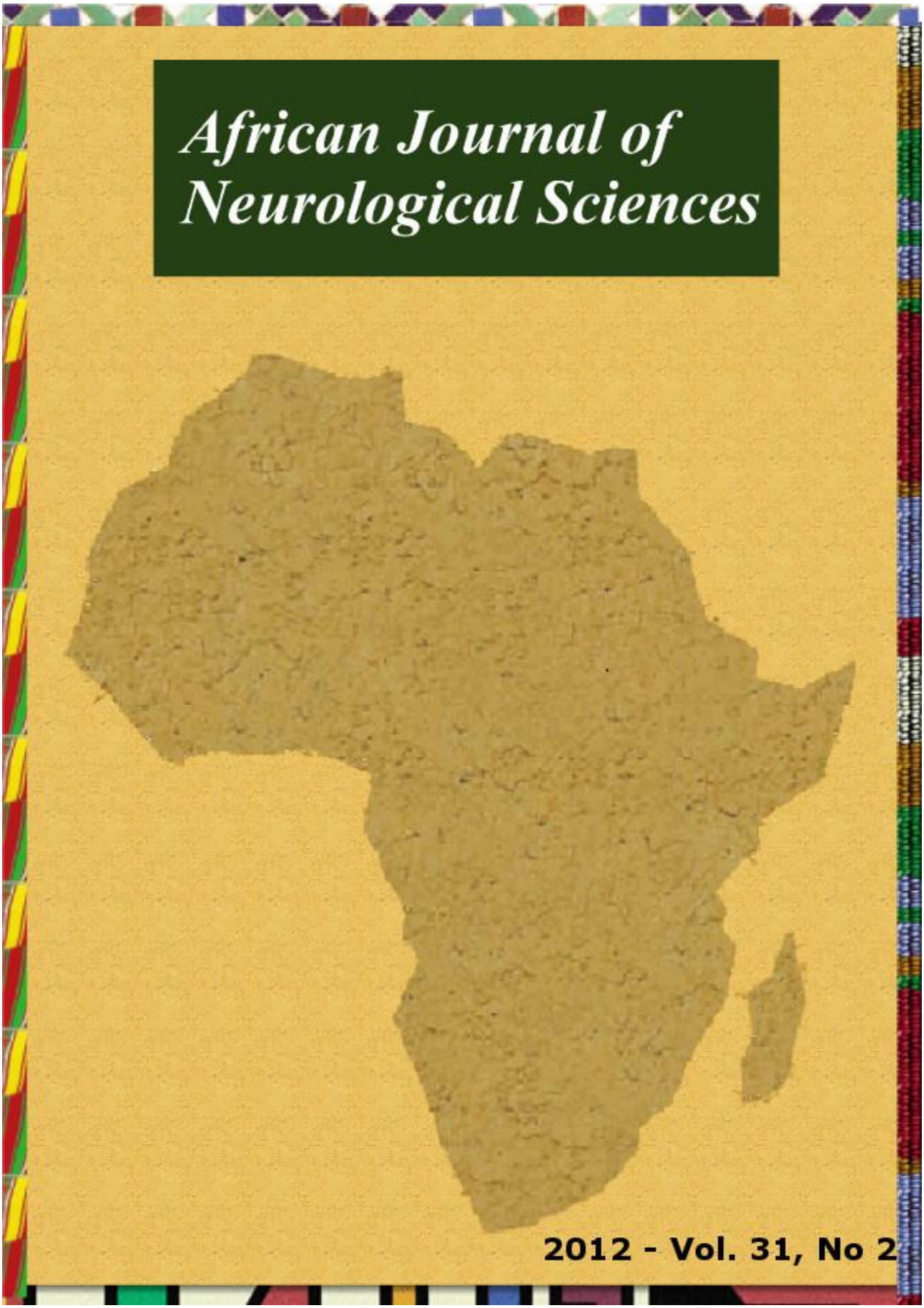
African Journal of
Neurological Sciences
2012 - Vol. 31, No 2

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CLINICAL STUDIES / ETUDE CLINIQUES

LES PARTICULARITES DE LA HERNIE DISCALE LOMBAIRE DE L'ADULTE JEUNE (18-25 ANS)

FEATURES OF LUMBAR DISC HERNIATION IN YOUNG ADULTS (18-25 YEARS)

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Mots clés : Hernie discale lombaire - Adulte jeune.
Key words:lumbar disc herniation-youngadults.

RESUME

Buts

La hernie discale lombaire est rare chez l'enfant et l'adolescent. Peu d'études ont été consacrées aux sujets de 18-25 ans. Nous avons voulu identifier d'éventuelles particularités de cette pathologie dans cette tranche d'âge à travers un échantillon pris en charge dans notre service.

Matériels et méthodes

Il s'agissait d'une étude rétrospective portant sur 52 patients colligés à l'hôpital de Grand Yoff et au CHU de Fann du 1er Avril 2004 au 31 Mars 2009. L'échantillon était représenté par des sujets de 18 à 25 ans, qui avaient consultés pour lomboradiculalgie avec mise en évidence au niveau de l'imagerie d'un conflit disco-radiculaire. Le suivi s'étalait de un mois à 48 mois.

Résultats

L'âge moyen était de 22,8 ans. On notait une prédominance masculine (86,5%). Les militaires représentaient 38,4%. La symptomatologie a été brutale dans 23,1% suite à un traumatisme. Le bilan radiologique retrouvait 6 cas de canal lombaire étroit et 6 cas d'anomalie transitionnelle associés à la hernie discale. On ne notait pas de signes de dégénérescence discale. L'étage L4-L5 était concerné dans 53,8%. Treize patients ont été opérés avec dans 46,2% des cas une disparition complète de la symptomatologie initiale à un an.

Conclusion

La hernie discale lombaire de l'adulte jeune est favorisée par les professions de force et les traumatismes du rachis lombaire. Le traitement doit être le plus conservateur que possible même si les résultats de la discectomie sont meilleurs que chez l'adulte plus âgé.

ABSTRACT

Aims

The lumbar disc herniation is rare in children and adolescents. Few studies are devoted to the 18-25 years old. We wanted to identify possible features of this disease in this age group through a sample management in our department.

Materials and methods

This was a retrospective study of 52 patients, collected inGrandYoff hospitalandatFann Hospital from 1st April 2004 to March 31, 2009. The sample was represented by subjects aged between 18 to 25, who had lombo-radicular pain with a disco-radicular conflict in imagery. The follow up ranged from one to 48 months

Results

The average age was 22.8 years. There was a male predominance (86.5%). The soldiers represented 38.4%. The symptoms were sudden in 23.1% following trauma. Radiological assessment found 6 cases of spinal stenosis and 6 cases of transitional anomaly associated with the herniated disc. No signs of disc degeneration. The L4-L5 level was involved in 53.8%. Thirteen patients were operated and in 46.2% of cases a complete disappearance of the initial symptoms one year.

Conclusion

Lumbar disc herniationin young adultsis favoredby the professionsof forceand traumaof the lumbar spine. Treatment shouldbe asconservative as possibleeven if the resultsofdiscectomyare better thanolderadults.

INTRODUCTION

La hernie discale lombaire est rare chez l'enfant et l'adolescent dominée par les causes traumatiques et l'activité sportive (10, 14, 22). Le traitement est le plus souvent conservateur avec cependant de meilleurs résultats chirurgicaux que chez l'adulte (4, 27). Entre l'adolescence et l'adulte âgé où domine la cause dégénérative, très peu d'études se sont consacrées aux sujets de 18 à 25 ans (15, 25). Nous avons voulu identifier d'éventuelles particularités cliniques, étiologiques et évolutives de cette pathologie dans cette tranche d'âge à travers un échantillon pris en charge dans notre service.

MATERIELS ET METHODES

Il s'agissait d'une étude rétrospective portant sur 52 patients, colligés à l'hôpital Général de Grand Yoff (HOGGY) et à l'Hôpital de Fann du 1er Avril 2004 au 31 Mars 2009. L'échantillon était représenté par des sujets de 18 à 25 ans, qui avaient consultés pour lomboradiculalgie avec mise en évidence au niveau de l'imagerie d'un conflit disco-radiculaire. Le bilan radiologique était constitué par les radiographies standards du rachis lombaire, le scanner et l'IRM. Le suivi s'étalait de 1 à 48 mois. Nous avons évalué le résultat fonctionnel à un an en classant les patients en 3 groupes en fonction de la reprise du travail :

- Une bonne évolution avec disparition complète de la symptomatologie et reprise du poste antérieur.
- Un groupe intermédiairerépondant aux critères suivants : lombalgie résiduelle, reprise du travail mais reclassement dans un autre poste.
- Une mauvaise évolution avec persistance de la sciatalgie et arrêt plus ou moins prolongé du travail.

RESULTATS

Pendant la période d'étude, 5672 personnes avaient consulté pour lombalgie ou lomboradiculalgie dont 83 âgés de 18 à 25 ans (1,5%). Il a été diagnostiqué une hernie discale chez 52 patients dans cette tranche

d'âge. L'âge moyen était de 22,84 ans. On notait une prédominance masculine (86,5%). Les militaires représentaient 38,4% des professions de nos patients (tableau 1).

La symptomatologie a été brutale dans 23,1% suite à un effort ou à un traumatisme et progressive dans 7,7% faite de lombalgie chronique. Les motifs de consultation étaient dominé par la lombalgie (76,9%) et les lomboradiculalgies (46,1%) (tableau 2).

La TDM (100% des patients) et l'IRM (44,2%) retrouvaient 2 cas d'arthrose inter apophysaire postérieure étagée, 6 cas de canal lombaire étroit constitutionnel, et 2 cas de spondylolisthésis associés. On ne notait pas de signes de dégénérescence discale (pincement discal, vide discal). On notait dans 6 cas (11,5%) une anomalie transitionnelle. L'étage L4-L5 était concerné dans 53,8%, L5-S1 dans 38,5% cas et L3-L4 dans 7,7% des cas.La hernie discale était médiane dans 53,8%, latérale dans 30,8% cas et exclue dans 15,4%. Un traitement médical a été institué dans tous les cas pendant 2 à12 semaines. Aucun de nos patients n'a bénéficié d'infiltration épidurale.

L'indication chirurgicale était posée chez 13 patients (25%) après échec d'un traitement médical de 3 à 6 mois; en cas d'apparition ou d'aggravation secondaire d'un déficit. Ceci représentait 3,2% de l'ensemble des discectomies réalisées pendant cette période. Tous les patients avaient bénéficié d'une discectomie par un abord inter-lamaire. Le taux de suivi de tous les patients était de 76,9%. Pour les patients opérés, l'évolution était satisfaisantedans 6 cas (46,2%), acceptable dans 2 cas (15,4%) et mauvaise dans 2 cas (15,4%). Aucun patient n'a été réopéré. Les autres patients avaient bien répondu au traitement médical et à la kinésithérapie.

DISCUSSION

Notre échantillon (52 patients) représentait la proportion des 18 -25 ans chez qui a été posé le diagnostic de hernie discale lombaire (1,5%). Ceci est dû à notre stratégie diagnostique qui consistait à ne demander les explorations radiologiques qu'en cas de persistance d'une lomboradiculalgie après un traitement médical initial de 2 semaines. L'échantillon aurait probablement été beaucoup plus important si une TDM lombaire avait été demandée de façon systématique.

On notait une prédominance masculine (86,5%) comme Pietila(16) sur une population de 14 à 25 ans, avec un sexe ratio 1,71/1. Il faut noter cependant que chez les moins de 16 ans, certains auteurs retrouvaient plutôt une prédominance féminine; la prédominance masculine n'apparaitrait qu'au-delà de 17 ans (17, 20). Cette distribution serait due à la croissance plus rapide des filles pendant l'adolescence, ce qui les rendrait plus vulnérable aux microtraumatismes du disque intervertébral que les garçons(24). Plusieurs facteurs ont été évoqués pour expliquer la survenue de cette pathologie chez les adolescents et les enfants. Parmi ces facteurs il faut citer les antécédents familiaux (frères et parents)de hernie discale lombaire (12)et le traumatisme lombaire. Le traumatisme, qu'il soit violent ou fait de microtraumatismes répétés par exemple lors de l'activité sportive est incriminé dans la survenue de la hernie discale dans cette tranche d'âge (2, 10, 17, 20). Il faut aussi citer la surcharge pondérale qui est un facteur reconnu quel que soit l'âge (2, 16). Les professions de force (militaires, chauffeur et maçon qui représentaient près de 85% de notre série) pourraient favoriser la survenue de cette affection. En effet ces professions sollicitent de façon importante le rachis lombaire (1, 26).

Dans la population pédiatrique et l'adolescence, les signes cliniques de la hernie discale ne sont pas spécifiques, dominés par le syndrome rachidien avec rareté des signes neurologiques (7, 11, 23). Dans notre série, nous n'avons retrouvé aucune particularité clinique par rapport à l'adulte plus âgé.

La stratégie des explorations complémentaires reste généralement à l'appréciation du clinicien et n'est pas codifiée. La bénignité de la hernie discale chez les sujets jeunes autorise à être un peu attentiste, mais le risque de passer à côté d'une affection grave (infectieuse dans notre contexte) plus fréquente à cet âge pourrait amener à recourir rapidement aux explorations radiologiques notamment l'IRM. Il faudrait donc un juste équilibre en s'aidant surtout de la clinique à la recherche systématique des signes associés. Les radiographies standards du rachis sont plus contributives chez les sujets jeunes que chez l'adulte montrant fréquemment des anomalies transitionnelles et les déformations rachidiennes en particuliers la scoliose (10, 16). L'analyse des images TDM et IRM doivent être rigoureuse pour éviter le piège des protrusions discales quasi constantes chez le sujet jeune du fait de la richesse en eau du nucléus (10). Quel que soit l'âge, les niveaux L4-L5 et L5-S1 sont les plus fréquemment touchés (10, 16, 26). Sur le plan topographique, les

hernies sont aussi bien médianes que postéro-latérales (10, 26). Les signes de dégénérescence discale sont par contre peu fréquents même s'ils sont présents à histologie (3).

Le traitement médical doit être de première intention surtout chez le sujet jeune pour éviter les troubles de la statique rachidienne ultérieure (8, 15, 18, 25) même si la plupart des auteurs rapportent des meilleurs résultats de la discectomie chez les enfants que chez l'adulte (8, 10). Nos patients opérés représentaient 3,2% de l'ensemble des discectomies pendant la période ; ce qui est comparable au chiffre de Pietila (2,3%) (16) dont les caractéristiques de l'échantillon sont proches du nôtre. Chez les adolescents ce taux se situerait entre 0,5 et 7% selon les études (8, 14). Les patients opérés représentaient 25% de notre échantillon. Ce pourcentage est important par rapport à ceux rapportés chez l'adulte plus âgé. Chez les adolescents, ce taux peut atteindre 50 à 60% dans certaines séries (9, 27). La durée moyenne du traitement médical avant l'indication de la chirurgie dans notre série variait entre 3 à 6 mois. Plusieurs tests sont utilisées pour évaluer les résultats de la chirurgie de la hernie discale (1, 5, 25). Nous avons utilisé un critère basé sur la reprise de l'activité professionnelle. Pour les patients opérés, nous avons eu de bons résultats dans 46,2% des cas contre 15,4% de mauvais résultats. Pietila retrouvait 35,1% de bons résultats. Chez l'enfant et l'adolescent ce taux varie entre 88 et 96% (15, 19, 21). Le taux de ré intervention (15%) serait semblable à celui de l'adulte (13, 21). Le temps de suivi moyen des patients opérés (1 an) n'a pas permis d'apprécier les conséquences de la discectomiesur leur statique vertébrale.

CONCLUSION

La hernie discale du sujet jeune est peu fréquente souvent favorisée par les traumatismes. Il existe des facteurs favorisants tels que la profession ; et la prédisposition génétique rapportée par certains auteurs. Les modalités cliniques se rapprochent de celles de l'adulte âgé. Le traitement doit être le plus conservateur que possible même si les résultats de la discectomie sont meilleurs que chez l'adulte.

Tableaux

Tableau 1 : répartition des patients selon la profession.

	Fréquence(Effectif)	Pourcentage (%)
Chauffeur	12	23,1
Etudiant - Elève	8	15,4
Militaire	20	38,4
Maçon	12	23,1
Total	52	100

Tableau 2 : les principaux signes cliniques.

	Fréquence (Effectif)	Pourcentage (%)
Lomboradiculalgie	24	46,1
Claudication neurogène	12	23,1
Sciatique parésiante	12	23,1
Queue de cheval	0	0
Syndrome rachidien	40	76,9
Signe de Lasègue	28	53,8

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CLINICAL STUDIES / ETUDE CLINIQUES

SEX-RELATED DIFFERENCES IN STROKE OUTCOME AT THE UNIVERSITY OF MAIDUGURI TEACHING HOSPITAL, NORTHEASTERN NIGERIA

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Key words: blacks, outcome, sex, stroke.

ABSTRACT

Background:

Studies have reported sex differences in stroke risk factor, presentation, morbidity and mortality. This study aims to determine the effect of sex on morbidity and 30-day fatality in patients with acute stroke.

Methods:

Ninety-one patients were recruited for the study. We documented sex differences in stroke presentation, stroke severity on admission and discharge, and 30-day in-hospital fatality. Continuous variables were assessed using the student t-test. While outcome measures were analysed using the logistic regression analysis. Results: There were 61 men (67%) and 30 women (33%) seen during the study period. Women were less likely to be formally educated (P = 0.024). Men were more likely to have lacunar strokes (P = 0.048), to smoke (P = 0.046) and take alcohol (P = 0.027). Men had a higher diastolic blood pressure at presentation (P = 0.046), even though they were more likely to be on antihypertensive medications pre-stroke (P = 0.036). Women were more likely to present with coma on presentation (P = 0.003), and suffer urinary tract infections (P = 0.023). Women were also more likely to have a severe stroke on admission (Barthel's ADL < 45, odds ratio OR = 5.30; 95% CI, 1.10 to 25.62 and mRS > 4, OR = 5.38; 95% CI, 1.53 to 18.96) and a poorer activity of daily living (ADL) status on discharge (OR = 4.40; 95% CI, 1.45 to 13.35).

Conclusions:

Sex differences in outcome exist in this study and women appear to have a poorer stroke outcome, more studies are needed to assess sex differences in response to therapy.

INTRODUCTION

Stroke is a leading cause of long-term disability, (1) and the second most common cause of death worldwide, accounting for about 8% of total deaths in developing countries. (5)

Men have a higher incidence of stroke, but women appear to have more severe strokes and a higher case fatality. (3) This has lead to an increasing concern for women with stroke with the 'Go red for women' campaign, due to the increasing burden and uniqueness of stroke in women. (37, 8, 45, 13, 24, 10)

Studies have reported sex-specific differences in stroke aetiology (37, 13, 24), presentations (45, 26, 44), diagnosis (39, 34, 47), treatments (13, 39, 36, 22) and outcomes (8, 13, 43, 19, 12).

Reports have shown that women hospitalized for stroke were less likely to be investigated (34, 47), have a carotid endarterectomy (34), or receive thrombolytic therapy. (13, 36, 40) While some studies are in agreement that women have more severe strokes and a lower quality of life than men (39, 43, 24, 38), others are in disagreement. (19, 17, 35)

Studies on sex difference in stroke mortality have been variable, some studies reported a higher mortality in women (24, 38, 4, 11), others reported a higher mortality in men (16, 42) and other studies reported no significant sex difference in stroke mortality (8, 19). These varying differences in mortality may be due to patient's characteristics and how stroke and mortality are defined. (42)

Reasons proposed for poorer outcomes in women include, older age and comorbidities; (24, 11) differences in acute stroke management; (8, 13, 34) and poorer functional recovery at rehabilitation. (33) Experimental studies are postulating cellular and pathophysiological basis for these sex differences, (25, 27) which is a subject for further researches.

Based on the above observation we sought to determine sex differences in stroke morbidity and mortality, as such differences may provide an opportunity for improved patient care.

MATERIALS AND METHODS

The study cohort was 91 stroke patients admitted through the accident and emergency unit or the neurology clinic of the University of Maiduguri Teaching Hospital (UMTH), North-eastern Nigeria. Stroke was clinically defined by the WHO criteria as rapidly developing clinical sign of focal and/or global disturbance of cerebral function, with symptoms lasting twenty-four hours or longer or leading to death with no apparent cause other than of vascular origin. (50)

During the five year period (2005-2009), two hundred and eighty-five (285) suspected stroke patients were attended to; one hundred and ninety-four patients were excluded from the study. Those excluded from the study were patients who had no computerized tomography (CT) or magnetic resonance (MRI) scan of the brain, those with a diagnosis of subarachnoid haemorrhage, subdural haematoma, those who died within 24hrs of admission and those with a past history of stroke. (Figure 1) All patients had an oral or written consent; consent was interpreted to some subjects into the local dialect for better understanding. History and examination was conducted and documented in the UMTH stroke proforma which included age and educational level. Risk factors for stroke such as hypertension (current blood pressure values 140/95 mmHg or features of long standing hypertension), atrial fibrillation (AF) (electrocardiographic evidence), transient ischaemic attack (TIA), diabetes mellitus (DM), smoking, alcohol consumption and a diagnosis of Human immunodeficiency virus (HIV) infection were recorded, this has been stated in an earlier study. (48) Medications taken by the patients before the stroke were also noted. Level of consciousness evaluated by the Glasgow Coma Score (a GCS < 8 is taken as coma). The distinction between ischaemic and haemorrhagic stroke was determined by CT or MRI. Patients with ischaemic stroke were categorized into; Total anterior circulation stroke (TACS), Partial anterior circulation stroke (PACS), Posterior circulation stroke (POCS) and Lacunar stroke.

Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). Disability and handicap were rated using the modified Rankin scale (mRS) and the Barthel ADL index (BI). These measures were also assessed at the time of discharge as outcome measures. The mRS identifies at a glance stroke disability, the BI assesses activity of daily living, but weighs heavily on motor functions, while the NIHSS provide the most prognostic information. (29)

Duration of hospital stay was recorded only for those who survived till time of discharge. Death within 30 days attributable to the stroke was recorded from date of stroke admission. All the above data were categorized based on sex.

Statistical Analysis

Student's t-test and the Z-test were used to assess continuous variables. The BI and the mRS were dichotomized for logistic regression analysis. The selected categories were severe stroke on admission (BI < 45 and mRS > 4), Poor ADL Status on discharge (BI < 45), independent on discharge (mRS <1 and BI > 90), and 30-day fatality was evaluated in a logistic regression analyses, controlling for age and clinical variables,

these results were expressed as odds ratios (ORs). All statistical data were analyzed using SPSS (version 16.1) software.

RESULTS

During the five year period 285 patients had a diagnosis of suspected stroke, 194 patients were excluded from the study as shown in Figure 1. Ninety-one patients were registered for the study. All recruited patients were blacks residing in Nigeria. There were 61 men (67%) and 30 women (33%), mean age of 56.2 +11.1 and 55.6 + 12.4 years in men and women respectively. Compared to men, women were less likely to be formally educated (P = 0.024).

Table 1 shows stroke subtypes. There was no statistical difference in stroke subtype; as 25 (83.3%) women compared with 48 (78.7%) men had CT evidence of infarction (P=0.812), while 5 (16.7%) women compared with 13 (21.3%) had haemorrhagic stroke (P = 0.812). Lacunar stroke was more common in men (P = 0.048), with no significant difference in other syndromes of ischaemic stroke.

Men were more likely to take alcohol (P = 0.027) and to smoke (P = 0.046). There was no significant sex difference in other risk factors when comparing history of hypertension, DM, TIA, AF, HIV infection. Men were more likely to be treated with antihypertensives compared with women (P = 0.036) There was no significant difference in the use of diabetic, antiplatelet and lipid-lowering medications (Table 1). . The clinical state at the time of presentation showed that women were more likely to be in coma compared to men (P = 0.003). Men were more likely to have a higher diastolic pressure at presentation (P = 0.047). There was no mean difference in random blood sugar (P = 0.772).

From the logistic regression in Table 2, women were about five times more likely to have severe stroke on admission (BI < 45, OR = 5.30; 95% CI, 1.10 to 25.62 and mRS > 4, OR = 5.38; 95% CI, 1.53 to 18.96), about four times likely to have a poor functional status on discharge (BI < 45, OR = 4.40; 95% CI, 1.45 to 13.35) and twice as likely to die from stroke within 30 days of admission (OR = 2.19; 95% CI, 0.72 to 6.65).

Urinary tract infection (UTI) was commoner in women (P = 0.023), with no major difference in other stroke complications (Figure 2). There was no sex difference in duration of in-hospital stay. (P = 0.168) Table 3, shows the summary of significant differences.

DISCUSSIONS

These data provide an evidence of differences by sex of stroke presentation and outcomes.

This study shows that women were less likely to be educated, to smoke or to take alcohol. Women were however more likely to present in coma, and have to a more severe stroke at presentation. Women were also more likely to be disabled and to be handicapped on discharge. Despite the higher likelihood of men receiving antihypertensive medications prestroke, they still had a higher DBP on admission. This may be a reflection of the general lack of optimal BP control among hypertensives in the African subregion (7, 31). Although, there was no sex difference in hypertension as a risk factor in this study; studies have shown that women were more likely to be hypertensive, (22, 2, 51) though this may not be so in black Africans with stroke. In the study by Andersen et al (2), they reported that hypertension was slightly more prevalent in men below the age of 50 years, after which the prevalence increased in women. Since our patients are younger we may not have similar findings.

We found no significant difference in risk factors such as DM, TIA and AF. Findings from other studies showed that women were more likely to have hypertension and AF (8, 13, 38, 11, 16), while men were more likely to have DM and heart disease (11, 16). Our finding of more frequent alcohol intake and smoking concurs with reports from other studies (8, 13, 11).

Our study showed that men were more likely to be on antihypertensives prestroke, and no sex difference in the use of lipid lowering, antiplatelets or antidiabetic medications. Our observation is divergent to the studies showing that women were more likely to have treatment of high blood pressure prestroke (31, 9). The study by Smith et al (44) showed that women were more likely to be treated with antihypertensives, and less likely to receive antidiabetic, antithrombotic and lipid-lowering medications during the course of stroke treatment. The study by Khan et al, (22) is also in agreement that women were more likely to receive antihypertensive

after a stroke. Report by Bushnell et al (6) on the use of statins showed that there was no sex difference in the use of statins or any statistical interaction between the effects of sex and statin use on the risk of stroke.

In our study lacunar strokes were commoner in men; this is congruent with a study by Foster et al (10) and divergent to some studies that reported lacunar strokes occurring more frequently in women with TACS. (44, 39, 35)

Women were reported to be older in several studies, (45, 13, 10, 44, 11) but this is not so in our study. The Framingham study (35) observed that women developed stroke an average of 5 years later than men. This difference in our study may be due to the relatively younger age of our cohort, smaller number of women participants and women in our community are less likely to seek medical attention early due to socioeconomic reasons, this may influence poorer outcomes and not reach the hospital alive. (32, 20, 49)

The women in this study were less likely to be educated compared to men; it has been shown that level of education influences socioeconomic status. A lower socioeconomic status not only increases the likelihood of having a stroke (20), but also impacts negatively on stroke presentation and care. (52)

Although other reports have shown no differences in stroke severity and case fatality rate (10, 17, 35); this study is in agreement with studies done elsewhere indicating that women were more likely have a severe stroke on admission and have worse outcomes after stroke, women were more likely to be disabled and handicapped on discharge, less likely to achieve activities of daily living independence and have a poorer quality of life. (8, 39, 43, 12, 24, 15) An excess of lacunar strokes in this study may contribute to the better outcome in men compared to women. A study by Sacco et al (41) observed that patients with lacunar stroke have a better outcome compared to those with nonlacunar strokes.

In keeping with a more severe stroke women were more likely to be comatose at presentation compared to men, as reported by Gall et al (11). Gargano et al (14) showed no sex difference in patients presenting with coma, but asserted that delay in presentation to the emergency room may explain some of the differences in symptoms.

Our study showed that women were twice as likely to die within thirty days from a stroke. This is consistent with some reports, (38, 11) but at variance with other studies. (8, 13, 10, 19) There are other studies that have shown lower rates of mortality in younger women than men and higher number in older women where the absolute burden of stroke is greater (24, 4). The higher mortality in women in other studies, were attributed to increasing age, a higher stroke severity and lower quality of care in women compared with men. (38, 4) There was no significant difference in the duration of hospital admission; this is congruent with a study by Zhu et al (53) who reported no sex difference in length of hospital stay. In our study UTI was commoner in women, and is in accordance with other studies. (13, 39)

Studies have shown that women were less likely to be investigated or treated with thrombolytics, (8, 13, 39, 47), but it is not universal. It is interesting to note from studies by Kent et al (21) and Sacco et al (40) that women were more likely to benefit from thrombolytic therapy. This may be an area of further research in our environment. Gargano et al (13) in their study explaining why women were less likely to be treated argued that women were older than men and this influences management owing to comorbid conditions. Women are less likely to have surgical interventions like carotid endarterectomy. (34) A study by Tell et al (46) observed that men were more likely to have carotid atherosclerotic disease than women, and may explain why men have higher endarterectomies.

Studies have postulated why women are likely to have severe stroke; Women brains are more likely to produce a stronger and more sustained inflammatory response compared to that of men in animal studies, consistent with increased immune responses (25, 27). In an experimental study with rats reported that oestrogen offers some neuroprotection in neuronal injury and this may be lost as women become older, (28) others have postulated the role of parity and increasing parity with increased mortality from both Ischaemic and haemorrhaghic stroke. (30, 18, 23) The main strength is the prospective nature of the study, regular follow-ups and various scoring systems used for stroke severity and disability.

The small sample size is a limitation of this study. We did not consider sex differences in recognition of stroke symptoms; as this may influence presentation and subsequent care. We also did not consider sex related effect of stroke care.

CONCLUSION

This study reveals sex differences in stroke presentation and outcome among Nigerians. After adjusting for cofounding variables we observed that women have more severe stroke on admission, and were more likely to be disabled and handicapped on discharge. In keeping with a severe stroke, they were more likely to be in coma on admission. Women were twice more likely to die from a stroke.

Acknowledgements

We acknowledge the contributions of Dr. A. Ahidjo of the radiology department and Dr. AA Gadzama of the Chemical pathology department.

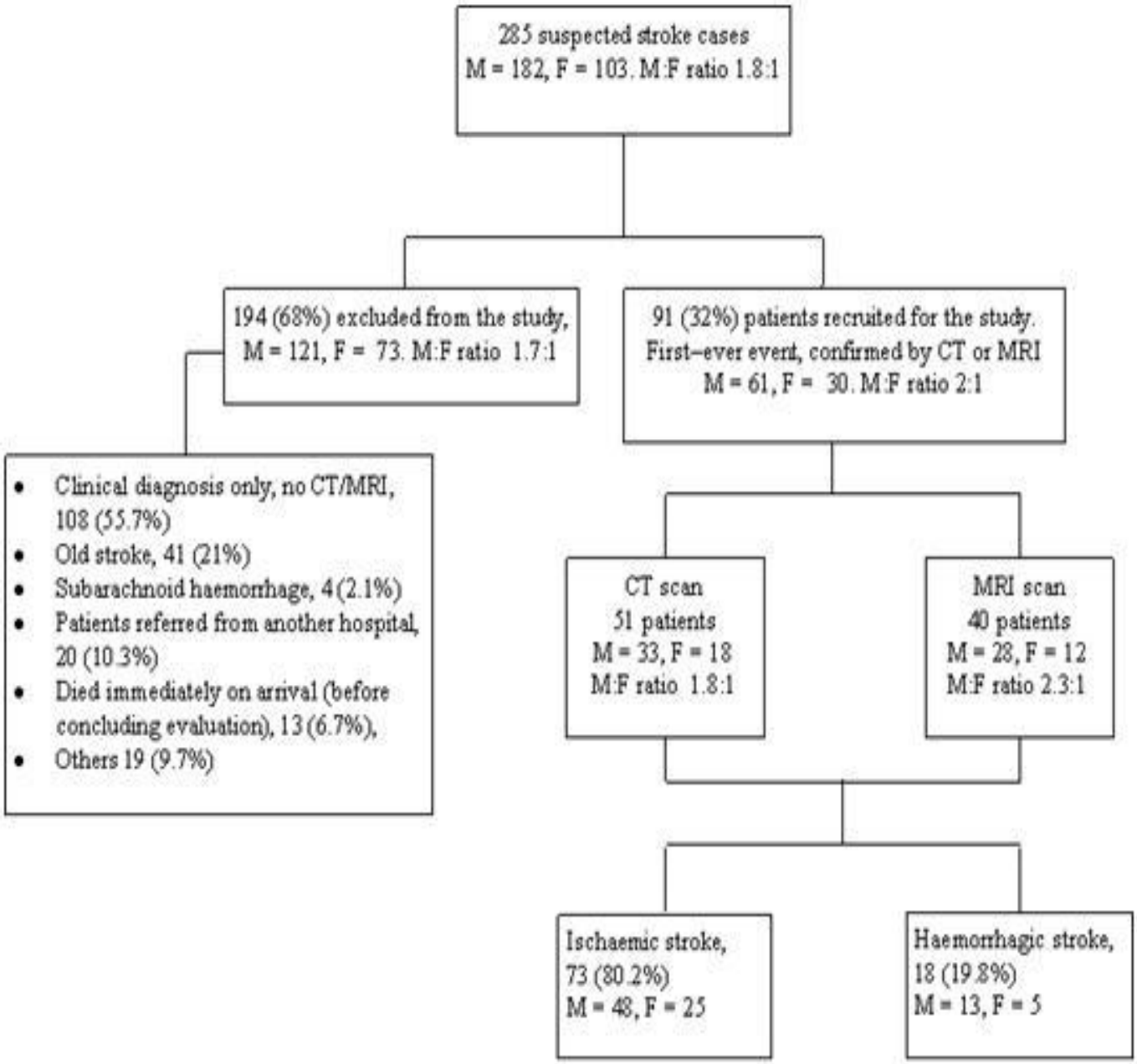

Figure 1. Inclusion and exclusion criteria, diagnosis and type of stroke. (48)

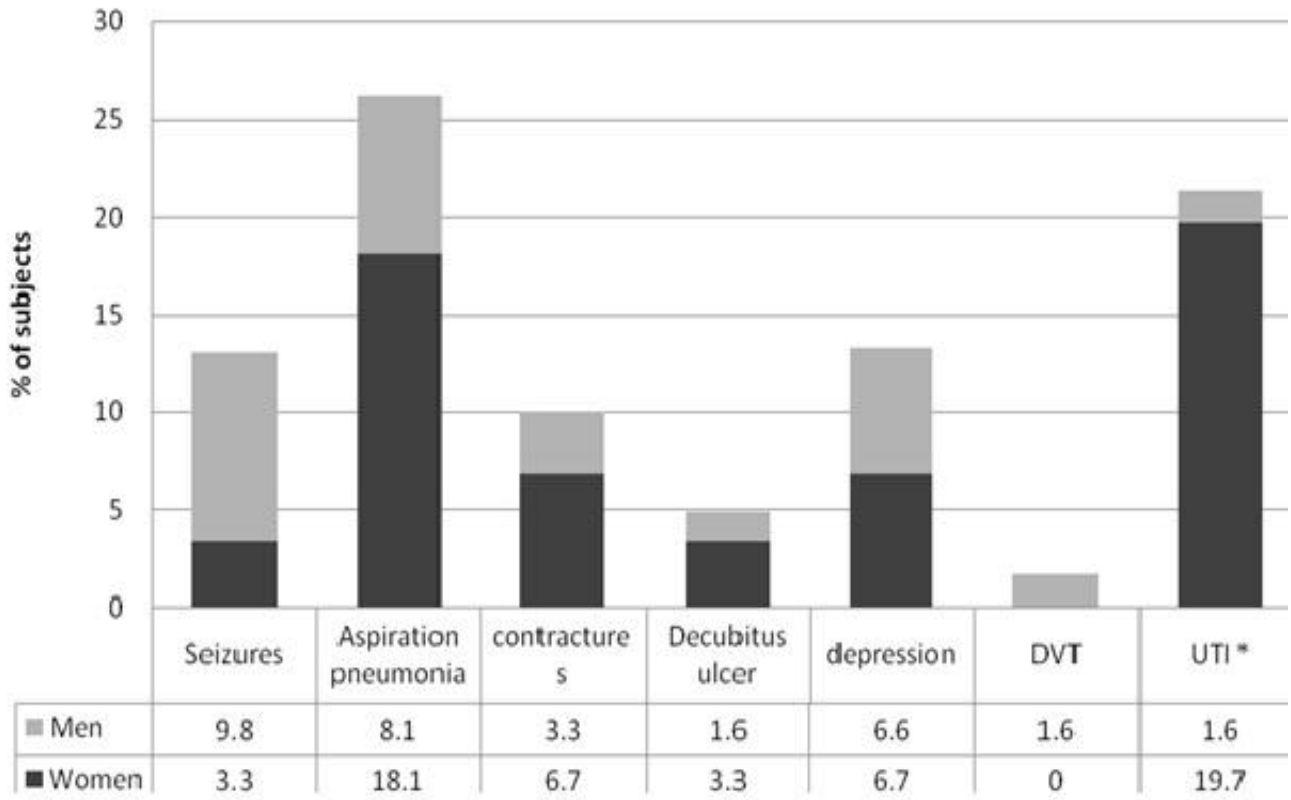

Figure 2. Stroke complications. Stacked bars are percentages of subjects with complications comparing sex groups. Asterisk * indicates P < 0.05.

TABLE 1. COMPARISON OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF SUBJECTS BY SEX

	Women	Men	P-value
Demographic characteristic			
Total	30 (33%)	61(67%)	0.004*
Mean age	55.6±12.4	56.2±11.1	0.823
Median age	55 (35-80)	57 (24-80)	
Formal Education †	4 (8.8%)	31 (33.18%)	0.024*
Stroke type			
Haemorrhagic	5 (16.7%)	13 (21.3%)	0.812
Ischaemic	25 (83.3%)	48 (78.7%)	0.812
Clinical syndrome of Ischaemic stroke			
TASC	8 (32.0%)	14 (29.2%)	0.976
PASC	15 (60.0%)	25 (52.1%)	0.626
POSC	1 (4.0%)	2 (4.2%)	1.000
Lacunar	1 (4.0%)	7 (14.6%)	0.048*

	Women	Men	P-value
Risk profile			
Hypertension	25 (83.3%)	49 (80.3%)	0.953
Diabetes	2 (6.7%)	3 (4.9%)	1.000
TIA	2 (6.7%)	5 (8.2%)	1.000
Smoking	0 (0.0%)	10 (16.4)	0.046*
Alcohol	1(3.3%)	15 (24.6%)	0.027*
HIV	1 (3.3%)	3 (4.9%)	1.000
Atrial fibrillation	2 (6.7%)	1 (1.6%)	0.511
Antiphospholipid syndrome	1 (3.3%)	0 (0.0%)	0.725
Heart failure	1 (3.3%)	1 (1.6%)	1.000
Prestroke medications			
Antihypertensive	3 (10%)	20 (32.8%)	0.036*
Antiplatelet	3 (10%)	9 (14.8%)	0.759
Lipid lowering agent	1 (3.3%)	3 (4.9%)	1.000
Diabetic medication	1 (3.3%)	2 (3.2%)	1.000
Clinical state at time of presentation			
Coma	9 (30.0%)	3 (4.9%)	0.003*
Mean SBP	148.5 ± 29.1	158.1 ± 37.9	0.225
(min-max)	(110-220)	(90-250)	
Mean DBP	90.5±18.3	100.1±22.6	0.046*
(min-max)	(60-130)	(40-150)	
Mean admission Random glucose	6.3±2.5	6.1±2.7	0.772
Duration of in-hospital stay (days)	43.0±33.1	33.9± 27.3	0.168
30-Day fatality	9 (30.0%)	9 (14.8%)	0.175

TACS - total anterior circulation stroke,
PACS - partial anterior circulation stroke,
POCS - posterior circulation stroke,
TIA - transient ischaemic attack.
SBP - systolic blood pressure,
DBP - diastolic blood pressure.
NIHSS - national institutes of health stroke scale.
* P - value < 0.05 from student's t - test.
† - At least a secondary school education

TABLE 2: INDEPENDENT PREDICTORS OF STROKE SEVERITY, DISABILITY AND 30-DAY MORTALITY AMONG FEMALE SEX.

Independent variable	OR	95% CI
Admission Barthel's ADL < 45	5.30	(1.10 - 25.62)*
Admission mRS > 4	5.38	(1.53 - 18.96 *
Discharge Barthel's ADL > 90	0.99	(0.31 - 3.20)
Discharge Barthel's ADL < 45	4.40	(1.45 - 13.35)*
30-Day fatality	2.19	(0.72 - 6.65)

Logistic regression analysis of variables, * P < 0.05

Table 3. Summary of significant differences

Women>Men	Men>Women
Less likely to be Educated	Smoking
Coma on admission	Alcohol
Severe stroke on admission	Hypertensive medication prestroke
Poor functional status on discharge	Lacunar strokes
Urinary Tract Infection	Higher diastolic BP on admission
More likely to die within 30 days	

NIHSS - National Institutes of Health Stroke Scale.

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REVIEW/MISE AU POINT

NEUROMYELITE OPTIQUE DE DEVIC

DEVIC'S NEUROMYELITIS OPTICA

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RESUME

La neuromyélite optique de Devic est un syndrome clinique rare associant une névrite optique unilatérale ou bilatérale à une myélite transverse. Cliniquement proche de la sclérose en plaque, avec néanmoins une évolution plus rapide et plus sévère, elle constitue une entité anatomo-clinique distincte. La séropositivité pour les NMO-IgG et les lésions médullaires longitudinalement étendues (3 ou plus segments spinaux) sont très caractéristiques de NMO. Le pronostic de la maladie apparaît plus péjoratif, justifiant des options thérapeutiques très agressives.

ABSTRACT

Devic's neuromyelitis optica is a rare clinical syndrome involving a unilateral or bilateral optic neuritis with a transverse myelitis. Clinically similar to multiple sclerosis, albeit with a more rapid and more severe, it is a distinct clinical and pathological entity. Seropositivity for NMO-IgG and longitudinally extensive spinal cord lesions (3 or more spinal segments) are very characteristic of NMO. The prognosis is more pejorative, justifying very aggressive treatment options.

INTRODUCTION

La neuromyélite optique de Devic (NMO) ou maladie de Devic est une affection inflammatoire démyélinisante du système nerveux central qui touche principalement la moelle épinière et les nerfs optiques. Elle a été décrite pour la première fois par Eugène Devic et son élève Fernand Gault à Lyon en 1894[8]. Pendant très longtemps, la maladie de Devic a été considérée comme une forme particulière de sclérose en plaques (SEP) et traitée comme telle. Cependant, des travaux récents ont mis en évidence des différences sur le plan clinique, épidémiologique, immunologique et anatomopathologique entre SEP et NMO [24]. Le traitement de NMO repose sur les immunosuppresseurs, c'est actuellement la meilleure option thérapeutique pour prévenir les rechutes.

EPIDEMIOLOGIE

La NMO est plus fréquente chez les femmes que chez les hommes (80%). L'âge d'apparition du syndrome est variable, de l'adolescence à l'âge adulte, avec un pic d'incidence médiane à la fin des trentaines. Cette maladie touche les caucasiens mais aussi les antillais [4] et les japonais [13].

Dans 1/3 des formes avec rechute, des antécédents personnels de maladies auto immunes incluant hypothyroïdie, lupus érythémateux systémique, syndrome de Sjögren, anémie de Biermer, maladie de Crohn, syndrome des antiphospholipides, la présence des anticorps anti-neutrophiles cytoplasmiques (ANCA), intoxication au Clioquinol, cholangite sclérosante primitive ou purpura thrombopénique idiopathique sont trouvés [16].

Certains auteurs stipulent que ces associations justifient la non inclusion de ces cas dans le cadre nosologique du syndrome de Devic [5].

Cette entité n'est pas une maladie héréditaire, mais il existe un cas rapporté de 2 sœurs homozygotes [16].

Les infections virales et bactériennes précédant ou accompagnant la NMO sont un phénomène connu. Le syndrome pseudo-grippal qui précède l'apparition de la maladie neurologique a été rapporté dans environ 25-30% des cas [24,2]. Parmi les cas où un agent infectieux avait été identifié (Sellner et al.), 69% étaient des femmes, l'âge moyen de survenue est de 21 ans (extrêmes:5-41 ans), et le cours a été essentiellement monophasique, avec une incapacité prolongée.[20].

Le virus varicelle zona (VZV) et la tuberculose ont été les déclencheurs infectieux les plus courants; Cependant, d'autres agents bactériens et viraux comme la chlamydia, cytomégalovirus, le VIH et l'Epstein Barr virus (EBV) ont été rapportés.

PHYSIOPATHOLOGIE

La maladie de Devic est une maladie auto-immune à médiation humorale, à la différence de la SEP, qui est une maladie à médiation cellulaire où l'infiltrat lymphocytaire est prédominant.

En 2004, l'équipe de la Mayo Clinic aux États-Unis a mis en évidence pour la première fois un marqueur sérique chez des patients atteints de NMO. Ce biomarqueur, appelé NMO-IgG est un auto-anticorps, a pour cible antigénique un canal hydrique, l'aquaporine 4 (AQP4) qui est exprimée uniquement par les astrcytes [11]. La recherche de cet auto-anticorps a donc été proposée comme test diagnostique de la maladie. NMO-IgG, a été associé avec 73% des patients ayant un syndrome de Devic, mais aussi avec 58% des patients ayant une SEP dans sa forme optico-spinale au Japan [12].

Actuellement, il n'existe pas de méthode de référence pour l'identification de l'auto-anticorps NMO-IgG. Même si cela reste controversé [9], les tests les plus sensibles et les plus spécifiques semblent basés sur la détection d'anticorps dirigés spécifiquement contre l'AQP4.

Dans le système nerveux central, l'AQP4 est d'expression ubiquitaire avec des régions de plus forte expression: l'hypothalamus, les régions péri-aqueducales, le nerf optique et la moelle épinière. Ce qui explique la fréquence des lésions en hypersignal adjacentes au 4ème et 3ème ventricule surtout en acquisition FLAIR. Ces localisations préférentielles correspondent précisément aux lésions encéphaliques qui ont été observées chez les rares malades qui ont une atteinte encéphalique à l'IRM [18]. Le rôle directement pathogène de cet auto-anticorps est fortement suspecté. Les données récentes de l'étude anatomopathologique des lésions de névrite optique avec myélite aigue soulignent que la perte d'expression astrocytaire de l'AQP4 est un élément très précoce dans la cascade lésionnelle de la maladie, précédant la perte astrocytaire, myélinique et axonale. Elle serait contemporaine du dépôt périvasculaire d'immunoglobulines [19,14].

CLINIQUE

Syndrome optique

Une névrite optique est révélatrice chez 50 à 65% des sujets, bilatérale dans un tiers des cas [3], l'atteinte est une névrite optique rétrobulbaire (papille optique d'aspect normal au fond d'œil), mais la neuropapillite (œdème et hémorragie péri-papillaire) est plus évocatrice, à la longue une atrophie optique s'installe.

L'atteinte est le plus souvent bilatérale soit d'emblée, soit plus fréquemment à quelques jours voire quelques mois d'intervalles. Une douleur oculaire rétrobulbaire peut s'associer, mais moins fréquemment que dans l'atteinte papillaire d'autre origine (SEP et étiologies granulomateuses). Le déficit des champs visuels est central. Les particularités cliniques sont la profondeur de la baisse d'acuité visuelle et la médiocrité de la récupération fonctionnelle.

Des cas d'anomalies oculomotrices, de syndrome de Claude Bernard Horner et de nystagmus ont été rapportés par certains auteurs [5].

Syndrome médullaire

L'atteinte médullaire dans la NMO est le premier événement dans 20% à 50% des cas. Son délai d'apparition est en moyenne de 2 ans [3]. Classiquement l'installation des symptômes est aigue atteignant l'acmé en quelques heurs ou en quelques jours. La topographie est volontiers cervico-dorsale et la présentation typique est celle d'une myélite transverse symétrique. Le tableau peut être dramatique à type de tétraplégie flasque associée à une détresse respiratoire nécessitant une assistance ventilatoire. Les poussées médullaires peuvent également adopter une topographie plus limitée comme des syndromes de Brown-Séquard, des monoparésies, voire des troubles sensitifs isolés. À la phase d'état, la paralysie sur un mode plégique d'au moins un membre et son caractère flasque seraient fréquents. Des phénomènes paroxystiques douloureux et moteurs sont souvent rapportés à distance des poussées.

EXAMENS COMPLÉMENTAIRES

IRM médullaire

Au cours d'un épisode de myélite, l'IRM médullaire révèle une augmentation de volume de la moelle et une image étendue sur plus de 3 corps vertébraux, apparaissant en hypersignal sur les séquences pondérées T2, avec en son centre un hypersignal dont l'intensité est identique à celle du LCR. Sur les séquences pondérées T1, ces anomalies apparaissent en hyposignal. Elles sont rehaussées par le gadolinium ce qui témoigne de l'altération de la barrière hémato-encéphalique. Les anomalies médullaires sont le plus souvent uniques, situées au niveau de la moelle cervicale et thoracique. Ces anomalies de signal sont observées lors de l'épisode de myélite mais se modifient à distance de l'épisode, la prise de gadolinium disparaissant et l'image T2 apparaissant moins étendue [17] (Encadré I).

IRM cérébrale

Par définition l'IRM cérébrale est normale en dehors de l'hypersignal étendu des deux nerfs optiques remontant jusqu'au chiasma. Cependant, la plupart des auteurs admettent la présence d'hypersignaux de la substance blanche encéphalique sur les séquences pondérées T2 surtout en corrélation à la durée d'évolution, sans remettre en cause le diagnostic de NMO [7].

Ponction lombaire

Le liquide céphalorachidien (LCR) est généralement anormal. La protéinorrachie est souvent élevée, excédant exceptionnellement 1g/l. Une pléiocytose est observée dans 1/3 des cas si le LCR est prélevé au moment d'une poussée [24]. La présence de bandes oligoclonales dans le LCR varie en fonction des études, 23% des cas dans la série de de Sèze et al [7], les bandes oligoclonale tendent à se négativer sur des tests successifs (Encadré II).

Anticorps NMO

La valeur prédictive positive des Anticorps NMO après un premier événement médullaire a été testée chez 26 cas de myélite transverse aigue définie par une lésion extensive sur plus de 3 espaces vertébraux à l'IRM médullaire [22]. Les Anticorps NMO étaient présents dans 11 cas. Aucun patient séronégatif n'a présenté de nouvel événement médullaire ou optique après un délai moyen de suivi de 21±19 mois. Ces résultats montrent que la présence des anticorps augmente le risque de rechute médullaire ou de névrite optique.

CRITERES DIAGNOSTIQUES

Les critères actuels de la neuromyélite optique de Devic reposent sur l'association de critères obligatoires (névrite optique, myélite aigue et absence de signes en faveur d'une atteinte d'autre que celle du nerf optique et de la moelle) à un critère secondaire majeur (IRM encéphalique initial normal, lésion médullaire étendue sur plus de 3 vertèbres, plèiocytose du liquide céphalorachidien) ou à deux critères secondaires mineurs (neuropathie optique bilatérale, neuropathie optique sévère avec une acuité visuelle à 1/10e et un déficit musculaire sévère d'au moins un membre) [24,25].

Toutefois, ces critères ne permettent pas de diagnostiquer les sujets atteints de neuromyélite optique de Devic dont les symptômes neurologiques concernent des régions du système nerveux central autre que le nerf optique ou la moelle épinière, et ceux dont l'IRM cérébrale montre des lésions identiques à celles d'une sclérose en plaques. Wingerchuk et al ont proposé une révision de ces critères diagnostiques [25] (Encadré III).

FACTEURS PRONOSTICS

Les facteurs pronostiques d'une évolution à rechute sont [16]:

- Un intervalle long entre les 2 premières poussées (RR = 2,16 par mois);
- L'âge de début tardif (RR = 1,08 par année);
- Le sexe féminin (RR = 10,0 femme versus homme);
- Un score EDSS (The Expanded Disability Status Scale) faible lors du premier épisode de myélite (RR = 1,84).

Les formes monophasiques, bien que plus sévères initialement, ont un meilleur pronostic à long terme que les formes à rechutes. Dans les formes à rechutes, 53 % des patients avaient besoin d'une aide à la marche, alors que 65 % des patients à forme monophasique marchaient sans aide [16] (Encadré VI).

TRAITEMENT

La neuromyélite optique de Devic est une urgence thérapeutique. Plus précoce et plus intense est la prise en charge initiale de la poussée, plus grandes sont les chances de récupération. Cette prise en charge en urgence repose sur une corticothérapie intraveineuse à forte dose (1g/jour pendant 5 jours). Considérant la prépondérance de la médiation humorale dans la maladie, les échanges plasmatiques doivent être rapidement proposés en cas de non-réponse à la corticothérapie [21]. Les immunoglobulines polyvalentes pourraient être également efficaces.

La deuxième préoccupation est la prévention des rechutes neurologiques qui ont une moindre probabilité de récupération si elles touchent un territoire déjà affecté par la maladie. L'azathioprine (2.5-3mg/kg/jour), associé ou non à une corticothérapie orale peut être proposé [26]. Pour les patients non répondeurs à ce dernier la mitoxantrone [23] et le rituximab [6] peuvent favoriser une rémission clinique.

Une étude réalisée en Chine par l'équipe de Yan-qing Feng et al a montré l'efficacité du traitement antituberculeux en dehors d'une tuberculose évolutive chez des patients NMO et qui résistent aux traitements corticoïdes [10]. On a noté une amélioration clinique et radiologique significative par rapport aux cas témoins.

CONCLUSION

La neuromyélie optique de Devic est une pathologie auto-immune à médiation humorale. Son pronostic est péjoratif justifiant des traitements agressifs notamment les immunosuppresseurs et les échanges plasmatiques à fin de l'améliorer.

Encadré I: Classification des lésions médullaires (adapté d'après Papais- Alvarenga et al 2002) [15].

Lésions étendues de type A avec sous types, parfois associés:
A1: Lésion ≥ à 3 segments vertébraux en séquence pondérée T2 sagittale et oedème médullaire;
A2: Lésion ≥ à 3 segments vertébraux en séquence pondérée T2 sagittale sans oedème médullaire;
A3: Cavitation médullaire en séquence pondérée T1 sagittale;
A4: Atrophie médullaire diffuse en séquence pondérée T1 sagittale, définie visuellement;
Lésions limitées avec sous types:
B: Lésions multifocales en séquence pondérée T2 sagittale toutes < 3 segments vertébraux.
C: Lésion unifocale en séquence pondérée T2 sagittale < 3 segments vertébraux.
Absence de lésion médullaire: sous type D

Encadré II:Les caractéristiques biologiques de la sclérose en plaque (SEP) et de NMO [1].

	SEP	NMO
LCR:		
Pléiocytose	cellularité normale ou < 50 cells/mm3	> 50 cells/mm3
Bande oligoclonale (%)	85-90	20-30
Sang:		
AAN (%)	20-30	>50
Autre auto AC	Rare	Fréquent
NMO- IgG	Absent	Sensibilité (73%) Spécificité (91%)

Encadré III: Critères diagnostiques révisés de Neuromyélie optique de Devic (Wingerchuk, 2006)

Critères diagnostiques de la maladie de Devic: Tous les critères absolus + 1 majeur ou 2 mineurs
Critères absolus
1. Névrite optique
2. Myélite
3. Pas d'atteinte en dehors du nerf optique et de la moelle épinière
Critères majeurs
IRM cérébrale normale au début
IRM médullaire : myélite étendue > 3 espaces vertébraux
LCR > 50 GB/mm3 ou > 5 neutrophiles/mm3
Critères mineurs
Névrite optique bilatérale
Névrite optique sévère (AV < 1/10) fixée sur au moins un oeil
Déficit moteur sévère (MRC grade 2) fixé sur au moins un membre

Encadré VI : Les caractéristiques des formes monophasiques et à rechutes de NMO [24]

	Monophasique	**A rechute**
Fréquence %	< 20	> 80
Age de début (ans, médian)	29	39
Sexe ratio (femmes)	50	80-90
Histoire de maladie autoimmune	rare	approximativement 50%
Névrite optique ou myélite (%)	48	90
Névrite optique bilatérale (%)	17	8
Névrite optique + Myélite (%)	31	0
Sévérité	plus grave	moins grave
Atteinte respiratoire	rare	approximativement 1/3
Mortalité à 5 ans (%)	10	32
Récupération	+	+/-

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REVIEW/MISE AU POINT

THE ROLE OF STATINS IN ALZHEIMER'S DISEASE: A META-ANALYSIS

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Keywords: Alzheimer's Disease; Meta-analysis; Prevention; Statins; Treatment

ABSTRACT

Background

In Alzheimer's disease (AD) Amyloid Beta (Aβ) is deposited in the form of extracellular plaques and previous studies have showed Aβ generation is cholesterol dependent. The use of statins in the prevention and treatment of AD is poorly explored. The aim of this work was, therefore, to perform a review of studies on the efficacy and safety of statins in the prevention as well as treatment of AD.

Methods and Findings

Medline and Cochrane Database of Systematic Reviews search was performed for original research articles published in English language in which participants received any type of statins for at least 6 months and evaluated for their cognitive changes. Selected articles were grouped into two, randomized controlled trials (RCTs) and observational studies, and meta-analyzed separately. Thirteen studies identified, 4 RCTs including 1153 AD patients with trial period ranging from 26 to 72 weeks and 9 observational studies including 21,819 study participants with follow up period of up to 12 years. The 4 RCTs assessed change in Alzheimer's Disease Assessment Scale- consisting of the cognitive subscale (ADAS-Cog) and when the results of each studies were combined there was no significant difference in ADAS-Cog between the statin and placebo group [Mean difference = -0.57, 95% CI, -1.39, 0.25, p=0.17]. Four of the 9 observational studies provided computed effect sizes in the form of Hazard ratio (HR) and common HR were computed and showed that statins had significant protective effect against AD [HR=0.69, 95% confidence interval (CI), 0.542, 0.882, p=0.003]. Three of the 9 observational studies were also combined for their Odds ratio (OR) and they showed that statins were protective against AD [OR=0.447, 95% CI, 0.299, 0.668, p=000]. Treatment related adverse effects were similar between statin and placebo [OR=2.84, 95% CI, 0.41, 19.69, p=0.29].

Conclusion

Though observational studies have shown statins' protective effect against AD, there is insufficient evidence to recommend statins for the treatment of AD, as RCTs failed to show significant efficacy. Statins are generally well tolerated in AD.

BACKGROUND

Alzheimer's disease (AD) is an age-related neurodegenerative disease characterized by a progressive loss of memory associated with other cognitive sphere deficits interfering with social and occupational functioning (20). The global prevalence of AD was estimated at 26.55 million in 2006 (3). It has also been projected that worldwide prevalence will quadruple to 106.2 million, with 1 in 85 persons living with AD by the year 2050 (3). AD is the commonest type of dementia encountered in older Patients (12). Dementia causes a significant financial burden to society, worldwide societal costs estimated at $315 billion in 2005 ($105 billion were for informal care) (32).There are a number of non-pharmacological and symptomatic pharmacological approaches to treat AD (9). None of these, however, can prevent, cure or stop the progression of the disease (9).

The brain is the most cholesterol-rich human organ (26). Hypercholesterolemia is one of the modifiable risk factors for AD (1, 23). A central event in the development of AD is thought to be abnormal processing of the cell membrane-associated amyloid precursor protein (APP) followed by deposition of toxic Aβ protein in the form of amyloid plaques in the extracellular space of the neocortex (7, 25). High cholesterol level may increase the activity of the β- or γ-secretase enzymes that generate Aβ from APP, and may decrease the flux of APP through the nonamyloidogenic α-secretase pathway (26, 24). Once Aβ has been produced, the cholesterol level could also influence its aggregation state (24). Several studies in cell culture and animals have demonstrated that treatment with cholesterol lowering drugs, such as statins, reduces the production of Aβ (28, 5). It was, therefore, hypothesized that reduction of Aβ levels by statins may have neuro-protective effects in patients with AD (33, 27).

Cholesterol forms an essential component of cell membranes, and has a crucial role in the development and maintenance of neuronal plasticity and function (26). Statin induced reduction in cholesterol concentration in the central nervous system may, therefore, cause neuro-cognitive deficits (18, 19, 13). The aim of this work was, therefore, to review the studies on the efficacy and safety of statins in the prevention and treatment of Alzheimer's disease as well as the role of baseline cholesterol level, Apolipoprotein (APO) E genotyping, age and cognitive level on the treatment outcome.

METHODS

Inclusion Criteria

- Randomized clinical trials (RCTs) in which study subjects were AD patients who received any type of statin for at least 6 months and cognitive changes were measured as outcomes using instruments such as ADAS-cog, Mini-Mental State Examination (MMSE) or other accepted cognitive measures.
- Observational studies in which study subjects were either AD patients or subjects at risk for AD who received any type of statin for at least 6 months and data on incident AD cases were obtained or change in cognition measured by accepted cognitive measure.

Search Strategy

A comprehensive systematic search for published articles and conference proceedings was undertaken with the electronic database Medline via PubMed, and Cochrane Database of Systematic Reviews, using the following combination of medical subject headings (MesH) terms or key words: "Statins" and "Alzheimer's Disease". The search was restricted to articles published in English language irrespective of the study place. Reference lists of identified articles were also searched.

Data Extraction

The summary statistics required for each trial and each outcome for continuous data were the mean change from baseline, the standard error of the mean change, and the number of patients for each treatment group at each assessment. Where changes from baseline were not reported, the mean, standard deviation and the number of patients for each treatment group at each time point was extracted. For binary data (commonly found in observational studies) computed effect sizes (OR, HR) and their corresponding confidence limits were sought.

Data Analysis

Outcome measures that were extracted from non-randomized studies analyzed separately from the outcome measures extracted from randomized trials to avoid bias (11).

Randomized trials

The outcomes measured in clinical trials of AD and cognitive impairment often arise from ordinal rating scales. Where the rating scales used in the trials have a reasonably large number of categories (more than 10), the data were treated as continuous outcomes arising from a normal distribution (17). Summary statistics (sample size (n), mean and standard deviation) were required for each rating scale at each assessment time for each treatment group in each trial for change from baseline. The mean change and standard deviation were calculated from the available data. All data extracted were then entered into Review Manager (RevMan), Version 5.1 (The Cochrane Collaboration, Oxford, England) for analysis. The duration of the trials varied from 26-72 weeks. A separate meta-analysis was conducted for each period. Some trials may contribute data to more than one time period if multiple assessments have been done.

Observational studies

For binary outcomes, such as progression of AD, severity of AD, the odds ratio, relative risk, or hazard ratio were used to measure treatment effect. The Comprehensive Meta-Analysis software (Biostat, Englewood, NJ, USA), Version 2 was used for data analysis.

In all cases the overall estimate from a fixed effect model is presented. Presence of heterogeneity was assessed using the Cochran Q statistic, and I2 statistic was also used to quantify the degree of statistical heterogeneity. If there was significant heterogeneity a random effects model will be presented. A 2-sided alpha error of less than 0.05 was considered to be statistically significant ($P<0.05$). Potential publication bias was assessed by visual inspection of the funnel plot produced by plotting the standard error against the mean difference of RCTs or log OR (HR) of observational studies.

RESULTS

The flow of studies through the review process is outlined in Figure 1. After a literature search and selection based on the inclusion criteria as described in the methods, a total of thirteen studies were identified that met inclusion criteria. All the thirteen studies (nine observational studies and four randomized controlled trials) were meta-analyzed separately. Tables 1 and 2 show RCTs and observational studies with their characteristics, respectively.

Of the 4 RCTs, 2 were undertaken in USA, 1 in Germany and the remaining one was an international study in which patients were recruited from 10 different countries. Six of the 9 observational studies were undertaken in USA and the remaining in Canada, France and the Netherlands. Overall, 1153 study subjects were included in the 4 RCTs with trial period ranging from 26 to 72 weeks. In the 9 of observational studies, a total of 21,819 study participants were included with follow-up period of up to 12 years.

Randomized Controlled Trials

The four studies assessed change in ADAS-Cog and as study periods varied between 26 to 72 weeks, separate meta-analysis was conducted for each period (table 3). When the four studies were combined there was no significant difference in ADAS-Cog between the statin group and placebo group ($p=0.17$) (table 3). As the Simons 2002 study was conducted for 26 weeks, data from ADCLT 2006, LEADe 2010, Sano 2011 and Simons 2002 at 6 months were combined and there was no significant difference in ADAS-Cog between the statin and placebo groups ($p=0.49$). As the ADCLT 2006 study was conducted for 12 months, data from ADCLT 2006, LEADe 2010 and Sano 2011 at 12 months were combined, and there was no significant difference in ADAS-Cog between the statin and placebo groups ($p=0.60$). Eighteen months data from LEADe 2010 and Sano 2011 on Change in ADAS-Cog were also combined using random effect model (due to presence of heterogeneity), and there was no significant difference in ADAS-Cog between the statin and placebo groups ($p=0.86$).

Data on change in MMSE were also available from the four studies and separate meta-analysis was conducted for each period as it was done for ADAS-cog (table 4). No significant beneficial effect on MMSE was seen with statin treatment at any time.

Three of the included RCTs (ADCLT 2006, LEADe 2010 and Sano 2011) also provided data on effect of statins on behavior using the instrument Neuropsychiatric Inventory Caregiver Distress Scale (NPI)) of AD patients. Data from these three studies were combined at the end point of each study and at 12 months (table 5). The effect was significantly different between groups only at 12 months (p=0.04) but not at end point (p=0.07) analysis. Eighteen months data from LEADe 2010 and Sano 2011 were also combined and found to be non significant (table 5).

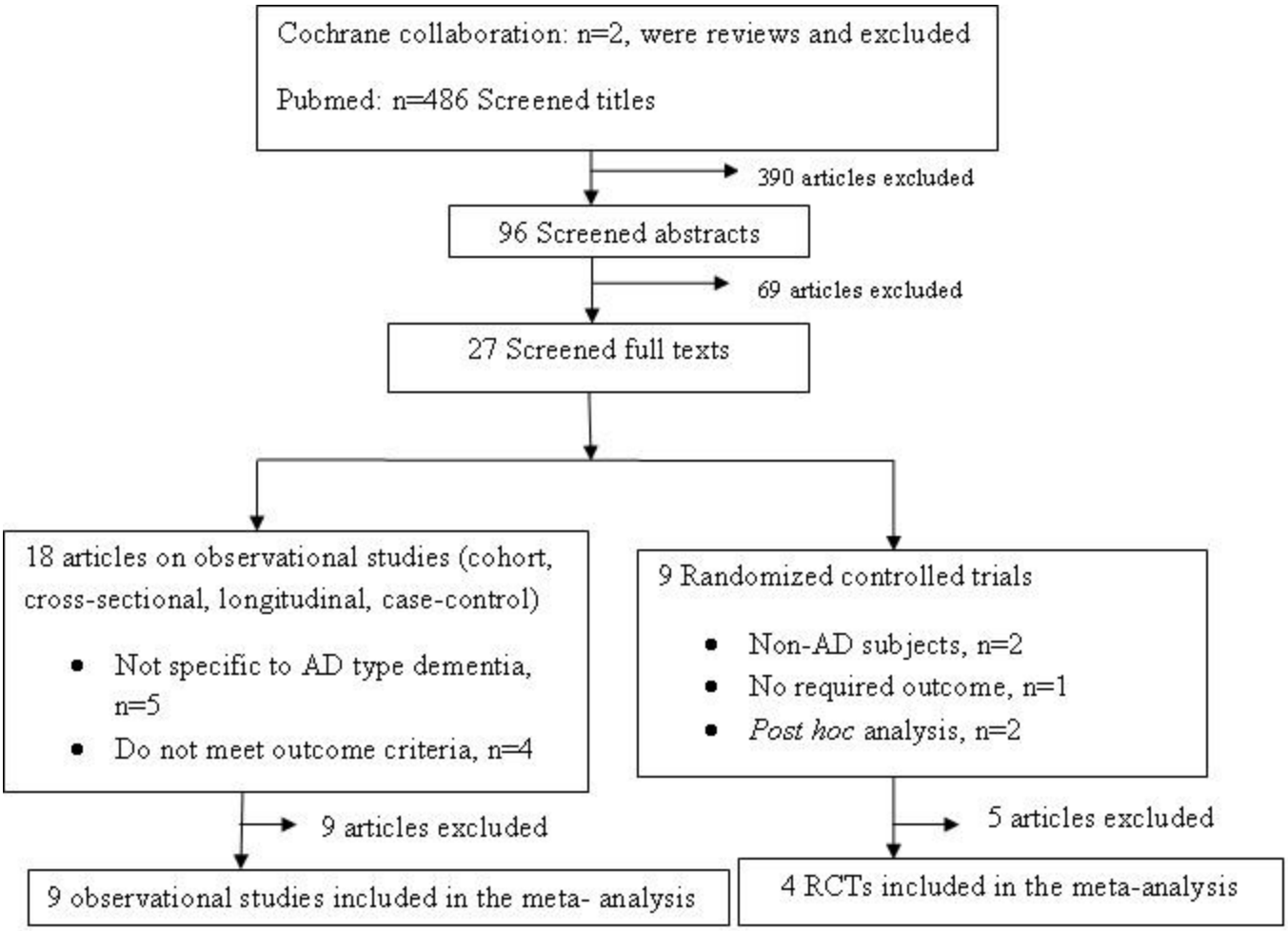

Fig. 1 Results of Pubmed and Cochrane collaboration database searches.

Observational Studies

One of the 9 included observational studies (i.e. Murali 2004) provided data using change in MMSE from baseline to follow-up period and the effect of statin on MMSE in statin users was not significant compared to statin non-users (p=0.429). Four of the remaining eight studies (Arvanitakis 2008, Higdon 2004, Li 2010, Rotterdam study 2009) provided computed effect sizes in the form of HR and the rest four (Hajjar 2002, Masse 2005, Peter 2005, Rockwood 2002) in the form of OR. The software used in the analysis (Comprehensive Meta-Analysis software) failed to accept data (OR, upper and lower limits) from Peter 2005 and reported that its upper and lower limit log values were not symmetric. Common HR computed from the above mentioned four studies showed that statin use had significant protective effect against AD [HR=0.69, 95% CI, 0.542, 0.882, p=0.003]. Computation of common OR from the above mentioned three studies also resulted in common OR=0.447, 95% CI, 0.299, 0.668, p=000, indicating that statin users had 0.447 times lower risk of AD compared to statin nonusers.

Baseline cholesterol level, APOE genotyping, age and cognitive level and treatment outcome:

Data provided in ADCLT 2006 revealed that patients who improved on the ADAS-Cog had higher baseline cholesterol levels than those who deteriorated. (Mean change in ADAS-Cog score -2.14 ±1.20 in atorvastatin + cholesterol >200mg/dl group, P=0.045 compared with placebo ≥200 mg/dl; 0.11±0.68 in atorvastatin + cholesterol <200mg/dl group).

ADCLT 2006 also indicated that significant difference was seen in ADAS-Cog performance at 6 months between the atorvastatin and placebo groups in individuals with an APOE ε4 allele (p=0.012) but not between the groups comprised of subjects without an APOE ε4 allele (p=0.967). However, Arvanitakis 2008 and Peter 2005 mentioned that there was no interaction of statins with APOE ε4 allele. Rotterdam study 2009 provided data that the protective effect of statin use was similar for persons with an ApoE4 allele (adjusted HR 0.50; 95% CI 0.26 to 0.94) and for persons without an ApoE4 allele (adjusted HR 0.61; 95% CI 0.32 to 1.18). Data from Higdon 2004 and Li 2010 revealed that, though overall interaction term for statin use-by-APOE ε4 was not significant, statin exposure was associated with a significantly lower risk of AD in the subjects < 80 years old at entry who had at least one APOE-ε4 allele and these data were combined and significant difference was seen [HR=0.31, 95% CI, 0.207, 0.739, p=0.004].

Among subjects treated with atorvastatin in ADCLT 2006, those who had improved on the ADAS-Cog at 6 months had baseline MMSE scores 2 points higher than those who continued to deteriorate (21.93±0.85 compared to 19.83±1.10, p<0.06).

Data provided in Rockwood 2002 indicated that the OR for those younger than 80 years was 0.26 (95% CI, 0.08, 0.88); while for those 80 years and older, it was 0.50 (95% CI, 0.13-1.88). The effect remains protective in those 80 years and older, the CI includes 1.0. Higdon 2004 and Li 2010 provided data on potential differential effect of statins in different age groups (<80 vs ≥80 years). Data from these two studies were combined and showed that statin use was associated with lower risk for probable AD in younger study subjects (HR=0.474, 95% CI, 0.298, 0.754, p=0.002), but not with study subjects ≥80 years (HR=1.464, 95% CI, 0.869, 2.467, p=0.152).

Safety:

LEADe 2010:

There were 60 (19.1%) atorvastatin-treated and 69 (21.2%) placebo-treated patients who experienced serious adverse events (SAEs), 6 of whom in the atorvastatin group and 1 in the placebo group considered treatment related by the investigator or sponsor. There were 9 deaths (2.9%) in the atorvastatin group and 6 (1.8%) in the placebo group. The SAEs for atorvastatin group were hepatitis, acute renal failure/rhabdomyolysis/pancreatitis, abdominal pain/ nausea/chest discomfort, transaminases elevation, liver disorder and gastrointestinal haemorrhage.

Simons 2002:

1 patient had muscle pain without elevation of creatine kinase, 1 patient was withdrawn because creatine kinase was elevated. No adverse effects were reported in the placebo group.

Sano 2011:

The groups did not differ in the number of subjects with SAEs (placebo group: 54/202 [26.7%]; treatment group: 56/204 [27.5%]; p = 0.91), the number of subjects with serious adverse events requiring hospitalization (placebo group: 46/202 [22.7%], active treatment group: 53/ 204 [25.9%]; p = 0.52), and the number of deaths (placebo group: 9/202 [4.5%], active group: 5/204 [2.5%]; p = 0.29). The most commonly occurring adverse events were falls, agitation, and anxiety.

Data from LEADe 2010, Sano 2011 and Simons 2002 on treatment related adverse events requiring treatment discontinuation were combined and no significant difference between statin and placebo groups was seen [OR=2.84, 95% CI, 0.41, 19.69, p=0.29].

DISCUSSION

In this systematic review and meta-analysis, both randomized controlled trials comparing statins use in the treatment of AD with matching placebo, and observational studies comparing statin users associated risk for AD (or cognitive decline) with matching non-users were reviewed and analyzed separately. Including non-randomized studies in reviews can be used to provide evidence of effects (benefit or harm) that cannot be adequately answered by reviews of randomized trials (11). To be included in the review, duration of the studies were expected to be at least six months. Six month was chosen as this was felt to be the minimum length of time required to be on treatment to allow a disease-modifying effect and before any cognitive benefit could be attained (17).

This review provides inconsistent evidence between RCTs and observational studies. Mean change in ADAS-Cog and MMSE from baseline were an outcome in the four of the RCTs and there was no significant difference between the statin and the placebo groups. Mean change in NPI from baseline was also an outcome in the three of the included RCTs, i.e., ADCLT 2006, LEADe 2010 and Sano 2011, and significant difference between the statin and the placebo groups was seen only at 12 months study period, not at end points. These indicated that statins were not efficacious in the treatment of AD. A previous systematic review of RCTs assessed treatment of dementia or AD by statins (17). This was published before the Sano 2011 results were available. Three studies were identified ADCLT 2005, LEADe 2010 and Simons 2002 as identified in this review, and there was no statistically significant treatment effect of statins on AD which is in agreement with the present review. While, common effect sizes computed from observational studies (common HR and OR) indicated that statins had strong protective effect against AD, though one of the studies (Murali 2004) failed to show significant protective effect. But the weight of Murali 2004 in the review of observational studies was very small (compared only 11 statin users with 22 statin non-users).

There was evidence from ADCLT 2006 that greater cognitive effect from the statin (atorvastatin) was seen in patients with higher cholesterol and higher MMSE at baseline. ADCLT 2006 and combined results from two of the observational studies (Higdon 2004 and Li 2010) provided evidence that greater cognitive and protective effects were seen in participants harboring an APOE ε4 allele. There was also evidence from observational studies that better protective effect against AD from statins was seen in those participants whose baseline age was younger than 80 years.

The statins were well tolerated and incidence of adverse effects was low. The statin group did not have a significantly higher rate of adverse effects requiring discontinuation of treatment when the data from the three of the RCTs, i.e., LEADe 2010, Sano 2011 and Simons 2002, were combined. There was no evidence that statins were detrimental to cognition.

The main strength of this review was inclusion of observational studies and their separate analysis to provide evidence on association of statin use with AD which was not elucidated in the review of RCTs only. Publication bias is a potential limitation when carrying out a review. This source of bias has been addressed by using funnel plot, and there was no evidence of publication bias as assessed by visual inspection of the funnel plot produced by plotting the standard error against the mean difference of RCTs or log OR (HR) of observational studies.

In summary, observational studies have shown that statins have strong protective effect against AD, whereas statins use in RCTs showed no significant effect on AD. This implies that there is insufficient evidence to recommend statins for the treatment of AD, as the level of evidence from RCTs outweighs than from observational studies. Negative clinical outcomes from RCTs accompanied by promising positive outcomes from observational studies signal a need for development of better randomized controlled study designs. Available RCTs designed to be run for shorter study periods than observational studies and that may affect the outcomes.

From ADCLT 2006 there was some evidence that atorvastatin treatment was more beneficial at six months in AD patients with higher MMSE and higher cholesterol levels at baseline. There was also evidence from ADCLT 2006 and observational studies that statin treatment was more beneficial in study participants harboring an APOE-ε4 allele. And observational studies also suggested that statin use was associated with lower risk for probable AD in younger study subjects (<80 years), but not with study subjects ≥80 years. From the present study, we recommend to use large scale RCTs to further assess the impact of treatment at an earlier stage of the disease process, effect of age, effect of APO E ε-4 allele and effect of baseline cholesterol level.

Disclosure
The authors report no conflict of interest concerning the mate¬rials or methods used in this study or the findings specified in this paper.

Table 1: Characteristics of included RCTs

Study ID	ADCLT 2006 (30, 31)	LEADe 2010 (6)	Sano 2011 (22)	Simons 2002 (29)
Method	RCT	RCT, multicentre	RCT, multicenter	RCT
Participants	63 AD patients (32 atorvastatin, 31 control), Age = 51 years. Total cholesterol, mean ±SE, mg/dl: Placebo =208.00±6.41, Atorvastatin = 207.97±5.98	640 patients (297=atorvastatin, 317=placebo with MITT), Age 50-90 years, Total cholesterol, mean (SD), mg/dl: Atorvastatin= 225.1 (33.7), Placebo= 223.1 (33.3)	406 AD patients (204 in the simvastatin, 202 placebo), age > 50 years, Total cholesterol (mg/dl): mean±SD: placebo (208.8 ± 28.6), simvastatin (215.0 ± 32.5).	44 AD Patients (20 placebo, 24 simvastatin) LDL-C mean(SD) (mg/dl) , (Simvastatin=137(42), Placebo=134 (32)
Interventions	Intervention: Atorvastatin 80mg/day Control: Matching placebo	Patients already receiving donepezil Intervention: Atorvastatin 80mg daily Control: Matching placebo	Treatment: initiation- simvastatin 20 mg, study- 40 mg/day. Control: identical placebo	Intrvention: 40 mg for 4 weeks then, 80mg simvastatin for the rest 22 weeks daily Control: Matching placebo
Outcomes (analyzed)	Change in ADAS-Cog, MMSE, NPI.	Change in ADAS-Cog, NPI, MMSE	Change in ADAS-Cog, NPI, MMSE	Change in MMSE and ADAS-Cog score
Study place and dutation	single site in USA, 1 year	Patients recruited from Australia, Austria, Canada, Denmark, Germany, South Africa, Spain, Sweden, UK and USA. 72 weeks trial period followed by 8 week atorvastatin withdrawal phase	45 sites in USA, Initiation 6 weeks plus study 18 months	Germany, 26 weeks

LDL-C= Low density lipoprotein cholesterol, SD= standard deviation, MITT= modified intent to treat, ID= Identification

Table 2: Characteristics of included observational studies

Study ID	Methods	Participants	Outcomes (analyzed)	Outcomes measured in	Study place and duration
Arvanitakis 2008 (2)	longitudinal	929 older Catholic clergy, mean baseline: Age 74.9 yrs, statin users= 119 (12.8%), statin nonusers= 810 (87.2%)	Incident AD	HR	USA, ≤12 years.

Study ID	Methods	Participants	Outcomes (analyzed)	Outcomes measured in	Study place and duration
Hajjar 2002 (10)	Case-control and Retrospective cohort	655 patients (113 statin users, 542 non-statin users), mean baseline age 78.7±0.3 years.	Incident AD	OR	USA,10.6±0.6 months
Higdon 2004 (14)	community-based prospective cohort	2,356 cognitively intact persons, mean baseline age 75.1 ± 6.1years	Incident AD	HR	USA, 3.9 ±2.8 years
Li 2010 (15)	Community based-Cohort -every 2 years follow-up	3,099 participants (711 statin users, 2,388 statin nonusers), mean baseline age (Statin users =74.2 ± 5.5 Statin nonusers =75.8 ±6.4)	Incident AD	HR	USA, 6.1 years
Masse 200 (16)	Observational study	342 AD patients, Mean (SD) age in years: 70 (7.4) at onset, 73.5 (7.3) at first visit, and 76.5 (7.5) at the end of the follow up (range 42 to 99).	Cognitive decline in AD patients.	OR	France, 34.8 months
Murali 2004 (4)	Pilot observational study	246 non-demented elderly subjects (35 LLA users, 211 LLA nonusers), mean baseline age LLA users =66 (6), LLA nonusers= 66 (6)	Cognitive change	Change in MMSE	USA, 2 years
Peter 2005 (34)	Cross-sectional, prospective study	4895 participants aged ≥65years, 4572 statin nonusers, 292 statin users Mean age (SD) in years: Nonusers= 75.7 (7.2), Statin users=73.0 (5.4)	Diagnosis of AD	OR	USA, Utah, Cache county. 3 years.
Rockwood 2002 (21)	Case-control design in population-based survey of Canada Study of Health and Aging (CSHA)	Participants (Canadians aged ≥65 years) from CSHA. Controls (n=823), Cases (n=326) , Statin users (n= 57), nonusers (n = 2234)	Association of statins use with AD	OR	Canada, 4 years.
Rotterdam study 2009 (8)	Prospective cohort study.	6992 (age ≥55 years) participants, mean baseline age (SD) in years= 69.4 (9.1)	Incident AD	HR	Netherlands, Rotterdam,9 years

LLA= Lipid lowering agents

Table 3. Change in cognition measured by change in ADAS-cog (error score). Mean difference obtained by subtracting weighted mean change in ADAS-cog score of placebo group from weighted mean change in ADAS-cog score of statin group.

Study period	Mean difference [95% CI]	P-Value
From baseline to end points	-0.57 [-1.39, 0.25]	0.17
From baseline to 6 months	-0.24[-0.93, 0.45]	0.49
From baseline to 12 months	-0.24[-1.15, 0.66]	0.60
From baseline to 18 months	0.19[-1.93, 2.31]	0.86

Table 4. Change in cognition measured by change in MMSE (correct score). Mean difference obtained by subtracting weighted mean change in MMSE score of placebo group from weighted mean change in MMSE score of statin group.

Study period	Mean difference [95% CI]	P-Value
From baseline to end points	0.57[-0.36, 1.50]	0.23
From baseline to 6 months	0.21[-0.15, 0.58]	0.25
From baseline to 12 months	0.27[-0.18, 0.73]	0.24
From baseline to 18 months	0.06[-0.92, 1.04]	0.90

Table 5. Effect of statin on behavior, measured in NPI change (error score). Mean difference obtained by subtracting weighted mean change in NPI score of placebo group from weighted mean change in NPI score of statin group.

Study period	Mean difference [95% CI]	P-Value
From baseline to end points	-0.77[-1.59, 0.06]	0.07
From baseline to 12 months	-1.03[-2.03, -0.04]	0.04*
From baseline to 18 months	-0.76[-2.01, 0.49]	0.23

**- Significant difference between statin and placebo groups*

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NEUROEPIDEMIOLOGY/NEUROEPIDEMIOLOGIE

PATTERNS OF ANTIEPILEPTIC DRUG USE AND SEIZURE CONTROL AMONG PEOPLE WITH EPILEPSY IN A SUBURBAN COMMUNITY IN SOUTHEAST NIGERIA

UTILISATION DES ANTIEPILEPTIQUES ET CONTROLE DES CRISES DANS UNE COMMUNAUTE D'UNE BANLIEUE DANS LE SUD-EST DU NIGERIA

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Keywords *- Active epilepsy - Antiepileptic drugs -Seizure control.*

ABSTRACT

Background

Epilepsy is characterized by episodic and unpredictable seizure recurrences which are often amenable to medical treatment. Simple and readily available medications can be used to control seizures in epilepsy. However, in many communities in developing countries seizure control among people living with epilepsy is still poor.

Method

We assessed the patterns of antiepileptic drug use and seizure control among persons living with epilepsy in a suburban community in Southeast Nigeria found in a two phase cross-sectional study. Detailed information on epilepsy treatment, seizure control and patterns of antiepileptic drug use (AED) by those diagnosed with epilepsy was determined by use of a semi-structured interviewer administered questionnaire. Further verification of the type of antiepileptic drugs (AEDs) was done by drug inspection.

Result

The total of 29 cases of active epilepsy comprising 16 (55.2%) males and 13 (44.8%) females were found. Those receiving AEDs at the time of survey were 7 (24.1%), 11(37.9%) who had previously used AEDs had stopped and the remaining 11 (37.9%) were AEDs naïve. Carbamazepine monotherapy was used by 57.1% (n=4) while phenobarbitone was used by 42.9% (n=3). The antiepileptic drugs were prescribed in all these cases by medical personnel. Over 82% of the persons with active epilepsy found were having more than one seizure per month.

Conclusion

Active epilepsy was prevalent in this suburban community with only 24.1% (n=7) of them receiving treatment with AEDs. Seizure control was poor even among those receiving AEDs and carbamazepine monotherapy was most commonly used AEDs.

INTRODUCTION

Epilepsy is one of the world's most prevalent non-communicable diseases with about 80% of the estimated 50 million people living with epilepsy residing in developing countries (20). Epilepsy is characterized by episodic and unpredictable seizure recurrences and these results in immense psychosocial consequences for sufferers and relatives alike. Despite these consequences, the overall prognosis of epilepsy remains good. Often time epilepsy is amenable to medical management with simple and readily available medications.

The goal of treatment is to maintain a normal lifestyle by complete seizure control with minimal side effects. Treatment is with pharmacological and non pharmacological methods. Antiepileptic drug (AED) therapy is the mainstay of treatment for the majority of patients. The selection of an AED is based on efficacy against specific seizure types and the adverse effect profile. Non-pharmacological strategies are primarily reserved for drug-resistant epilepsy. If the seizures are provoked by external factors, for instance sleep deprivation or excessive alcohol, simple avoidance might be sufficient to prevent further attacks. AEDs are highly successful in suppressing seizures in most patients. With correct, early and uninterrupted therapy, up to 75% of patients with epilepsy eventually become seizure free, many of them within 5 years after diagnosis (3) while about 25% of patients may not respond to any kind of therapy (3).

AEDs differ in many important aspects including their efficacy against different seizure types, their side-effect profiles, their potential for pharmacokinetic interactions, and their ease of use. Several antiepileptic drugs exist, these include the older antiepileptic drugs generally regarded as ¡°old¡± or ¡°established¡± AEDs (carbamazepine, phenobarbitone, phenytoin, valproic acid, e.t.c) and the newer antiepileptic drugs (vigabatrin, lamotrigine, felbamate, gabapentin, topiramate, e.t.c). Except for a better side effect profile, there are no convincing data to show that newer drugs compared with older ones, achieve superior seizure control (3). Older AEDs have several advantages including long-term experience, lower cost and known efficacy. The AEDs most frequently prescribed in the developing world are phenobarbital and phenytoin, (6) they are the cheapest and are prescribed in 65-85% of cases (6).

Initiation of therapy for newly diagnosed patients is with a single antiepileptic drug. Combination therapy is recommended when two successive AEDs given as monotherapy have failed. Agents with a low risk of pharmacokinetic interactions are preferred for combination therapy and success of combination therapy can be improved by paying attention to mechanisms of action and using lower dosages (2). With correct, early and uninterrupted therapy, up to 75% of patients with epilepsy eventually become seizure free, many of them within 5 years after diagnosis (3). About 25% of patients may not respond to any kind of therapy. Antiepileptic drugs (AEDs) are highly successful in suppressing seizures in most patients.

MATERIAL AND METHODS

Study area: The study was conducted in Ukpo an Igbo speaking community in Southeast Nigeria. Ukpo is the headquarters of Dunukofia Local government area in Anambra State Nigeria. The population of Dunukofia local government according to the 2006 National population census report is 96,517 and it has 20,708 households by ownership status of dwelling units (11). The people of Ukpo are predominantly subsistent farmers and they also trade on farm produce. There are a few civil servants under the school system and the Local government employment. The major religion of the people is Christianity with few who are still adherents of Africa traditional religions. The people are acquainted with orthodox treatment since the establishment of a health clinic in the community in the Eastern region of Nigeria. This together with the advent of Christianity had not succeeded in modifying much of the cultural beliefs and practices about epilepsy. This health clinic came under the management of Nnamdi Azikiwe University Teaching Hospital (NAUTH) in 1997 and it became a centre for medical student training in community medicine and recently has become the epicenter of the Neuro-epidemiology and Community Neurology centre of the Neurology unit of the Department of Medicine, Nnamdi Azikiwe University. In addition there is another health centre and two maternity homes and a handful of patent medicine stores in the community but no pharmacy store. Drugs are sourced from these patent medicine stores or the pharmacy sections of the health centers and from pharmacies in neighboring communities.

THE SURVEY

The study was a two phase cross-sectional descriptive study. The first phase was preceded by a census of households. Household interviewed were selected using computer generated random numbers. Every member of a selected household was interviewed. A total of 6800 persons from 1700 households in the community were selected and interviewed in the first phase taking into consideration the design effects and epilepsy prevalence.

The first phase of the study was a door-to-door using a modified version of the WHO protocol (15) for detecting the presence of neurological diseases in the community which was forth and back translated into the local vernacular of the community. This protocol was validated in the area and found to have a sensitivity of 100% and specificity of 65% for active epilepsy. In the second phase all those identified as possibly having epilepsy were evaluated by neurologists and senior residents in neurology. Epilepsy was diagnosed based on the ILAE guidelines (9) and electroencephalogram (EEG) was done in for 19 (65.5%) of the persons with active epilepsy. Detailed information on epilepsy treatment, seizure control and patterns of antiepileptic drug use was determined by use of a semi-structured interviewer administered questionnaire. Further verification of the type of AEDs was done by drug inspection.

Ethical approval for the study was obtained from the Ethical Committee of the Nnamdi Azikiwe University Teaching hospital Nnewi and permission to conduct the study from the Ministry of Health Anambra State, Nigeria. Informed consent was obtained from the traditional ruler and his council, from household heads and adults subjects and from parents or close family relatives of children. All the subjects gave their consent. Parents or close family members acted as proxy for Children and persons unable to understand and respond to the questions during all the phases of the survey.

STATISTICAL ANALYSIS

Data collected was entered into the research instrument and confidentiality maintained. Data collected was analyzed using Statistical Package for the Social Sciences SPSS version 15 (SPSS Chicago Inc., IL, USA). Prevalence values with their 95% confidence intervals were calculated, relevant percentages, frequencies, means and standard deviation were calculated. Fisher's exact test was used to compare percentages where necessary. Findings were represented with relevant tables.

LIMITATIONS

The analysis of antiepileptic drug use was restricted to those on AEDs at the time of survey whose drug type and dosage regimen were verifiable.

RESULT

In the first phase of the study 6800 persons were screened that included 3249 (47.8%) males and 3551 (52.2%) females. Seventy six persons were identified at the first phase as possibly having epilepsy. At the second phase 29 persons were found to have active epilepsy giving a prevalence of 4.3 per 1,000 (95% CI: 2.7 - 5.9). The identifiable seizure types on clinical assessment were generalized seizures 62.1% (n=18) and partial seizures 37.9% (n=11).

The patterns of AEDs use is shown in Table 1. At the time of study 24.1% (n=7) of the persons with active epilepsy were receiving AEDs, while 37.9% (n=11) of the persons with active epilepsy who had previously use AEDs had stopped. The remaining 37.9% (n=11) had never been treated with AEDs. AEDs monotherapy was used by all the subjects (100.0%) still receiving AEDs at the time of survey and these were prescribed by medical staffs (medical doctors). Carbamazepine was used by 57.1% (n=4) and phenobarbitone by 42.9% (n=3) of the persons with active epilepsy.

The duration of seizures and seizure frequency are shown in Table 2. The mean duration of seizures for patients with active seizure was 6.07 ± 4.6 years. The duration of seizure was 5 years or less for 58.6% (n=17) of the persons with active epilepsy. The seizure frequency was more than one seizure episode per month for 82.8% (n=24) of cases of active epilepsy and less than one seizure episode per month for the remaining 17.2% (n=5). There was no statistically significant difference (P>0.05) in seizure episodes

between those on AEDs and those not receiving AEDs (Table 3), this also applied to the difference in seizure types and the type of antiepileptic drug prescribed (Table 4).

DISCUSSION

Epilepsy one of the most common chronic neurologic diseases the world over is amenable to medical treatment. This study concerned a population sample representative of the Ukpo community in Dunukofia local government area of Anambra state Nigeria. The prevalence rate of 4.3 per 1,000 (95% CI 2.7-5.9) found in this present study was lower than 5.3/1000 and 37/1000 reported by Osuntokun et al (14, 15) in Igbo-ora and Aiyete Southwest Nigeria respectively and 6.2/1000 by Longe and Osuntokun (10) in Udo Southsouth Nigeria. However Osuntokun et al (14) had acknowledged that the existence of health facilities in Igbo-Ora would have contributed to the lower prevalence of epilepsy in Igbo-ora compared to Aiyete which was only 20KM away. The established health care facilities spanning for over more than four decades now in Ukpo might account for the low prevalence in this present study. Furthermore the point in time of this study and difference in the definition of active epilepsy between the present study and that of Osuntokun et al (14) might also be contributory.

Simple and readily available medications can be used to control seizures in epilepsy. Up to seventy five percent of patients with epilepsy will eventually become seizure free within 5 years of diagnosis (3) while about 25% of patients may not respond to any kind of therapy (3). In our study the percentage of persons with active epilepsy using antiepileptic drugs at the time of survey was 24.1% (n=7). This is comparable to 27.5% found by Aziz et al (1) in Urban Pakistan. However at Igbo-ora a suburban community that is comparable to Ukpo, Osuntokun et al (14) reported that 4% (n=4/101) were not on AEDs. This was about three decades ago. During door to door surveys the percentage of persons with active epilepsy on AEDs had varied between studies conducted in the developing countries and between communities within the same country. In a community study in Turkey, Aziz et al (1) found that 30% of the epileptic population was on AEDs. The percentage of people living with epilepsy (PWE) on AEDs is less in studies conducted in rural communities. Aziz et al (1) reported 1.9% in rural Pakistan while Dent et al (5) reported 4.2% in a rural community in Southern Tanzania.

The AEDs that the patients were using at the time of the study were carbamazepine (57.1%) and phenobarbitone (42.9%). Prior to the study, three persons had used phenytoin. Phenobarbitone and/or phenytoin were used by the persons with epilepsy found by Osuntokun et al (14) at Igbo-ora and Dent et al (5) in Southern Tanzania. Phenobarbitone has been successfully used to treat epilepsy by primary health workers in rural Africa (21). Phenobarbitone is recommended by the World Health Organization (WHO) as the drug of choice for management of seizures in developing countries (8). Previous studies had noted phenobarbitone and phenytoin to be the most often prescribed AEDs in the developing world, the two drugs being the cheapest were prescribed in 65-85% of treated epileptic patients (6). In a study, Ogunniyi et al (12) in a hospital series at Ibadan in 1998 found that phenobarbitone was the single most commonly prescribed antiepileptic agent during that period.

The World Health Organization reported carbamazepine as the third most prescribed AED in developing countries and is prescribed for only 5 to 20% of cases (6). However, the use of carbamazepine is gaining acceptance due to its favorable anticonvulsant efficacy and supplementary psychotropic use (13) and this might in part explain the high use of carbamazepine found in our study. This is further supported by a recent finding in a study conducted in Ilorin, Nigeria by Sanya and Musa (17) on private practitioners' perspective of epilepsy management that 64.8% of the respondents prescribed carbamazepine, while 25.4% and 14.1% prescribed phenobarbitone and phenytoin respectively. Antiepileptic drug monotherapy was used by all the patients in this study who were still on AEDs at the time of survey. This is encouraging as monotherapy should be the aim for most people with epilepsy (19). Optimum seizure control can be obtained with a single drug for between 70% and 80% of patients (18, 19).

The frequency of seizure was high among the PWE in our study. The majority of those with active epilepsy (82.8%) had more than one seizure episode per month. There was no statistically significant difference between the episodes of seizures in those using AEDs and those not receiving AEDs at the time of survey. Though the number of persons in this study that were on AEDs was few to make reasonable conclusions, various factors which may be patient related or health care related however, are known to contribute to poor seizure control in epilepsy. The major health care related problem identified in our study was under dosage. The patients in our study on AEDs at the time of the survey were grossly under dosed. The maximum dosages of the drugs were carbamazepine 200mg daily (plain not controlled release formulation) and

phenobarbitone 60mg daily despite continuing seizures. Antiepileptic drugs are highly successful in suppressing seizures in most patients and with probable adequate dosing and education of both the patients and health care providers in this community epilepsy control will be improved. Another health care related factor that may have also contributed to the poor seizure control was the choice of antiepileptic drug used. Carbamazepine was used for three patients we found to be having primarily generalized seizure based on clinical assessment using the ILAE guidelines.

Self withdrawal from AED therapy was high in our study. We found that 37.9% (n=11) of the persons with active epilepsy had used AEDs previously but had stopped at the time of study. This is higher than 27% reported by Aziz et al (1) in a mixed rural and urban community in Turkey. The major reason found in this study to be responsible for permanently discontinuing AEDs was patients' dissatisfaction arising from the continuity of the seizures despite the use of AEDs. Other workers have also reported in the past that the majority of patients who permanently discontinue their antiepileptic medication do so of their own accord (4, 7). About one-third (37.9%) of the persons with active epilepsy in our study had never used antiepileptic drugs, this is similar to other reports were up to one-third of the epileptic population were never on medication (16).

CONCLUSION

Active epilepsy was prevalent in this suburban community in Southeast Nigeria. Among the PWE less than one third were receiving treatment with AEDs. Seizure frequency has high even among those receiving AEDs. More than a quarter of the PWE had never been treated with antiepileptic while more than half of those who were started on antiepileptic drug have discontinued of their own accord despite continuing fits.

Table 1 Patterns of Use of Antiepileptic Drugs

Characteristics	Number of subjects	Percentage
Use of AED		
Number with active epilepsy	29	100.0
Number receiving AED at time of survey	7	24.1
Number that had previously used AED(s)	11	37.9
Number that never used AED(s)	11	37.9
AED regimen		
Monotherapy	7	100.0
Polytherapy	0	0.0
Type of AED (a)		
Phenobarbitone	4	42.9
Carbamazepine	3	57.1

(a) Analysis limited to those using AEDs at time of survey because of problems of recall. However three patients with active epilepsy had used phenytoin before the time of survey.

Table 2 Seizure duration and control

Characteristics	Number	Percentage
Duration of seizures		
<5 years	17	58.6
6-10 years	8	27.6
> 10 years	4	13.8
Total	29	100.0
Mean duration of seizures	6.07 ± 4.6	
Frequency of seizures (a)		
≤ 1 per month	5	17.2
>1 per month	24	82.8
Total	29	100.0

(a) Seizure frequency the year prior to survey

Table 3 Seizure frequency and Antiepileptic drug (AEDs).

Seizure Frequency	On AEDs (%)	Not on AEDs (%)	Total (%)
≤ 1 per month	1 (3.4)	4 (13.8)	5 (17.2)
>1 per month	6 (20.7)	18 (62.1)	24 (82.8)
Total	7(24.1)	22 (75.9)	29 (100.0)

Fisher's exact test (2-sided) P =1.0

Table 4 Seizure type and type of antiepileptic drug prescribed

Seizure Frequency	Carbamazepine (%)	Phenobarbitone (%)	Total (%)
Generalized	3 (42.9)	3 (42.9)	6 (85.7)
Partial	1 (14.3)	0 (0)	1 (14.3)
Total	4 (57.1)	3 (42.9)	7 (100.0)

Fisher's exact test (2-sided) P =1.0

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CASE REPORT/CAS CLINIQUE

A RARE NEURONAL TUMOR OF THE CEREBELLUM WITH MYOID FEATURES

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Key-words: *liponeurocytoma, cerebellum, myoid differentiation, immunohistochemistry*

ABSTRACT

We report an extremely rare tumor presenting with myoid features in the left cerebellar hemisphere in a 62-year-old man. This tumor consisted of medium to large round cells with focal lipomatous and myoid differentiation. Immunohistochemically, the tumor cells expressed synaptophysin, GFAP (glial fibrillary acidic protein) and focally desmin. From these findings, we concluded that this tumor was a liponeurocytoma with myoid features. To the best of our knowledge, this report constitutes the second described case of liponeurocytoma with myoid differentiation in the cerebellum.

INTRODUCTION

Cerebellar liponeurocytoma is morphologically composed of uniform round cells with neuronal differentiation and lipomatous features. It typically affects adults and has a favourable prognosis. Initially described as a lipomatous medulloblastoma, the World Health Organisation Working group proposes the term "cerebellar liponeurocytoma" primarily to distinguish this entity from medulloblastoma and to avoid over treatment of this benign tumor.

Here, we report to the best of our knowledge the second case in the literature of cerebellar liponeurocytoma with myoid features and discuss the histogenesis of this rare tumor.

CASE SUMMARY

The patient was a 52-year-old man who presented with a 4-month history of headache of gradual onset, vomiting and decreased visual acuity. His past medical and family history were unremarkable. Neurological examination revealed cerebellar syndrome. Magnetic resonance imaging (MRI) showed a relatively well-defined, poorly enhancing, round lesion in the left cerebellar hemisphere hyperintense on T2-Weighted Images, causing moderate mass effect [Figure1]. At surgery, a 5,7cm x 4,7cm, well circumscribed mass, located in the cerebellar left hemisphere was removed. Ten percent formalin-fixed specimens were paraffin-embedded, cut at 3 µm, and stained with eosin-hematoxylin-saffron.

Microscopically, the tumor was composed of small round cells to polygonal with eosinophilic or clear cytoplasm resembling oligodendrocytes [Figure 2]. In some areas, the tumor cells were mixed with lipomatous cells [Figure 3] and myocyte-like cells [Figure 4]. The tumor shows no mitotic figures.

An immunohistochemical study was performed. After heat-induced epitope retrieval, dewaxed 3µm sections were incubated with the following antibodies: synaptophysin (Cell Marque, Rabbit polyclonal), GFAP (glial fibrillary acidic protein) (Cell Marque, Clone G-A-5, Mouse monoclonal), Mib1 (Cell Marque, Clone sp6,

Rabbit monoclonal) and desmin (Cell Marque, clone D33, Mouse monoclonal). Revelation was performed after a streptavidin-biotin-peroxidase technique with diaminobenzidine.

Tumour cells expressed synaptophysin [Figure 5], GFAP [Figure 6] and focally desmin [Figure 7]. The Mib 1 antibody stained less than 1% of tumour cell nuclei.

The tumor was classified as a cerebellar liponeurocytoma with myoid differentiation grade II accordind to the WHO grading.

Her postoperative period was uneventful with no evidence of tumour recurrence after 12 months.

DISCUSSION

Liponeurocytoma is a rare cebellar neoplasm of adults that is histologically characterized by neuronal differentiation with focal lipidization and low proliferative potential.

Since the first report [2] by Bechtel in 1978 as a mixed mesenchymal and neuroectodermal tumor of the cerebellum, several terms “medullocytoma” [3], “lipomatous glioneurocytoma”[4] and “lipidized mature neuroectodermal tumor of the cerebellum” [5] have been proposed as to emphasize its resemblance to central neurocytoma.

In 2000 [1], the WHO classification of tumours of the central nervous system proposed the term “cerebellar liponeurocytoma” to distinguish this tumor from medulloblastoma because of the outcome and to avoid aggressive treatment to this benign tumor.

This tumor classically manifests at the fifth decades like our case (mean 50 years) [6] without significant gender predilection. This is in contrast with the age distribution of medulloblastoma. The clinical features are non-specific.

This tumour is predominantly located in the cerebellar hemispheres like our observation followed by the vermis. Histologically, the cerebellar liponeurocytoma features a monotonous pattern of round cells with focal lipidization and neuronal differenciation reflected by immunoreactivity to neuronal markers [1]. The Mib1labelling index is even lower.

In the literature data, only one case has been reported with additional immunoreactivity to desmin [5] in a 67 year-old woman. This myogenic feature hasn’t anysignificance.

The most important differential diagnosis is medulloblastoma but the occurrence of the latter in children and the high Mib-1 labelling index can distinguish between these two tumors.

The histogenesis of cerebellar liponeurocytoma has remained unclear. The immunoreactivity to neuronal antigens suggests that the fat containing cells result from lipomatous differentiation of tumour cells. The cell of origin is a precursor cell with commitment to neuronal differentiation but a capacity for divergent astrocytic and myogenic differentiation.

Some studies suggests that this tumor is derived from the external granular layer of the cerebellum. [7] Several genetics studies suggests that medulloblastoma are distinctly different from liponeurocytoma [8] with particular higher frequency mutation of TP53 in liponeurocytoma than in medulloblastoma.

A complete surgical resection is recommended as the initial treatment but there is no consensus regarding the treatment of this rare tumor specifically adjuvant chemo-or radiotherapy. The prognosis of liponeurocytoma is favourable [8].

CONCLUSION

The cerebellar liponeurocytoma is a histopathologically and genetically distinct entity. The distinction between liponeurocytoma and medulloblastoma is very important since the medulloblastoma requires adjuvant radio/chemotherapy.

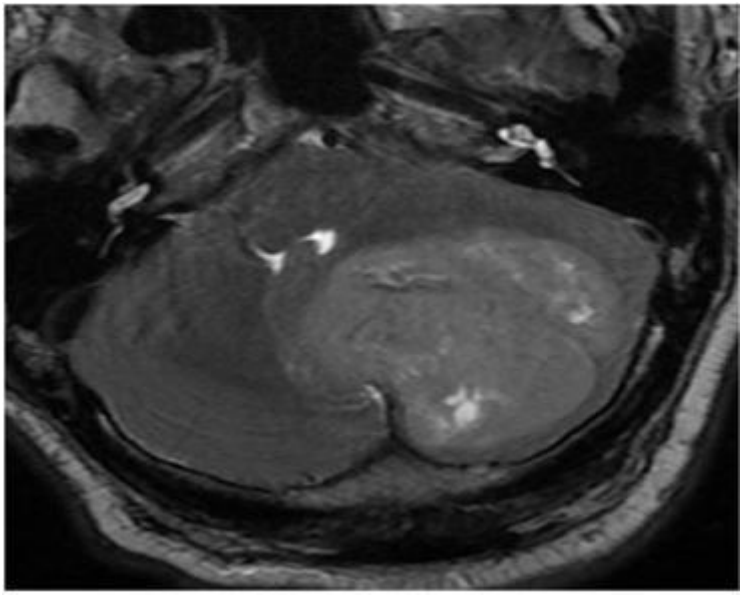

Figure 1:
T2-Weighted MRI of cerebellar tumour.

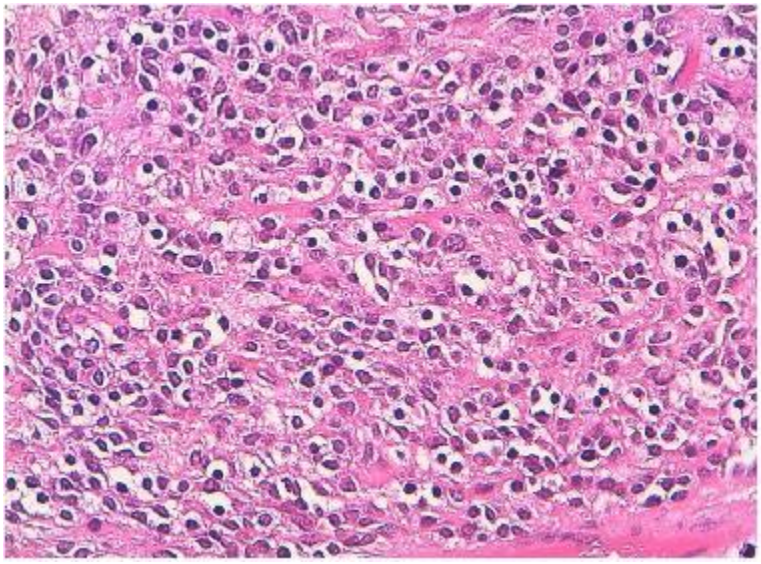

Figure 2:
Hematoxylin-eosin-saffron stain x 250: tumour cells showing a round nuclei with a clear cytoplasm resembling neoplastic oligodendrocytes.

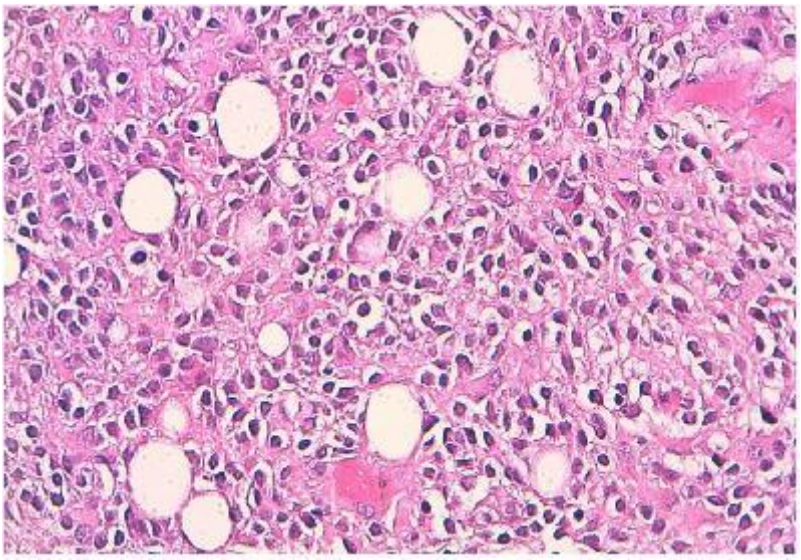

Figure 3:
Hematoxylin-eosin-saffron stain x 250: Isomorphic small cells with focal lipomatous differentiation.

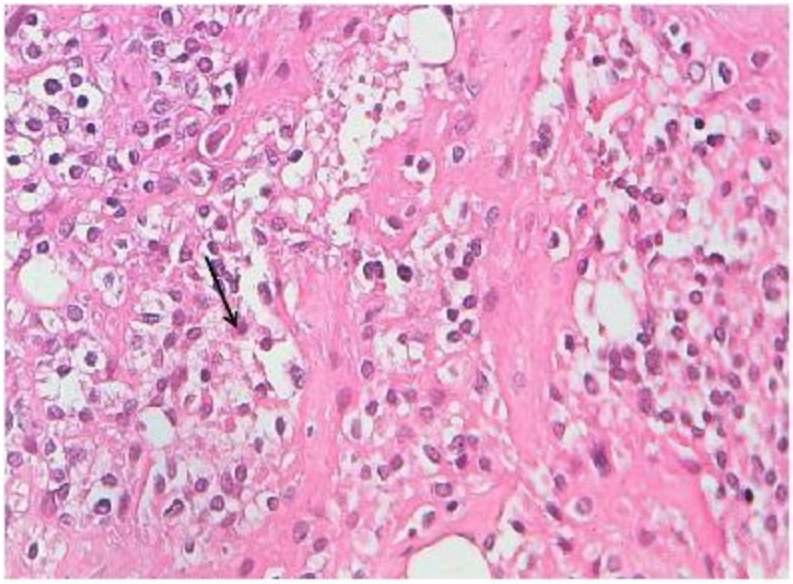

Figure 4:
Hematoxylin-eosin-saffron stain x 250: myocyte-like cells (arrows)

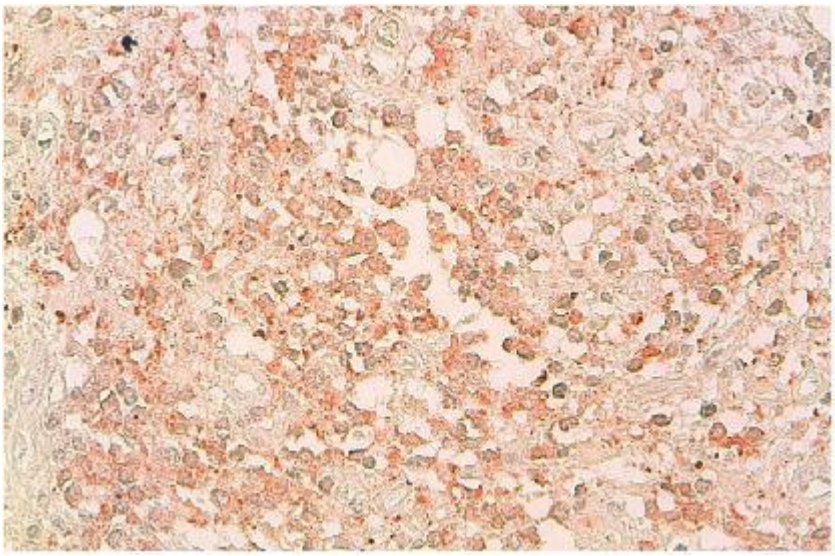

Figure 5:
Immunoreactivity with anti-synaptophysin, DAB x 100. Small tumour cells express neuronal marker.

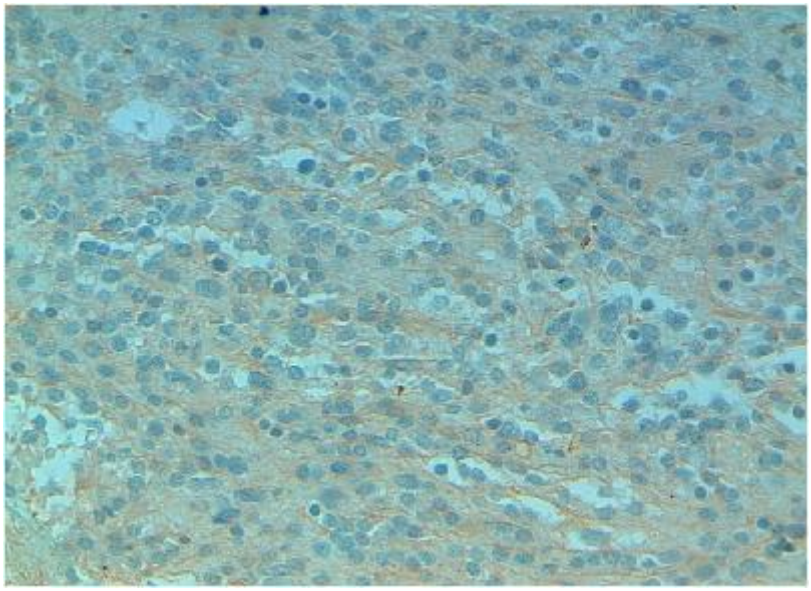

Figure 6:
Immunoreactivity with GFAP

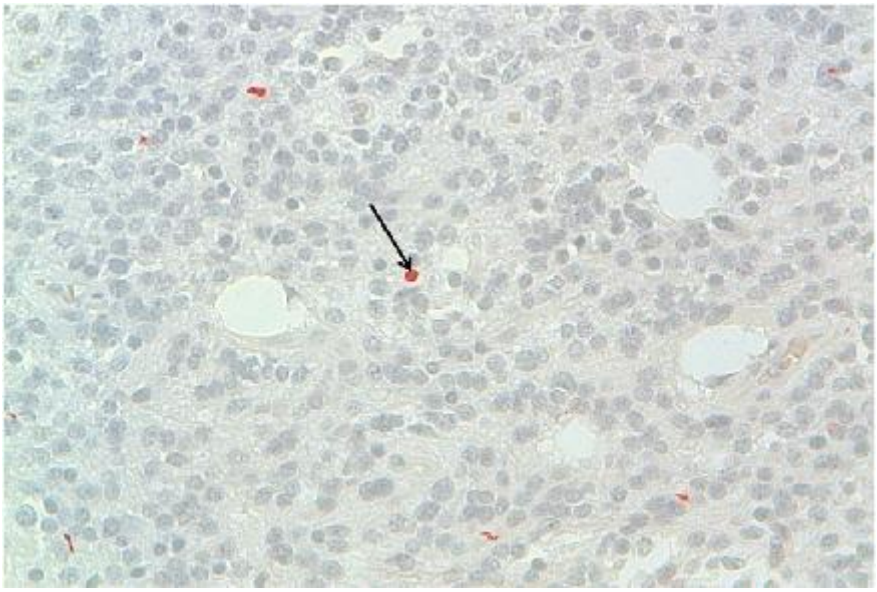

Figure 7:
Immunoreactivity with anti-desmin, DAB x 100. Positivity of some tumor cells, indicating an myogenic differentiation. (arrows)

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CASE REPORT/CAS CLINIQUE

CLINICAL EXPERIENCE AND OUTCOME OF PITUITARY SURGERY IN KENYAN PATIENTS AT THE KENYATTA NATIONAL HOSPITAL

EXPÉRIENCE ET RÉSULTATS DE LA CHIRURGIE HYPOPHYSAIRE CHEZ DES PATIENTS KENYANS AU KENYATTA NATIONAL HOSPITAL

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Key Words: Pituitary tumors, Trans-sphenoidal, Hypophysectomy, Craniotomy

ABSTRACT

Introduction
Surgical extirpation of pituitary lesions and can be perfomed by craniotomy or trans-sphenoidal hypophysectomy. This could be for pituitary ablation, excision of pituitary adenomas, craniopharyngiomas, suprasellar meningiomas and other types of tumors of the sellar region. Despite this being a common neurosurgical procedure there is a paucity of data on the local Kenyan experience and outcomes following pituitary surgery.

Study Design and Site
A retrospective study at the Kenyatta National Teaching and Referral Hospital.

Objectives
To evaluate the clinical presentation, management and outcome of patients undergoing surgery for pituitary lesions at the Kenyatta National Hospital.

Patients and Methods
Following ethical approval, patients' records were retrieved and assessed for clinical and radiologic features of pituitary lesions, surgical treatment and post operative outcome. All the data was coded and analysed using Statistical Package for Social Sciences (SPSS) version 16.0.

Results
Sixty five patients, 39 (60%) female and 26 (40%) male patients were included. The mean age was 36.88 years (+ 14.689). The most common presentation were visual disturbances reported by 57 (87.7%) of the patients having reduction in visual acuity, while 37 (56.9%) had bitemporal hemianopia. Sixty two (95.4%) patients were operated during the study period and of these 28 (45.2%) by the transphenoidal approach as opposed to 34 (54.85%) by craniotomy. The pterional trans-sylvian approach was the most prevalent of transcranial hypohysectomies accounting for 17 (50%) patients, while 15 patients (44.1%) were operated by the subfrontal approach and two patients were operated via midline trans-callosal approach. Majority (96.4%) of trans-sphenoidal hypophysectomies were by sub-labial incision. Fifty (76.9%) of the patients had good functional outcome while 11 (16.9%) and 4 (6.2%) suffered moderate and severe disability respectively. Patients' age (p=0.0029), duration of symptoms prior to surgery (p=0.0018) and surgical management versus conservative (p=0.001) significantly affected patient outcome. There was no statistically significant difference in outcome between patients of different sex (p=0.058) or the type of operation performed (p=0.191).

Conclusion
Transsphenoidal and trans-cranial approaches are effective and safe treatment strategies for pituitary lesions with low morbidity, mortality and recurrence rates.

INTRODUCTION

Pituitary adenomas account for 10 to 15 % of all intracranial tumors and in addition to suprasellar tumors such as craniopharyngiomas, meningiomas, germinomas and low grade gliomas, account for a significant portion of the surgical workload of any neurosurgical practice30. Tumors of the suprasellar region assume importance because of their anatomical proximity to the anterior visual apparatus and neuroendocrine structures (the pituitary gland and hypothalamus) which influences their clinical presentation and progression.

Surgical extirpation is the treatment of choice for pituitary adenomas and other types of tumors of the sellar region and clivus. Pituitary and sellar mass lesions presenting with chiasmatic syndrome, ophthalmoplegia, pituitary apoplexia or endocrine derangement can undergo successful surgical removal34. Access to the pituitary may be achieved by craniotomy via subfrontal, pterional and sub-temporal approaches. In addition, the transsphenoidal route is widely accepted as the approach of choice for intrasellar lesions and some centers have also advocated the transsphenoidal route for tumors with subdiaphragmatic origin and subsequent suprasellar extension9. These subdiaphragmatic lesions are thought to be more easily removed by a transsphenoidal approach because the expanded sella provides a widened aperture to the suprasellar compartment and also diaphragmatic protection from pial invasion26. Further, the transsphenoidal approach has a number of variations, including the sublabial transseptal, transnasal endoscopic, endonasal rhinoseptoplastic, and transnasal septal displacement26, 37.

However, despite the major advances, reported success rates and low morbidity and mortality, there is a paucity of local data regarding the Kenyan experience and outcomes of this popular procedure. Kenyatta National Hospital is a teaching and referral hospital with a bed capacity of over 2000 patients. Through this centre the majority of neurosurgical referrals are managed. We reviewed the records of patients who were treated for pituitary tumors in the neurosurgical unit.

METHODS

Following ethical approval, the records of patients who presented to the Kenyatta National Hospital and underwent surgery for pituitary lesions from June 2000 to June 2010 were retrieved and reviewed. Patient biodata, type and duration of symptoms, hormonal profile and management modalities were recorded in a pre-formed questionnaire. A data entry interface was created through which codified data was entered and data analysis carried out using Statistical Package for Social Sciences (SPSS) version 16.0. Frequencies and means were computed for description of the various variables and presented in prose form and as pie charts and graphs. The association between categorical variables was calculated using Chi-square test while comparison of mean values was performed using the one-way analysis of variance test (ANOVA).

RESULTS

Biodata and Clinical Presentation A total of 65 patients fit the inclusion criteria during the study period and their files were retrieved and reviewed. There were 39 (60%) female as compared to 26 (40%) male patients (Figure 1).

The mean age was 36.88 (+ 14.689) with a range from 2 years and 6 months to 72 years. Majority of the patients (55%) were aged between 26 and 45 years whereas pediatric patients (aged less than 13 years) and elderly patients (over 61 years) accounted for 5% each (Figure 2).

The most common presentation were visual disturbances reported with 57 (87.7%) of the patients having reduction in visual acuity, while 37 (56.9%) had bitemporal hemianopia on confrontational and formal perimetry. Fundoscopy findings were reported for 39 patients with 24 (61.5%) of these being normal and optic atrophy and papilledema being reported for 29% and 9.5% respectively. The right and left eyes were each affected in 8 cases (12.3%) with bilateral involvement in 41 (63.1%) and 8 patients had no ocular involvement. Forty eight patients (73.8%) reported headaches while only 6% and 5% reported vomiting or convulsion respectively.

Amenorrhea and primary infertility were the presenting complaint of 11 (16.9%) patients while 14 (21.5%) and 8 (12.3%) had galactorrhea and gynecomastia respectively. Ten patients (15.4%) had acromegalic features of hypergnathia and enlarged hands and feet. In addition, 9 (13.8%) patients had erectile dysfunction, while 4 (6.2%) had atrophic testes with gynoid habitus and female hair distribution (Figure 3).

One patient aged two years and six months presented with features of precocious puberty. She had progressive breast development since eight months of age and at presentation was at tanner stage IV with growth of pubic hair from 11 months of age. In addition she experienced monthly mensrual-like flow from 1 year of age and had a post-pubertal uterus on ultrasound. She was however reported to have a normal growth rate.

Admission blood pressures were measured and recorded for all the patients and were classified using the World Health Organisation-International Society of Hypertension guidelines. Majority of the patients (65%) had optimal blood pressures while 7.5% and 5% had moderate and severe hypertension (figure 4). Also recorded were admission random blood sugars, of which 49 (75%) were normoglycemic and 12.5% each were gucose intolerant and within diabetic range each (Figure 5).

Data of the hormonal profile was also retrieved where available. Prolactin levels were recorded for 47 patients with 22 (46.8%) of them having hyperprolactinemia as compared to 21 (44.7%) and 4 (8.5%) having normal and low levels respectively. Majority of the patients were euthyroid (72.4%) while 10.3% and 17.3% were hyperthyroid and hypothyroid respectively. Cortisol levels were recorded for 41 patients of whom 4 had hypercortisolemia levels and 9 had normal with 8 patients having low levels (Table 1).

With regards to imaging, all the patients included in the study had a CT scan done while a further 8 (12%) and 5 (7.7%) had an MRI and 4-vessel angiography done respectively. The location of the lesion was described as completely intrasellar 15 (23.1%), sellar with suprasellar extension 40 (61.5%), suprasellar 5 (7.7%) or sellar with supra-, infra- and parasellar extension 5 (7.7%) (Figure 6).

Sixty two (95.4%) patients were operated during the study period, of these 28 (45.2%) by the transsphenoidal approach as opposed to 34 (54.85%) by craniotomy. In addition, there were 2 patients who had initially undergone transsphenoidal hypohysectomy who were re-operated transcranially for recurrences at 2 years and 4 years. The three patients who were not operated are included in the table below:

The pterional trans-sylvian approach was the most frequent of transcranial hypohysectomies accounting for 17 (50%) of these operations. Further, 15 patients (44.1%) were operated by the subfrontal approach with frontal lobe retraction and two patients were operated via midline trans-callosal approach. With regards to the 28 patients operated trans-sphenoidally, majority 27 (96.4%) were by sub-labial incision with blunt dissection up to the maxilla and nasal crest. Septal mucosa was then stripped up to the vomer which was excised. The ostia of the sphenoid were then identified, the body of sphenoid nibbled and the floor of the sella turcica opened. The tumor was then exposed, biopsied and removed by curette and suction.

One 37 year old patient who developed progressive blindness, erectile dysfunction and general weakness for 2 years had a pituitary tumor on CT and MRI with a sellar component, suprasellar extension, sphenoid bone erosion obliterating the sphenoid sinus and extension to both cavernous sinuses. He was scheduled for endonasal endoscopic biopsy as he was a poor anaesthetic risk for general anaesthesia due to persistent hypotension secondary to adrenocortical insufficiency.

Fifty (76.9%) of the patients in this series had good functional outcome with marked improvement in visual function, normalised post-operative hormone levels and regression of symptoms while 11 (16.9%) and 4 (6.2%) suffered moderate and severe disability respectively. There was no early post-operative mortality among this cohort. There was no statistically significant difference in outcome between patients of different sex (p=0.058). However, patients' age was a significant indicator of outcome. Pediatric patients in this series had good functional outcome in comparison to patients above 61 years who developed severe disability (p=0.0029). In addition, the duration of symptoms prior to surgery significantly affected patient outcome (p=0.0018). Majority of the patients (24) who presented within 6 months had good outcome compared to none of the patients who presented after 5 years of symptoms. Findings on fundoscopy had a significant on visual outcome as patients in whom optic atrophy was reported had a higher incidence of blindness and thus severe disability in comparison with those in whom the fundoscopy was normal. Patients who were operated

had a higher incidence of good functional outcome as compared to those managed conservatively (p=0.001) irrespective of the type of operation performed (p=0.191).

Transient fluid-electrolyte imbalance and diabetes insipidus (DI) was the most common postoperative complication (7.7% of the patients) in the present series. Hypothyroidism occurred in 6.2% of the patients as the second most common complication. In addition 2 patients has recurrences of tumor with clinical and radiological evidence at 2 and 4 years and had to undergo craniotomy and excision. Post-operative rhinorrhea was reported in 6.2% of the patients and was managed conservatively.

DISCUSSION

Although pituitary tumors are the most commonly encountered intracranial neoplasms, their true incidence has not been established with certainty. In literature, the prevalence of these tumors in autopsy series is reported to be 5-20%7, 27, 32 while most recent series estimate the prevalence of clinically apparent pituitary lesions to comprise approximately 10-15 % of all intracranial lesions10, 18. Improvement in radiographic imaging, biochemical detection of hormonal abnormalities, and microsurgical techniques have raised the number of surgical procedures, and in some series pituitary adenomas represent approximately 25% of surgically resected intracranial neoplasms; however, this may reflect a bias that reflects the interests of the surgeon or institution.

In the current study, there is a slight majority of 39 (60%) female as compared to 26 (40%) male patients. Previous studies report that pituitary tumors tend to afflict both sexes equally3, 5, 18. In addition, the mean age was 36.88 years (+ 14.689) with most of the patients (55%) were aged between 26 and 45 years and fewer patients at both extremes of age. There is a wide range of reported mean ages in literature ranging from 39.8 years40 to 50.4 years10. Reported incidence rates demonstrate an increase with age for both clinically apparent and autopsy diagnosis of pituitary tumors. In this regard, autopsy analyses and imaging studies report that more than 30% of people 50 - 60 yr of age harbor clinically undetected tumors 5, 7, 28, 31. Further, it is widely reported that pituitary adenomas are infrequent in childhood accounting for only about 3.5- 8.5% of pituitary adenomas which are diagnosed before the age of 20 yr 23, 33. Childhood tumors exhibit a female preponderance, and it has been suggested that they are smaller, less invasive, and less aggressive than tumors of adults23.

Patients with pituitary tumors present with signs and symptoms related to mechanical effects of an expanding tumor within the sella turcica (headaches, visual disturbances and cranial nerve palsies), excessive or impaired hormone production3. The most common presentation in this series, were visual disturbances reported by 57 (87.7%) of the patients with reduction in visual acuity. Chang10 reported that in an American population, over one half of patients presented with visual disturbance while other studies have reported a prevalence rate of up to 90%19, 39. The classic bitemporal field loss is found in chiasmatic compression and was described by 37 (56.9%) of the patients. These patients frequently complain of bumping into objects on one or both sides of the contracted visual field, reflecting both unilateral and bitemporal field loss. However, early compression may lead to upper quadrantic defects secondary to inferior chiasmal fiber compression.

Central vision may be affected by direct compression of the intracranial optic nerve. This may present as a blurring of vision or scotomatous central field defects. This is more common in individuals with a “post-fixed” chiasm - an anatomical variation where the chiasm is situated further back, thus exposing more optic nerve to the compressive effects of an expanding adenoma 25. If compression has been longstanding, fundoscopy may reveal optic atrophy which was observed in 10% of the current population. In our study, 50 (87.7%) the patients had improved visual function following surgery. The reported results in literature of visual outcome after surgical management of pituitary and sellar tumors vary considerably among studies, with improvement rates ranging from 36 to 80% 2, 4, 20, 21, 24, 25. Hypertension is an important complication of pituitary tumors and contributes to the increased morbidity and mortality of this condition. In the current study, 12.5% of the patients had moderate and severe hypertension. Bondanelli6 reported that the prevalence of hypertension in acromegalic patients is about 35%, ranging from 18 to 60% in different clinical series, while Chanson11 reported a range of 20% to 50% of patients. The exact mechanisms underlying the development of hypertension in pituitary lesions are still not clear but may include several factors including chronic hypervolemia (the plasma volume is 10% to 40% above normal due to increased renal sodium reabsorption at the distal tubule level) 12, 22. In addition, hypertension can also result from endothelial dysfunction29 and it has been postulated that insulin resistance and diabetes may also play a role in the onset of hypertension13. Recent studies indicate that an increased sympathetic tone could play an important role in

development and maintenance of elevated blood pressure6. With regards to surgical approaches, 28 (45.2%) patients were operated by the transsphenoidal approach as opposed to 17 (45.83%). 15 (37.5%) and 2 patients by pterional, subfrontal and midline trans-callosal approaches respectively. However, as the current study was retrospective in nature the indications for choice of approach were not accurately captured in data. When analysed over time, more of the recent surgeries were increasingly via of the transsphenoidal route. This not-withstanding, there was gradual shift towards the transsphenoidal route likely guided by an increase in proficiency and the reported lower morbidity in other populations.

The choice for transphenoidal approach as opposed to craniotomy is determined by a number of factors including degree of suprasellar extension, cavernous sinus invasion, tumor consistency, brain invasion and cerebral edema as well as encasement of the optic apparatus41. Tumors with significant suprasellar extension, especially through the plane of the hypothalamus and floor of the third ventricle, have been correlated with significantly worse postoperative outcomes 14, 35. As such, particular features of suprasellar extension that mandate additional consideration prior to an operation are intraventricular extension, displacement or edema of the hypothalamus, displacement/compression of the proximal branches of the ACA, and involvement of the perforating arteries off the ICA and ACA1, 15, 17, 38.

Firm tumor consistency creates an inherent limitation in the ability to completely deliver the suprasellar tumor component via any transsphenoidal approach. Tumor consistency remains one of the most important, yet elusive, factors in the consideration of an trans-sphenoidal versus open craniotomy for skull base tumors. If a tumor's consistency is known to be fibrotic ahead of time (as in some cases of reoperation), thus making it less amenable to suction, dissection and gross total resection, this should provide added support for consideration of an open approach. On the contrary, a primarily cystic or hemorrhagic appearance on MR imaging, especially a fluid-fluid level, can often lend support to selecting a less invasive approach for sellar region tumors 16. In the future, a priori knowledge of tumor consistency may lend major support to the selection of a skull base approach from above versus below and warrants further research. Although cavernous sinus invasion is by no means a contraindication to selecting a transsphenoidal approach, its presence is known to limit the extent of tumor resection 42. In addition, the anatomical relationship of the tumor to the optic chiasm, the degree of circumferential encasement of the optic nerve, and invasion of the optic foramina each require careful preoperative consideration. In the majority of suprasellar pituitary adenomas, the plane between the tumor pseudocapsule and arachnoid membrane is preserved, and the tumor can be safely debulked or removed in its entirety from below. If visual loss is the major indication for surgery, the surgeon must be satisfied that the transsphenoidal approach can safely and effectively decompress the optic nerve and chiasm. Otherwise, the patient may be better served by an open craniotomy with direct visualization of these structures, such as a frontoorbital or supraorbital subfrontal eyebrow craniotomy 36.

CONCLUSION

In conclusion, key advances have been made to improve the ability to safely treat patients with larger and increasingly complex tumors of the anterior and middle skull base since the re-emergence of the transsphenoidal approach. Nevertheless, patient selection remains of paramount importance in guiding the decision to perform a particular surgical approach for a given tumor, and it remains clear that, for the time being, some patients with large sellar and parasellar region tumors are better served by performing one of many variations of an open craniotomy (such as a pterional, frontoorbital, subfrontal, or interhemispheric approach)8. This study highlights the experience and outcomes following pituitary surgery in a Kenyan referral hospital. It demonstrates that good surgical outcomes can be achieved by both the trans-sphenoidal and craniotomy approaches based on the indications and tumor characteristics. There is a need to carry out a prospective study with closer assessment of hormonal profile and response to surgery as well as perioperative management and longer follow-up for outcome. It however, demonstrates the current clinical status and lays a foundation for further inquiry of this subject that is central to neurosurgical practice.

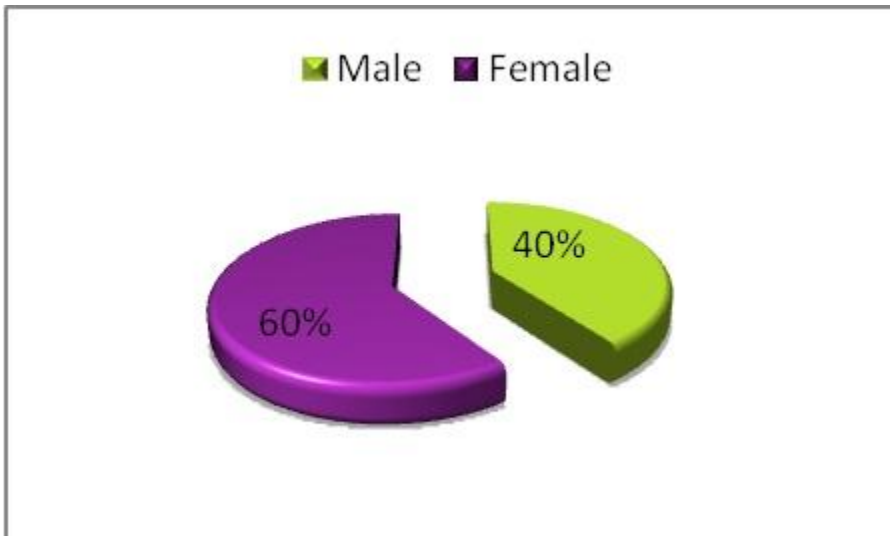

Figure 1: Illustration of the patient distribution by sex

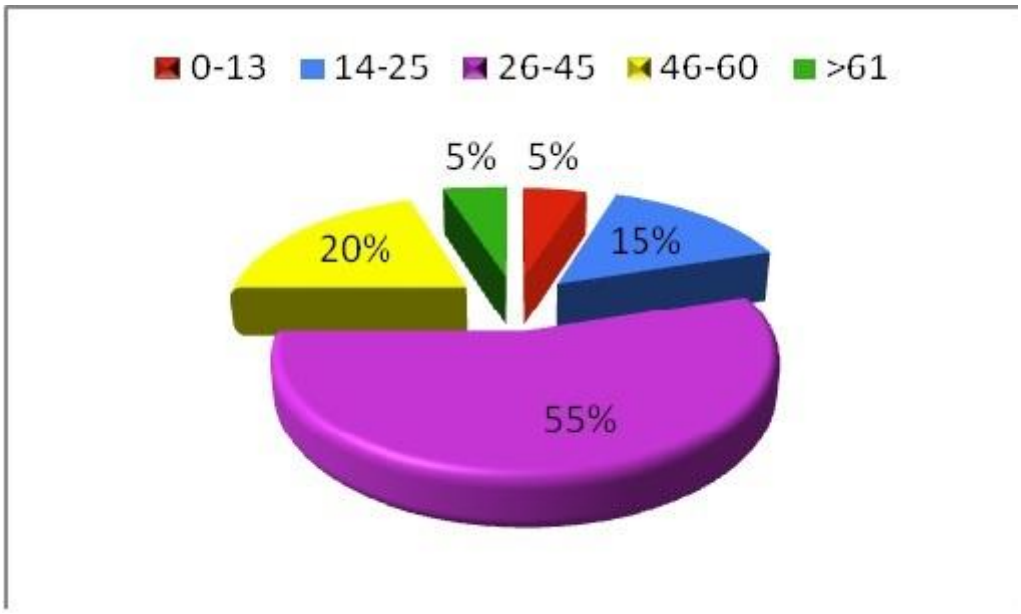

Figure 2: A pie chart demonstrating the distribution by age of patients with pituitary tumors managed at the neurosurgical unit. The majority of the patients were aged between 26-45 years.

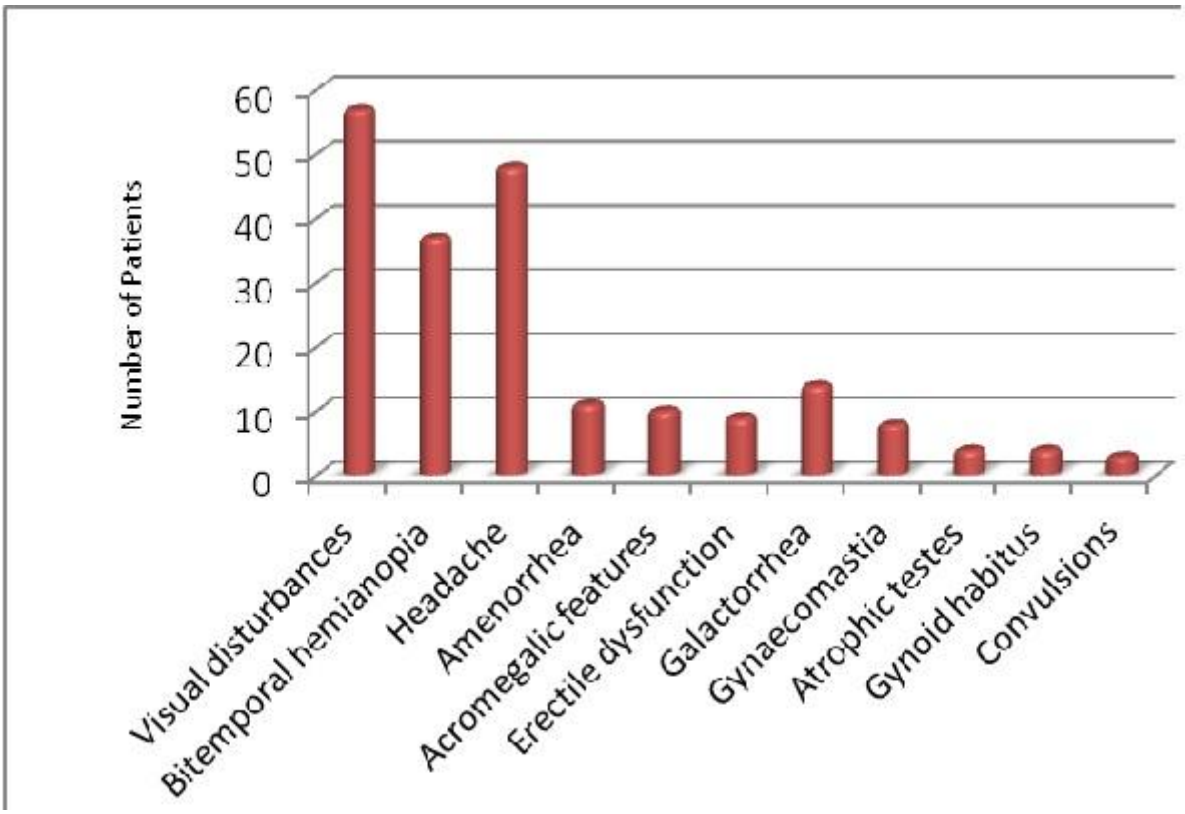

Figure 3: A bar graph showing the frequency of common presentations of patients with pituitary lesions

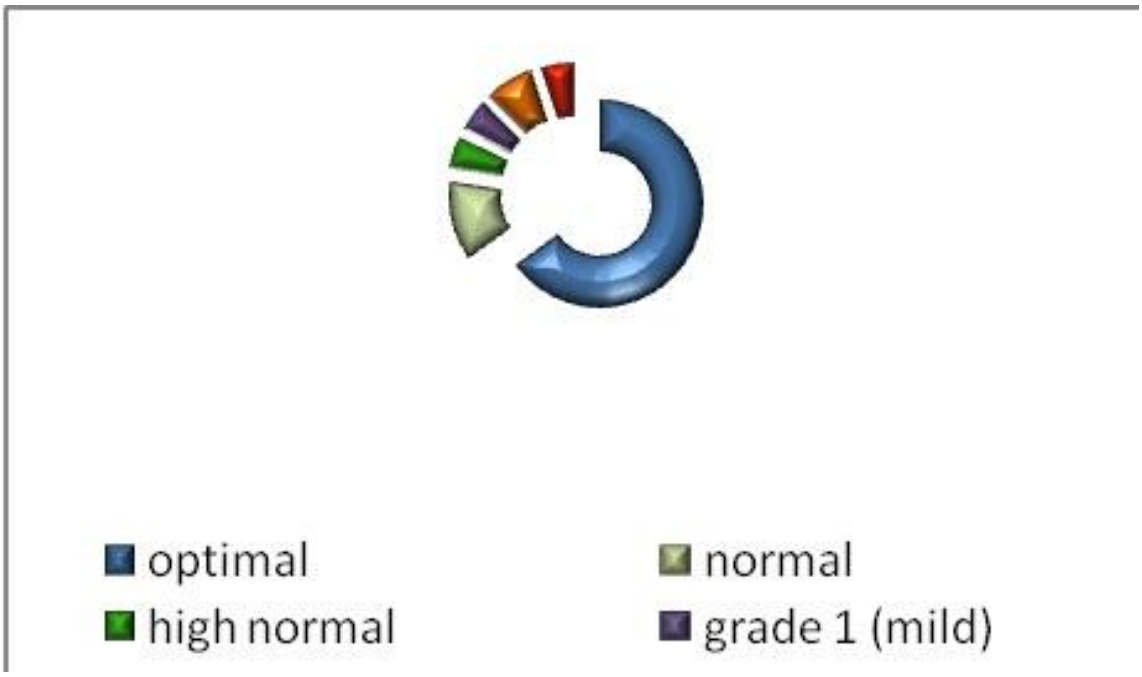

Figure 4: An illustration of the distribution of admission Blood Pressure accoring to the World Health Organisation-International Society of Hypertension guidelines. Grades 1, 2 and 3 refer to the severity of hypertension

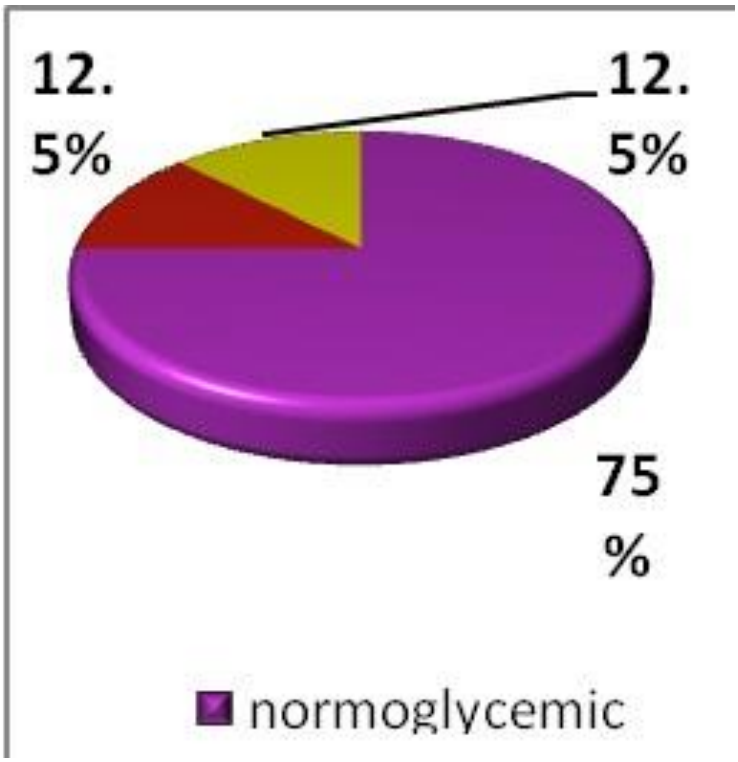

Figure 5: A pie chart representing the proportions of with the various blood sugar levels. Where normoglycemic refers to random blood sugars ¡Ü6.9mmol/L, glucose intolerance (7-11 mmol/L) and diabetes (¡Ý11.1 mmol/L).

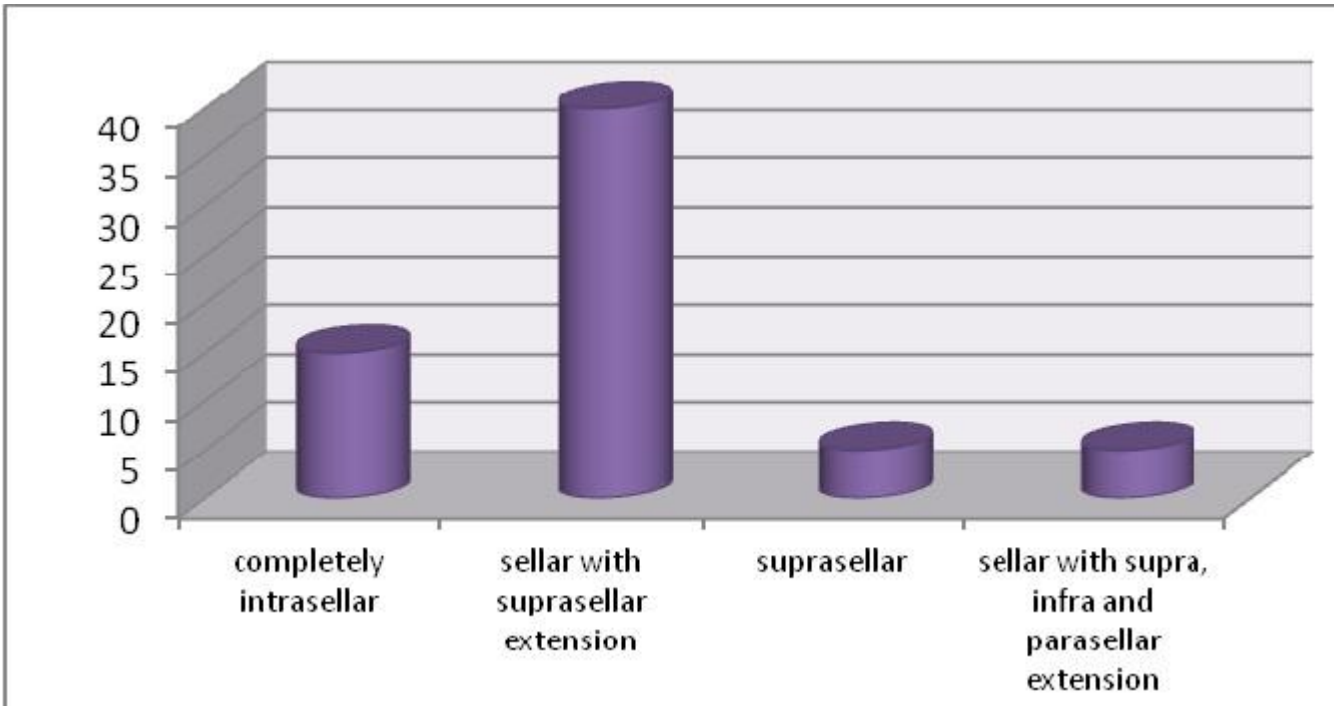

Figure 6: Location of pituitary lesions as seen on CT scan

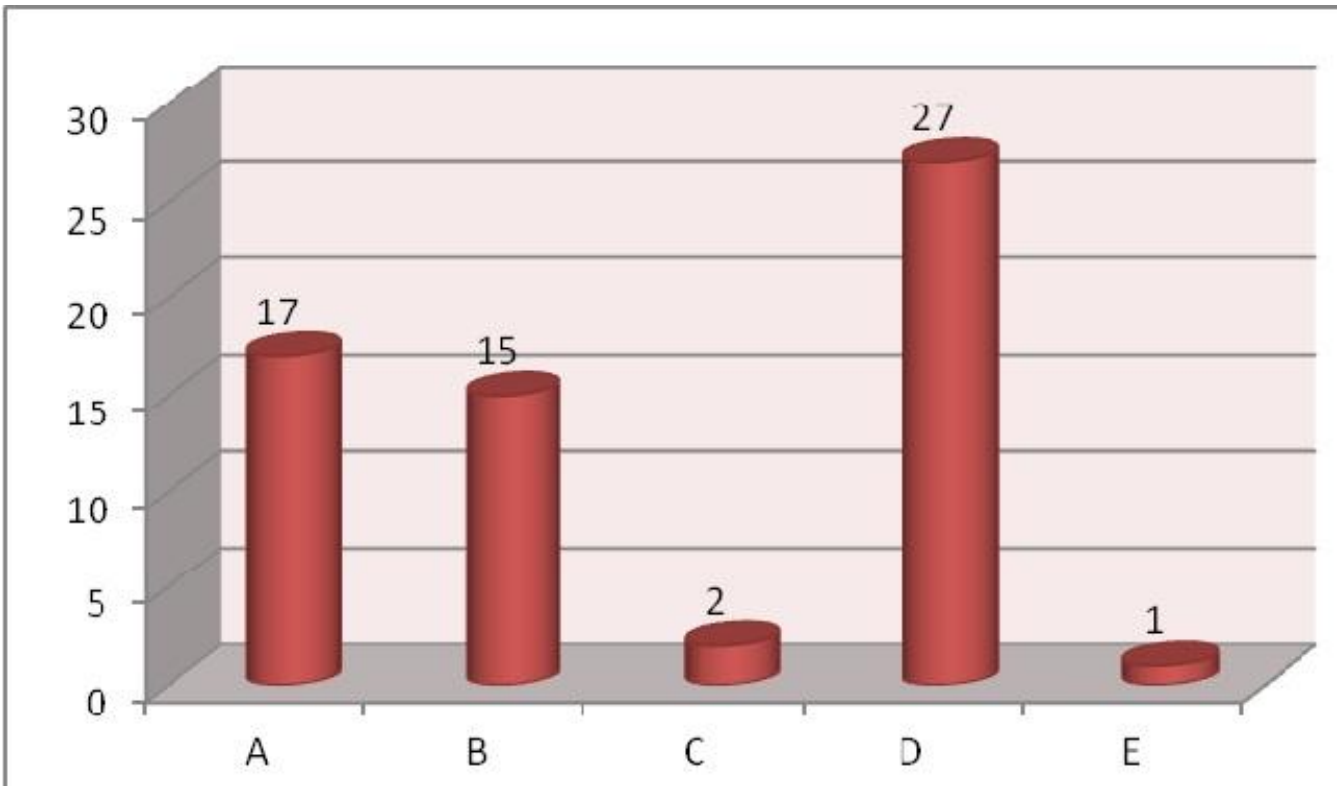

Figure 7: The various approaches to sellar and parasellar lesions
KEY

A- pterional trans-sylvian approach
B- subfrontal approach with frontal lobe retraction
C- midline trans-callosal craniotomy
D- Sublabial trans-sphenoidal approach
E- Endoscopic trans-nasal biopsy

Table 1: The hormonal profile of patients with pituitary tumors managed at the neurosurgical unit

Hormone	Levels	
Prolactin (n=47)	High	22 (46.8%)
	Normal	21 (44.7%)
	Low	4 (8.5%)
Thyroid profile TSH,T3,T4 (n=49)	Hyperthyoid	5 (10.2%)
	Euthyroid	39 (79.6%)
	Hypothyroid	5 (10.2%)
Cortisol levels AM and PM (n=41)	High	8 (19.5%)
	Normal	18 (43.9%)
	Low	15 (36.6%)

Hormone	Levels	
Growth hormone levels (n=15)	High	10 (66.7%)
	Normal	4 (26.7%)
	Low	1
FSH (n=7)	Normal	5
	Low	2
Testesterone (n=2)	Normal	2
	Low	0
Estradiol (n=5)	High	2
	Normal	2
	Low	1

Table 2: Patients with pituitary tumors who were not operated. RVD=Retroviral disease, HAART= Highly Active Antiretroviral Therapy, CT= Computed Tomography

1.	A 54 year old RVD patient on HAART who developed bilateral blindness over a period of 4 months, he declined surgery and was lost to follow up.
2.	A 72 year old man who had progressive visual deterioration over 5 year who had a large suprasellar mass on CT, and a normal 4-vessel angiogram who developed dementia and cognitive impairment.
3.	An 88 year old patient with bilateral blindness for 4 years who also had metastatic bronchogenic carcinoma

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CASE REPORT/CAS CLINIQUE

HYDATIDOSE DU RACHIS CERVICAL : A PROPOS D'UN CAS

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RESUME

L'hydatidose intéresse l'os dans 0,5 à 2 % des cas, dont 44 % de localisations au niveau rachidien. L'étage cervical est la moins fréquente des localisations rachidiennes. Cette atteinte est grave par le risque de compression médullaire haute, et surtout par son caractère récidivant. Les auteurs présentent l'observation d'un jeune patient admis pour une tétraplégie progressive, due à une hydatidose vertébro-médullaire cervicale ; son diagnostic a été évoquée sur l'imagerie par résonance magnétique et confirmée par l'étude anatomopathologique.

INTRODUCTION

Le kyste hydatique est le résultat du développement chez l'homme de la forme larvaire de l'échinoccocus granulosis [8]. L'hydatidose osseuse est une affection rare représentant 0,5 à 2% malgré son caractère endémique dans les pays du Maghreb [1]. Les localisations rachidiennes sont les plus graves et fréquentes liées vraisemblablement à la richesse vasculaire du rachis [3]. Elle associe parfois une atteinte médullaire justifiant le terme d'hydatidose vertébro-médullaire. La localisation au niveau du rachis cervical est exceptionnelle. Le diagnostic est souvent tardif par son manque de spécificité et sa latence cliniques et soulève des problèmes diagnostiques résolus ces dernières années par l'avènement de l'IRM. La problématique de l'hydatidose vertébro-médullaire cervicale est surtout thérapeutique et pronostique [7].

OBSERVATION

Il s'agit d'un patient âgé de 40 ans, sans antécédents pathologique notable, admis dans le service de neurochirurgie pour la prise en charge d'une tuméfaction de la région postérieure du cou associée à une lourdeur des quatre membres. Le début de la symptomatologie remontait à 4 mois. Le patient avait été victime d'une chute de sa hauteur avec un impact cervical. La symptomatologie s'est aggravée par l'installation progressive d'une lourdeur des quatre membres plus marquée à gauche dans un contexte d'apyrexie, d'amaigrissement non chiffré et d'altération de l'état général.

À l'examen clinique, le patient était conscient. Il était noté une tuméfaction cervicale postérieure, mobile par rapport au plan superficiel, fixée au plan profond, indolore et non inflammatoire. L'examen neurologique relevait une tétraparésie plus marqué à gauche, un syndrome tétra pyramidal et des troubles de sensibilité profonde.

L'IRM médullaire, réalisée en séquences pondérées T1 et T2 sagittales, T2 en écho de gradient en coupes axiales et T1 après injection intraveineuse de produit de contraste révélait la présence d'un processus lésionnel ostéolytique du corps vertébral et de l'arc postérieur de la troisième vertèbre cervicale responsable d'une compression médullaire cervicale avec une extension dans les parties molles para vertébrales mesurant 30 mm x 20 mm de grand axe, en hypo signal T1 hyper T2 rehaussé après injection intraveineuse de produit de contraste (Figure 1) Un complément scannographique et une radiographie standard du rachis cervicale ont été réalisés et ont visualisé un aspect hétérogène des vertèbres C2 et C3 avec présence d'images lacunaires osseuses intéressant les corps vertébraux et les arcs postérieurs, s'étendant par endroit aux parties molles adjacentes avec un recul du mur postérieur associé à une luxation antéro-postérieure C2-C3 .

Le patient a été opéré par voie postérieure avec réalisation d'une laminectomie décompressive de C2 et C3 avec ostéosynthèse C1-C4 pour stabilisation rachidienne (Figure 2) Le diagnostic d'hydatidose a été confirmé par l'examen anatomopathologique de la pièce opératoire (Figure 3). La radiographie pulmonaire et l'échographie abdominale étaient sans anomalie. Le patient a été mis sous traitement anti helminthique au long cours. L'évolution sur une durée de 6 mois a été marquée par une récupération d'une force motrice permettant la marche avec double aide.

DISCUSSION

L'hydatidose est une anthropozoonose due au développement chez l'homme de la forme larvaire d'un cestode de l'espèce échinoccocus granulosis. Elle atteint préférentiellement le foie et le poumon. L'hydatidose vertébrale est rare et ne représente que 1 à 2% de toutes les localisations viscérales. Elle reste néanmoins la localisation la plus fréquente des hydatidoses osseuses (44%) [9]. Cette fréquence peut s'expliquer par la richesse de la vascularisation vertébrale et/ou par le phénomène de l'embolie paradoxale : lors d'une augmentation brutale de la pression intra-abdominale, le sang des veinules du système porte se drainerait dans le plexus rachidien. Du fait de cette inversion de courant veineux, l'embryon hexacanthe parviendrait au tissu spongieux vertébral en évitant le filtre hépatique et pulmonaire [2]. Sa localisation est généralement dorsale (80%), rarement lombaire (18%) et exceptionnellement cervicale.

La localisation du kyste hydatique au niveau des régions cervico et maxillo-faciales est extrêmement rare avec seulement quelques rares cas rapportés dans la littérature (environ 0,2 %) [5]. L'hydatidose vertébrale atteint souvent le sujet jeune entre 10 et 30 ans, avec une légère prédominance masculine (60%). L'atteinte hydatique rachidienne est souvent primitive, alors que les lésions médullaires sont secondaires à la migration des vésicules hydatiques à travers les trous de conjugaison ou à des destructions osseuses. Comme c'est le cas dans notre observation, les larves affrontées à la résistance mécanique de l'os se développent par vésiculation exogène, les espaces sous-périostés sont progressivement envahis. Le périoste est ensuite rompu permettant la constitution de collections ossifluentes dans les parties molles, réalisant des «abcès froids hydatiques» pouvant migrer à distance. Dans notre cas, le syndrome rachidien cervical a précédé le tableau de compression médullaire qui est due principalement à des destructions osseuses majeures, À l'inverse des infections bactériennes et en l'occurrence la tuberculose, le disque intervertébral reste intact au début [8].

L'état général reste longtemps conservé et la température souvent normale en dehors des surinfections. Les rachialgies, souvent inaugurales, dominent le tableau clinique [2]. La localisation cervicale est grave car elle peut entraîner une tétraplégie complète par la compression de la moelle par le matériel hydatique et la récidive fréquente après traitement. Les collections ossifluentes peuvent constituer un mode de révélation de l'affection sous forme d'une tuméfaction locale fistulisée ou non. La radiographie standard permet de préciser la topographie, les rapports et la multiplicité des lésions, de suivre l'évolution et d'orienter les explorations radiologiques ultérieures. L'image lacunaire d'ostéolyse est la plus caractéristique. Les destructions corticales aboutissent à un tassement cunéiforme ou en galette des corps vertébraux [1], ce qui augmente le risque d'atteinte médullaire. A la tomodensitométrie l'ostéopathie hydatique se traduit par des images hypodenses, plus ou moins bien limitées, de taille et de forme variables, de densité inférieure à celle de l'os et sans reconstruction osseuse. Elle apprécie l'atteinte des parties molles et l'extension intracanalaire. En post-opératoire, elle permet un «second look radiologique» à la recherche de lésions résiduelles ou récidivantes [1]. L'IRM est actuellement l'examen de choix devant toute compression médullaire. Elle permet grâce aux coupes multiplans d'étudier directement le contenu canalaire, d'apprécier le degré de souffrance médullaire et de préciser les rapports des vésicules hydatiques avec le fourreau dural [6]. Les vésicules hydatiques sont en hyposignal sur les séquences pondérées T1, non modifiées par l'injection de produit de contraste et en hypersignal sur les séquences pondérées T2. Dans les kystes multivésiculaires, les cloisons apparaissent de signal intermédiaire en T1 et hypointense en T2. Un rehaussement des parois et des cloisons peut se voir si les kystes sont remaniés [4,10] c'est le cas de notre cas . A l'heure actuelle, le traitement de l'hydatidose vertébrale ne peut être que chirurgical permettent l'éradication aussi complète que possible des lésions rachidiennes et extra-rachidiennes. Son indication et ses résultats dépendent de l'étendue des lésions, de leur localisation et de la présence ou non de complications [8] Le traitement médical à base de Mebendazole n'a pas encore fait ses preuves dans la localisation vertébro-médullaire. Il est destiné aux formes inopérables ou de mauvais pronostic, mais aussi comme thérapeutique adjuvante de la chirurgie. Les récidives sont très fréquentes (30 à 40% des cas) et la mortalité se situe entre 3 et 14%.

CONCLUSION

L'hydatidose vertébro-médullaire cervicale est grave du fait de sa localisation au niveau d'un véritable carrefour neurologique, du nombre de vertèbres atteintes et du degré de compression médullaire, aboutissant à un état grabataire souvent important. La TDM et surtout l'IRM, toujours précédées par un bilan radiologique standard, permettent de caractériser les lésions, de dresser un bilan d'extension précis et de rechercher les lésions résiduelles ou récidivantes en post-opératoire.

ICONOGRAPHIE

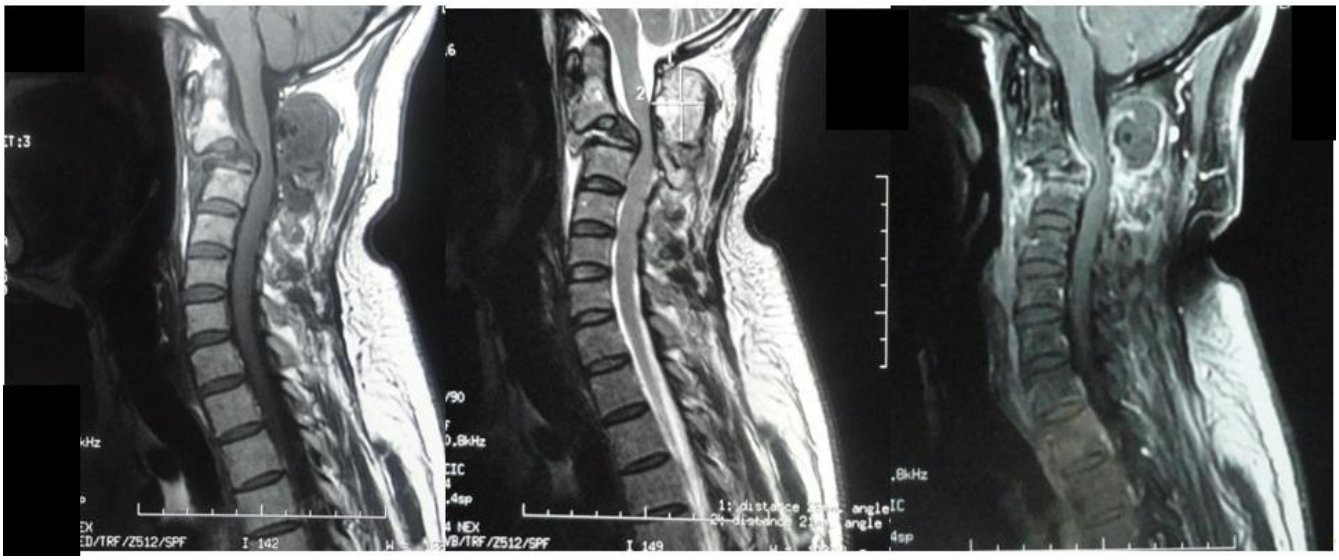

Figure 1 : IRM médullaire en coupe sagittales réalisée en séquences pondérées
T1(a), T2(b) et T1 après injection intraveineuse de produit de contraste(c), montrant une lésion ostéolytique du corps vertébral et de l'arc postérieur de C3 avec extension dans aux parties molles para vertébrales, en hypo signal T1 hyper T2 rehaussé de manière hétérogène après injection intraveineuse de produit de contraste

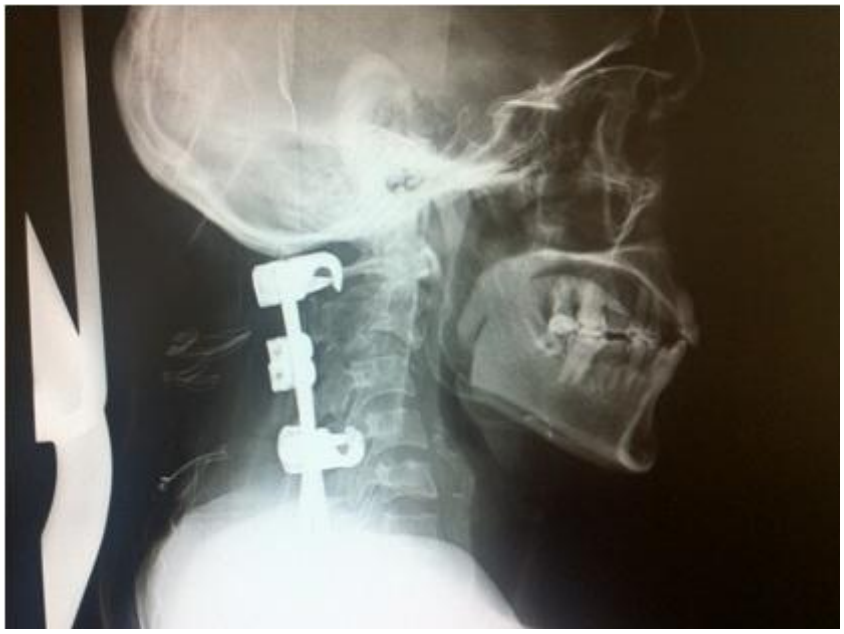

Figure 2 : Radiographie de contrôle du rachis cervical

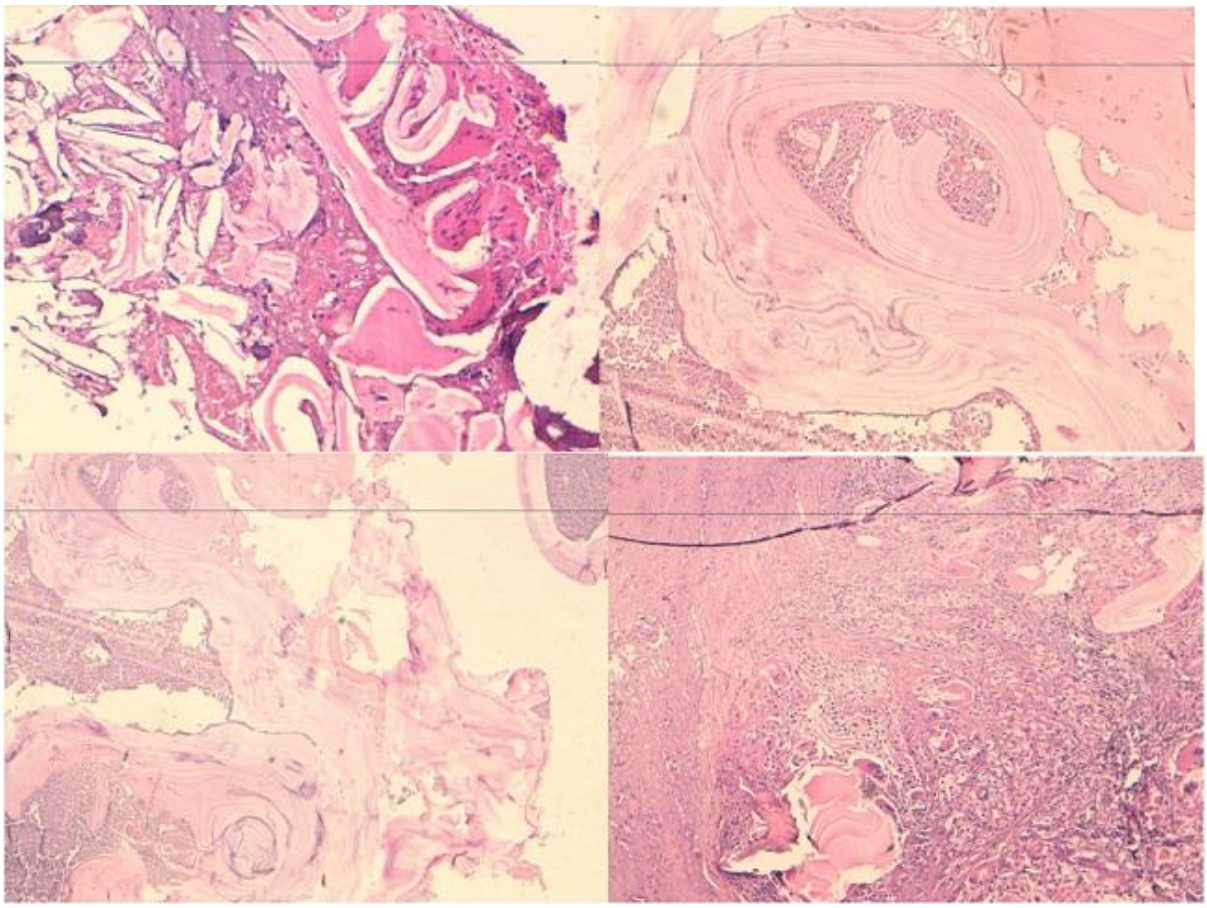

Figure 3 : Etude histologiqque de la masse cervicale
Agrandissement (*5 et *10) montrant des membranes anhistes et de la compression médullaire (agrandissement *10 et *20) montrant une réaction granulomateuse

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ANATOMY / ANATOMIE

TERMINAISON DU CÔNE MÉDULLAIRE, DU SAC DURAL ET PROFONDEUR DU CANAL VERTÉBRAL CHEZ LE NOIR AFRICAIN

CONUS MEDULLARIS POSITION, DURAL SAC LEVEL AND VERTEBRAL CANAL DEPTH ON BLACK AFRICAN SUBJECTS.

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Mots clés *: cône médullaire, sac dural, ponction lombaire, canal vertébral, IRM lombaire.*
Keywords*: conus medullaris, thecal sac, lumbar puncture, vertebral canal, lumbar spine MRI*

RESUME

Objectifs
Déterminer la taille et la terminaison du cône médullaire, la terminaison du sac dural et la profondeur du canal vertébral des sujets noirs africains.

Matériels et méthodes
Les coupes sagittales d'IRM lombaire en pondération T1 et T2 étaient revues pour 77 Noirs africains. La terminaison du cône médullaire et du sac dural était déterminée en référence au segment vertébral ou au disque adjacent.

L'épaisseur maximale du cône médullaire, la profondeur du canal vertébral et l'épaisseur de la graisse sous cutanée étaient mesurées.

Résultats
Il y avait 39 hommes et 38 femmes avec un âge moyen de 47,29 ans. Le cône médullaire se terminait majoritairement (87%) entre le tiers inférieur de T12 et le disque L1L2; il était plus bas chez les personnes âgées ($p = 0,0027$). Le sac dural se terminait entre le tiers moyen de S1 et le tiers inférieur de S2 pour 91% des sujets. L'épaisseur moyenne du cône médullaire était de 7,3 ± 0,8 mm. La profondeur moyenne du canal vertébral était de 77,87 ± 20,18 mm; elle était supérieure à 100 mm pour 9,1% de sujets et était corrélée à l'épaisseur de la graisse sous cutanée lombaire ($r = 0,67$).

Conclusion
La terminaison du cône médullaire et du sac dural du Noir africain est comparable à celle des sujets caucasiens. Dans 9,1% des cas la profondeur du canal vertébral est supérieure à la longueur habituelle des aiguilles à ponction (100 mm).

SUMMARY

Objectives
To determine the thickness and position of the conus medullaris, level of thecal sac and depth of the vertebral canal in black African subjects.

Materials and methods
Sagittal T1 and T2 - weighted MRI sections of the lumbar spine of 77 black African subjects were reviewed. The position of conus medullaris and thecal sac were determined in reference to the adjacent vertebral segment or disk. The thickness of the conus medullaris, the depth of the vertebral canal and the thickness of the adjacent subcutaneous fat were measured.

Results
There were 39 males and 38 females, with a mean age of 47.3 ± 14.0 years. In 87% of cases, the position of the conus medullaris was between the lower-third of T12 and the L1-L2 intervertebral disk. Age significantly influenced this position (p = 0.0027). The level of the thecal sac was mainly (91%) located between the middle-third of S1 and the lower-third of S2. The mean thickness of the conus medullaris was 7.3 ± 0.8 mm. The mean depth of the vertebral canal was 77.9 ± 20.2 mm. It was greater than 100 mm in 9.1% of cases and correlated with the thickness of sub cutaneous fat (r = 0.67).

Conclusion
The position of the conus medullaris and the dural sac of black African subjects are comparable to that of Caucasians. In 9,1% of cases the vertebral canal depth is greater than the length of common needles used for lumbar puncture.

INTRODUCTION

La ponction lombaire (PL) est un acte médical largement pratiqué, car elle seule permet de recueillir du liquide céphalospinal (LCS) pour toute analyse lors des différentes pathologies du système nerveux central. C'est aussi un temps essentiel de la myélographie opaque, de la sacco-radiculographie et du myélo-scanner. Cet acte est cependant susceptible de léser le cône médullaire, et peut donc donner lieu à des pathologies de mauvais pronostic, notamment une atteinte irréversible des centres réflexes de la fonction sphinctérienne. La connaissance de la localisation de la terminaison du cône médullaire est donc indispensable pour éviter toute lésion de celui-ci lors d'une ponction lombaire, d'une chirurgie ou d'une radiothérapie de la région lombaire.

Chez le sujet caucasien, le cône terminal est le plus souvent situé en regard du bord inférieur de L1 (12, 9, 6, 3). Des variations potentielles liées à l'âge (5, 11), au sexe (7, 3, 11), à la morphologie et éventuellement à la race (7) ont été évoquées. En 1935, Needles et al concluaient au terme d'une étude par autopsies que la terminaison du cône médullaire était située plus bas pour les Noirs américains comparativement aux Blancs américains (7). L'Imagerie par Résonnance Magnétique (IRM) permet chez le sujet vivant une étude fiable de la moelle épinière, sans traumatisme et sans irradiation; de nombreux auteurs l'ont déjà appliquée à l'étude du cône médullaire (13, 9, 6, 3, 5, 11, 10, 8). Tous ces travaux ont été réalisés sur des sujets caucasiens et leurs conclusions ne peuvent pas à priori être transposées aux populations Noires africaines. Nous avons entrepris une étude dont l'objectif était de déterminer la taille et le niveau de la terminaison du cône médullaire et du sac dural des adultes Noirs africains à partir des coupes IRM du rachis lombaires réalisées au Centre Hospitalier Universitaire de Yaoundé (CHUY). Le but de cette étude étant d'améliorer la connaissance de l'anatomie du cône médullaire des sujets Noirs africains; afin de contribuer à réduire les risques d'accidents et incidents traumatiques du cône médullaire liés à la ponction lombaire.

MÉTHODES

Patients

De façon consécutive, les images des patients ayant passé une IRM du rachis lombaire au CHUY de juin 2008 à juillet 2011 ont été systématiquement examinées. Les examens d'IRM étaient demandés par les médecins traitants pour les indications suivantes : lombalgies, lombosciatalgie, troubles sensitifs et/ou

moteurs des membres inférieurs. Quatorze patients ont été exclus pour une tumeur rachidienne ou médullaire (04), une anomalie de hauteur des disques ou des corps vertébraux (06), un trouble significatif de la statique rachidienne (03) ou antécédent de chirurgie du rachis (01). Finalement, 77 sujets noirs africains ont été retenus pour l'étude de la terminaison et de l'épaisseur du cône médullaire, ainsi que de la profondeur moyenne du sac dural et de l'épaisseur de la graisse sous cutanée lombaire.

Technique

Tous les examens étaient réalisés sur un appareil IRM de 0,2 T (Signa Profile Excite, Lightspeed VCT, GE Healthcare). Les protocoles utilisés étaient les suivants : coupes sagittales en séquences pondérées T1 spin écho (TR/TE 500/18 ; 4 mm d'épaisseur, 5 mm d'intervalle, FOV 280 x 280 mm) et T2 spin écho (TR/TE 4240/114 ; 4 mm d'épaisseur, 5 mm d'intervalle, FOV 350 x 350 mm).

Conformément à la méthode utilisée dans des études antérieures, la terminaison du cône médullaire ou du sac dural était déterminé en référence au segment vertébral adjacent. Chaque vertèbre était divisée en trois (tiers supérieur, moyen, inférieur) et les disques intervertébraux étaient considérés sur toute leur hauteur comme un segment à part entière (9, 3, 5, 11, 2, 10, 8, 4). Chaque segment obtenu était numéroté pour faciliter l'analyse statistique (tiers supérieur de T12 = 1 ; disque L1L2 = 8 ; tiers moyen de S2 = 30). (Figure 1)

L'épaisseur maximale du cône médullaire était mesurée dans un plan antéropostérieur sur une coupe sagittale médiane du rachis lombaire en pondération T2 (Figure 2).

La profondeur du canal vertébral était mesurée sur une coupe sagittale médiane du rachis lombaire en pondération T1, sur une ligne droite allant de la surface cutanée au centre du canal vertébral en passant entre les apophyses épineuses de L4 et L5 ; cette ligne étant considérée comme le trajet idéal à suivre lors d'une ponction lombaire (Figure 3). L'épaisseur de la graisse sous cutanée (apparaissant en hypersignal) était mesurée sur cette même ligne (Figure 4).

Collecte des données et analyse statistique

Toutes les mesures et interprétations étaient effectuées par les deux premiers auteurs. Le consensus était obtenu pour toutes les variables retenues.

Les données étaient collectées et analysées grâce aux logiciels Epi info 3.5.1.0 et Epidata 2.2.1.171.

Les tests de Mann Withney/Wilcoxon et ANOVA ainsi que la régression linéaire, étaient utilisés pour rechercher la corrélation entre les variables mesurées et l'âge ou le sexe. Toute différence était jugée statistiquement significative pour une valeur de $p < 0.05$.

RÉSULTATS

Des 91 sujets éligibles, 77 ont été retenus (84,61%) pour cette étude parmi lesquels on comptait 39 hommes (50,6 %), soit un sex-ratio de 1,02 H/F. L'âge moyen était de 47,29 ± 14,03 ans (hommes : 48,97 ± 14,66 ans ; femmes : 45,57 ± 13,33 ans) avec des extrêmes allant de 16 à 82 ans.

Dans notre échantillon, le cône médullaire se terminait entre le tiers inférieur de T12 (2,6 %) et le tiers inférieur de L2 (1,3 %) soit en moyenne au tiers moyen de L1 (Figure 5). Dans 87% des cas (67 cas/77), la terminaison du cône se situait entre le tiers inférieur de T12 et le disque L1L2. Il n'y avait pas de différence statistiquement significative du niveau de cette terminaison entre les hommes et les femmes ($p = 0,9727$). L'âge avait un effet statistiquement significatif sur la terminaison du cône médullaire ($p = 0,0027$; $r2 = 0,17$) qui se situait dans 33,3 % des cas au tiers moyen de L1 pour les sujets de moins de 20 ans et dans 22,1 % des cas au tiers inférieur de L2 pour les patients de plus de 70 ans.

Le sac dural se terminait entre le disque L5-S1 (1,3 %) et le tiers moyen de S3 (1,3 %), soit en moyenne au tiers supérieur de S2 (Figure 6). Pour 91% de nos patients, cette terminaison se trouvait entre le tiers moyen de S1 et le tiers inférieur de S2. Il n'y avait pas de différence statistiquement significative du niveau de la

terminaison du sac dural entre les hommes et les femmes (p = 0,5118). L'âge n'avait pas d'effet statistiquement significatif sur la terminaison du sac dural (p = 0,7655 ; r2 = 0,00).

L'épaisseur du cône médullaire variait de 5,8 à 9,6 mm avec une moyenne de 7,3 ± 0,80 mm. Cette épaisseur n'était influencée ni par le sexe (p = 0,1558) ni par l'âge (p = 0,3390 ; r2 = 0,01).

La profondeur du canal médullaire variait de 11 à 133 mm avec une moyenne de 77,87 ± 20,18 mm. Elle était supérieure à 100 mm pour 09,1 % (7 cas / 77) des patients dans notre échantillon. L'épaisseur de la graisse sous cutanée, mesurée sur le même trajet variait de 3 à 83 mm avec une moyenne de 31,75 ± 17,56 mm. Il y avait une corrélation linéaire entre la profondeur du canal vertébral et l'épaisseur de la graisse sous cutanée lombaire (r2 = 0,67).

DISCUSSION

Dans ce travail, nous avons cherché à déterminer la taille et le niveau de la terminaison du cône médullaire et du sac dural dans un échantillon de 77 adultes noirs africains ayant effectué une IRM au CHU de Yaoundé. Nos résultats sont dans l'ensemble conformes aux données de la littérature (tableau III).

Ainsi, dans notre échantillon, la terminaison du cône médullaire se situe entre T12 (tiers inférieur) et L2 (tiers inférieur), avec une moyenne au tiers moyen de L1. Toutefois, dans la seule étude menée sur une population entièrement noire africaine comme la nôtre, Gatonga et al. (4) avaient trouvé une terminaison moyenne au tiers supérieur de L2. Cette variation pourrait s'expliquer par les différences méthodologiques entre les deux travaux. Gatonga et al. ont étudié par autopsies 112 cadavres comportant majoritairement des hommes (sex ratio 2,05H/1F), tandis que notre étude portait sur 77 patients vivants avec quasiment autant de femmes que d'hommes (1,02H/1F). Même s'il n'y avait pas de corrélation entre le sexe et la terminaison du cône médullaire dans nos deux études, d'autres auteurs travaillant sur des échantillons plus larges avaient trouvé qu'elle se situait plus bas pour la femme que pour l'homme (7, 3, 11).

Dans notre échantillon, la terminaison du cône médullaire était d'autant plus bas située que l'âge était avancé (p = 0,0027 ; r2 = 0.17) ; ceci confirme les résultats obtenus par Kim et Soleiman (11). La dégénérescence arthrosique progressive des vertèbres et des disques intervertébraux avec l'âge pourrait expliquer une modification de la terminaison du cône médullaire lors du vieillissement. Une étude portant sur des sujets âgés comparativement à des sujets jeunes et sains est nécessaire pour le vérifier.

La terminaison du sac dural est comparable dans notre étude à celle retrouvée par d'autres (6, 11, 2). Seul Mac Donald avait trouvé une corrélation entre cette terminaison et le sexe (6) mais dans son échantillon, la distribution n'était pas normale et la segmentation vertébrale adoptée intégrait les disques intervertébraux comme faisant partie des vertèbres.

Connaitre la profondeur moyenne du canal vertébral est important dans l'attitude du clinicien qui réalise une ponction lombaire car une insertion trop profonde de l'aiguille pourrait entrainer des dommages tandis qu'une insertion insuffisante obligerait à reprendre le geste causant des douleurs supplémentaires au patient. Certaines aiguilles à ponction lombaire disponibles sur le marché ne dépassent pas 100 mm de longueur alors que 09,1 % de nos patients avaient une profondeur du canal supérieure à ce seuil ; ceci pourrait expliquer certains échecs de ponction. Cette profondeur est fortement influencée par l'épaisseur de la graisse sous cutanée (r2 = 0.67). On pourrait envisager que la flexion du dos de même que la pression au point de ponction telles qu'obtenues en pratique courante lors de la réalisation de la ponction lombaire puissent entraîner une réduction de l'épaisseur de la graisse sous cutanée et raccourcir le trajet de l'aiguille à ponction. Il a déjà été démontré que la flexion du rachis ne faisait pas varier la position du cône médullaire (1); mais son effet sur la profondeur du canal vertébral reste à rechercher. Il serait par ailleurs intéressant d'explorer le lien éventuel entre l'épaisseur de la graisse sous cutanée et la taille ou l'indice de masse corporelle des patients dans une autre étude.

L'épaisseur du cône médullaire dans la population mérite d'être connue, car elle peut servir de référence objective pour évaluer ses variations pathologiques (épaississement tumoral ou sclérose post radique par exemple), rechercher des variantes anatomiques et mettre en évidence des différences avec d'autres populations.

La petite taille de notre échantillon (77 patients) est due au fait que l'IRM reste une technologie nouvelle et assez méconnue des patients et même des cliniciens dans notre pays. En outre, elle est onéreuse par rapport aux revenus de la population (100 000 FCFA ou 150 euros au moins) et reste hors de portée de la majorité des patients.

Notre étude est donc préliminaire et nécessite d'être poursuivie avec un échantillon plus large.

CONCLUSION

Les terminaisons du cône médullaire et du sac dural se situent dans notre échantillon au tiers moyen de L1 et au tiers supérieur de S2 respectivement et ne semblent pas différer de celles des sujets caucasiens.

La profondeur moyenne du canal vertébral est de 77,87 ± 20,18 mm et elle est d'autant plus élevée que la couche graisseuse sous cutanée à l'étage lombaire est épaisse. L'épaisseur moyenne du cône médullaire dans notre population est de 7,3 ± 0,80 mm.

La présente étude devra être poursuivie sur un échantillon plus large et plus représentatif afin d'en renforcer la puissance.

REMERCIEMENTS
Au Docteur MOIFO Boniface, pour lecture et corrections.

FIGURES

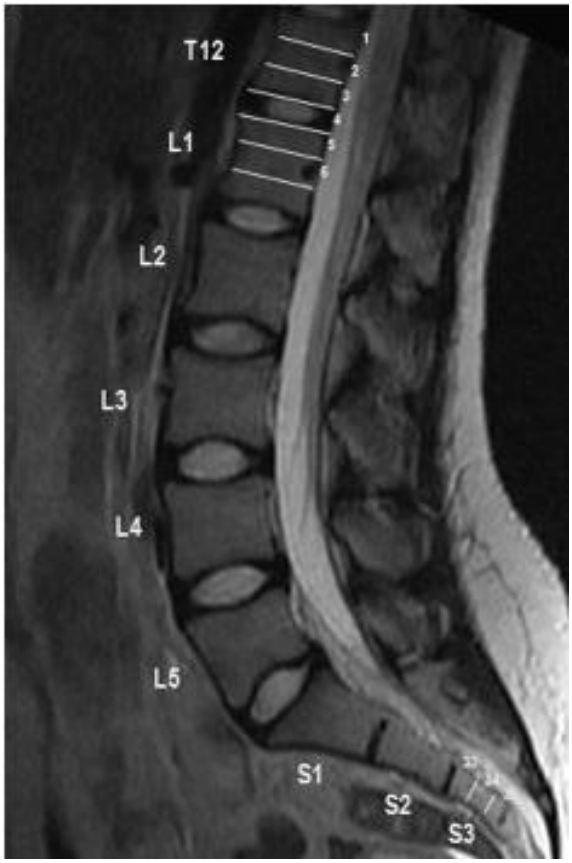

Figure 1 : segmentation du rachis en vue de l'analyse statistique.

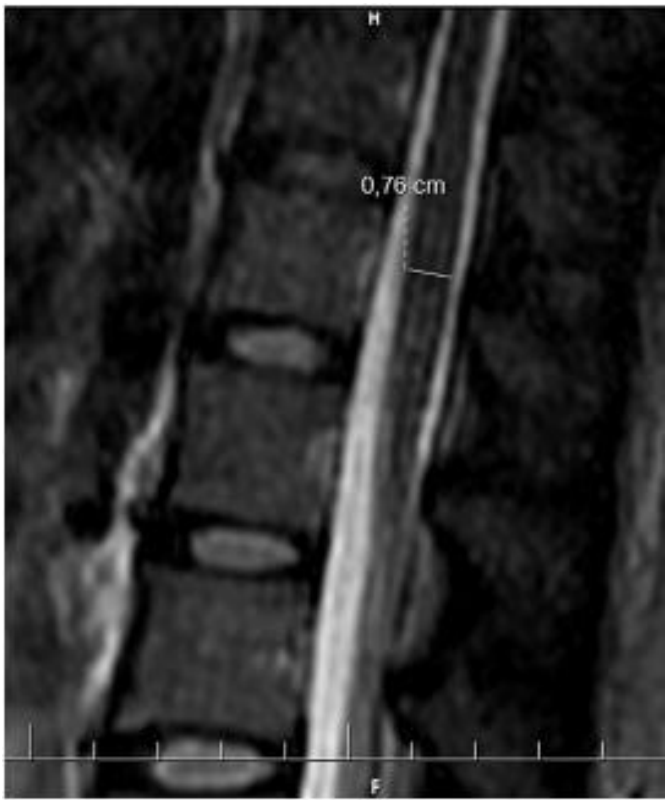

Figure 2: mesure de l'épaisseur maximale du cône médullaire sur une coupe sagittale médiane du rachis lombaire en pondération T2.

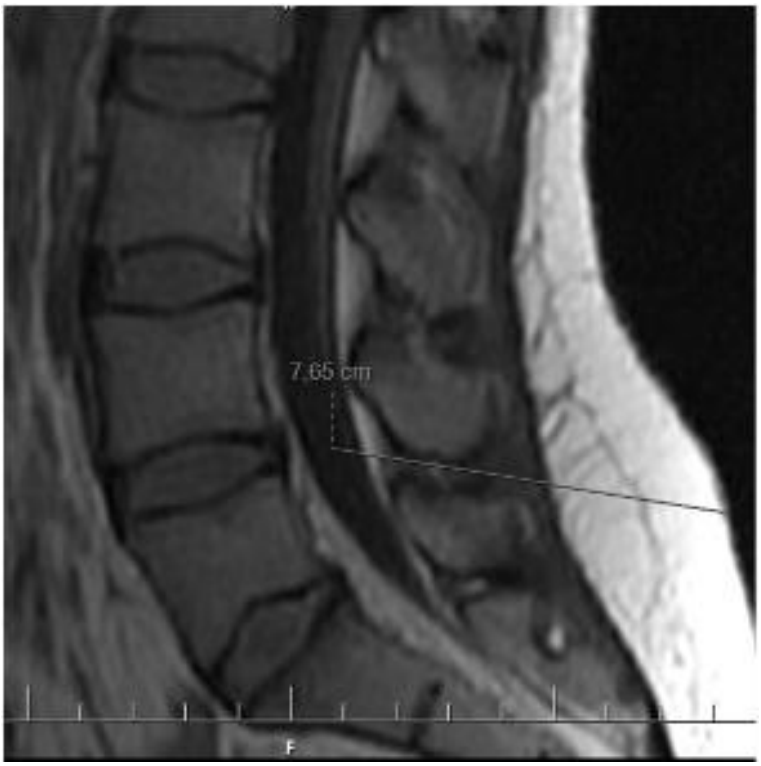

Figure 3: mesure de la profondeur du canal vertébral sur une coupe sagittale médiane du rachis lombaire en pondération T1.

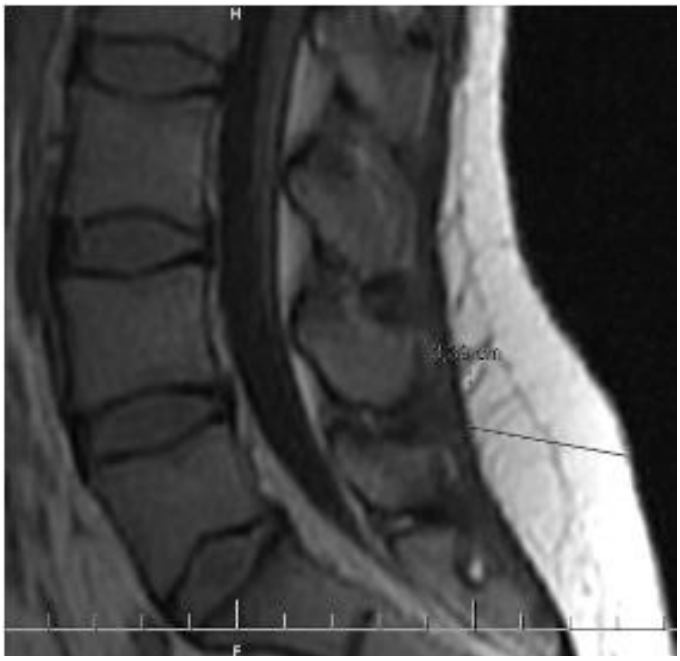

Figure 4: mesure de l'épaisseur de la graisse sous-cutanée lombaire sur une coupe sagittale médiane du rachis lombaire en pondération T1.

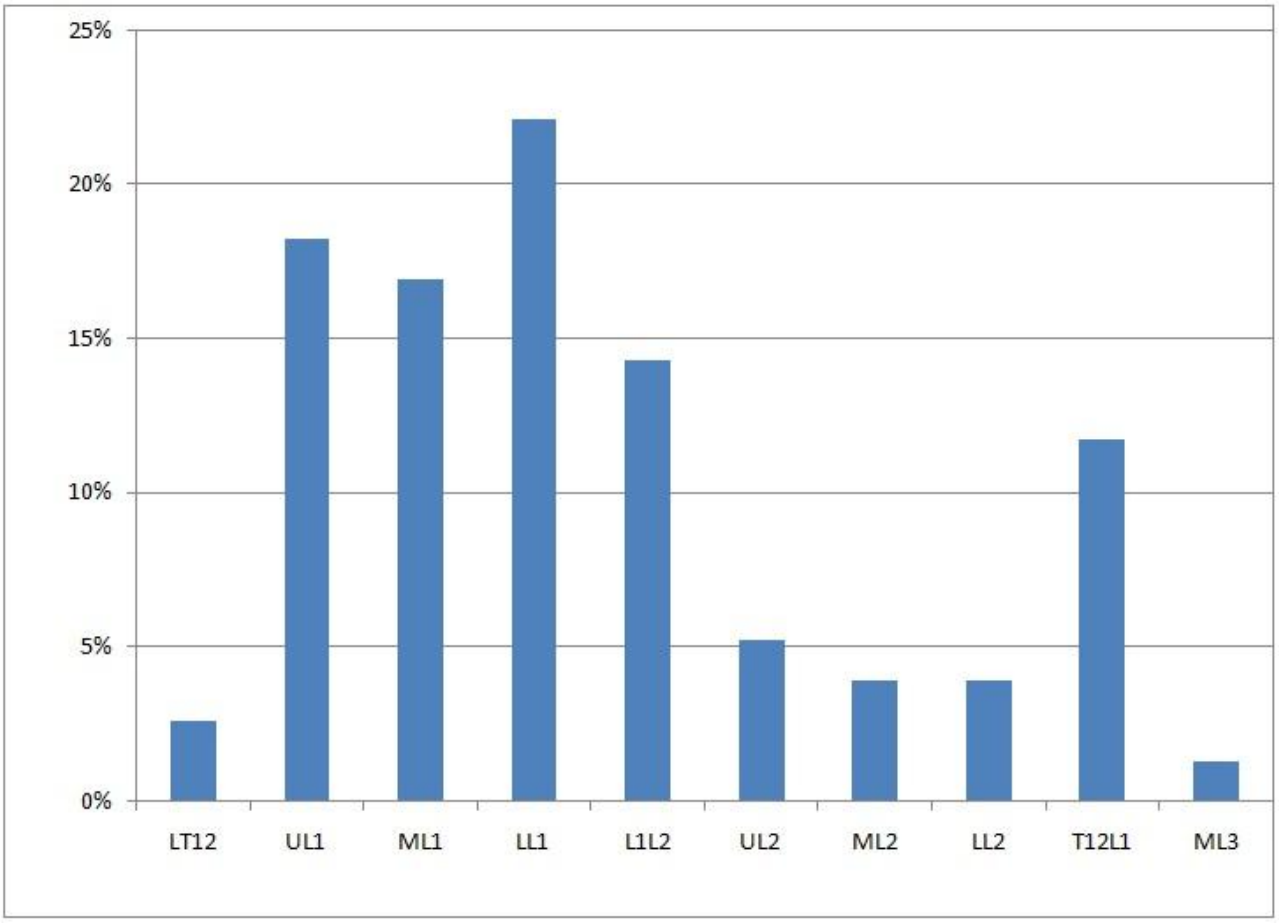

Figure 5 : distribution du siège de la terminaison du cône médullaire.
U : upper = tiers supérieur.
M : middle = tiers moyen.
L : lower = tiers inférieur.

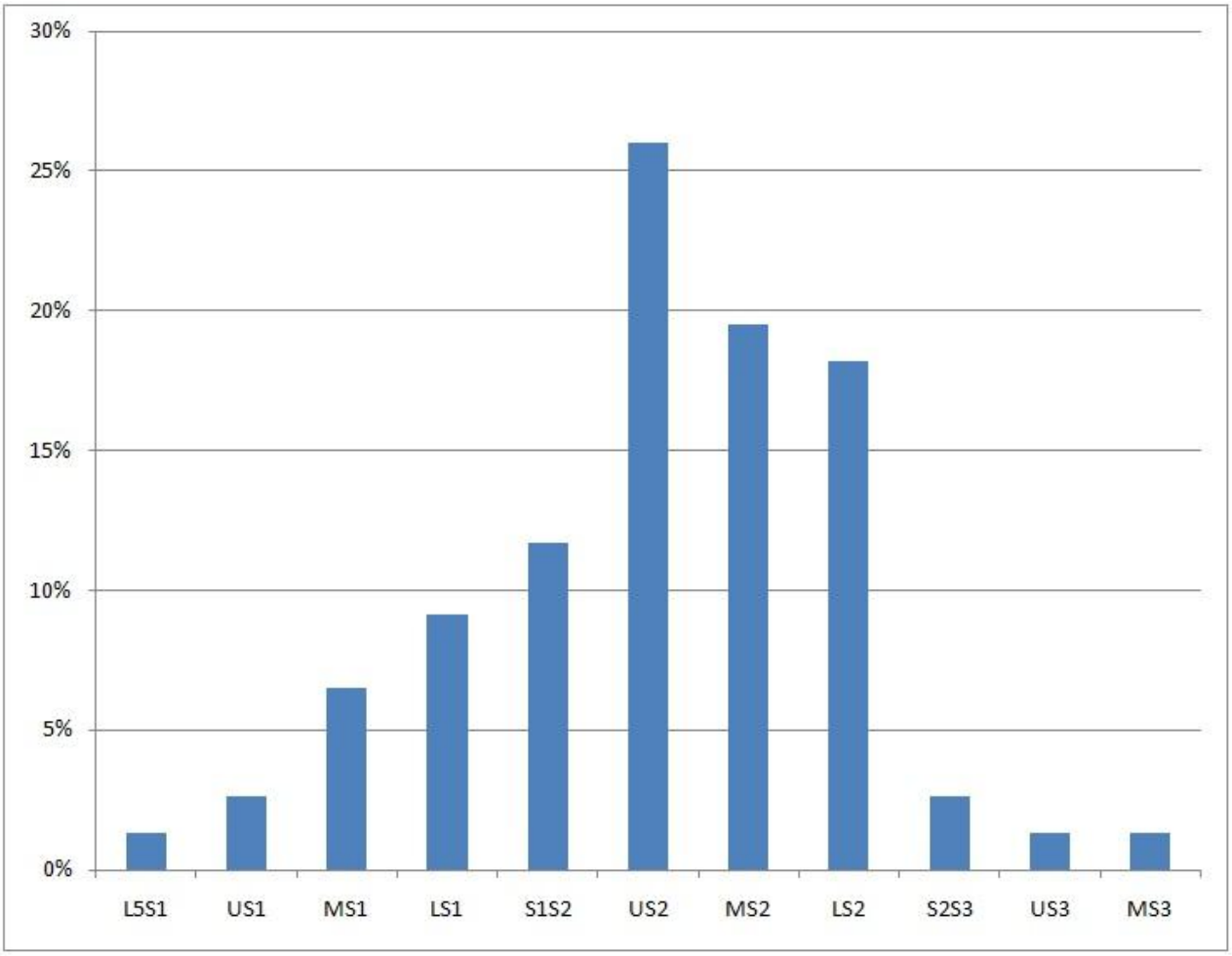

Figure 6: distribution du siège de la terminaison du sac dural.
U : upper = tiers supérieur.
M : middle = tiers moyen.
L : lower = tiers inférieur.

TABLEAUX

Tableau I : répartition de la terminaison du cône médullaire

Terminaison du Cône	Femmes	Hommes	TOTAL	
			Nb	%
T12				
Tiers inférieur	0	2	2	2,6
Disque T12-L1	6	3	9	11,7
L1				
Tiers supérieur	5	9	14	18,2
Tiers moyen	7	6	13	16,9
Tiers inférieur	10	7	17	22,1

Terminaison du Cône	Femmes	Hommes	TOTAL	
Disque L1 - L2	5	6	11	14,3
L2				
Tiers supérieur	1	3	4	5,2
Tiers moyen	2	1	3	3,9
Tiers inférieur	2	1	3	3,9
TOTAL	38	39	77	

Tableau II : répartition de la terminaison du sac dural

Terminaison du sac dural	Femmes	Hommes	TOTAL	
			Nb	%
Disque L5-S1	0	1	1	1,3
S1				
Tiers supérieur	1	1	2	2,6
Tiers moyen	3	2	5	6,5
Tiers inférieur	5	2	7	9,1
Disque S1-S2	4	5	9	11,7
S2				
Tiers supérieur	10	10	20	26
Tiers moyen	8	7	15	19,5
Tiers inférieur	6	8	14	18,2
Disque S2-S3	0	2	2	2,6
S3				
Tiers supérieur	0	1	1	1,3
Tiers moyen	1	0	1	1,3
TOTAL	38	39	77	

Tableau III : terminaisons moyennes du cône médullaire et du sac dural dans la littérature.

Auteurs	Population	Méthode	Terminaison du cône médullaire	Terminaison du sac dural	Facteurs de Corrélations	
					Cône médullaire	Sac dural
Needles,1935	240[196H,44F]	Autopsies	UL2[MT12-LL3]	NE	-	-
Wilson, 1989	100 [63 H, 37 F]	IRM	L1 [T11T12 - L2L3]	NE	-	-
Saifuddin,1997	504[231H,273F]	IRM	LL1[MT12-UL3]	NE	Sexe: pas de corrélation	-
					Age : pas de corrélation	-
Mac Donald, 1999	136 [47 H, 89 F]	IRM	ML1* [LT11 - ML3]	MS2*[US1 - US4]	Sexe : pas de corrélation	Sexe : p=0.00261
Demiryurek, 2002	639 [296 H, 343 F]	IRM	T12-L1 [T11T12-UL3]	NE	Sexe : p < 0.01	-
					Age : pas de corrélation	-
Jin Tae Kim, 2003	690 [347 H, 343 F]	IRM	LL1 [UT12-UL3]	NE	Age : p < 0.001	-
Soleiman,2005	635[347H,343F]	IRM	ML1[LT11-UL3	US2[LS3-US5]	Sexe: p < 0.006	Sexe: pas de corrélation
					Age: p < 0.001. r=0.13	Age: pas de corrélation
Binokay,2006	682 [282H,400F]	IRM	NE	US2[L5S1-US3]	-	Sexe: pas de corrélation
					-	Age: pas de corrélation
Sevinc,2006	364[157H,207F]	IRM	L1L2[T11T12-L1L3]	-	Sexe: pas de corrélation	-
Rahmani,2009	289[111H,178F]	IRM	UL1[UT12-ML2]	NE	Sexe: pas de corrélation	-
					Age: pas de corrélation	-
Gatonga,2010	112[82H,40F]	Autopsies	UL2[LT12-LL3]	NE	Sexe: pas de corrélation	-
Moulion,2011	**77[39H,38F]**	**IRM**	**ML1[LT12-LL2]**	**US2[L5S1-MS3]**	**Sexe: pas de corrélation**	**Sexe: pas de corrélation**
					Age: p =0,0027 ; r=0.17	**Age: pas de corrélation**

** : médiane. NE : non étudié. U : upper = tiers supérieur. M : middle = tiers moyen. L : lower = tiers inférieur.*

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OBITUARY / NECROLOGIE

Dr DIDIER MUDJIR BALANDA

OKITO Jean-Pierre Kalala [1]

1.

E-Mail Contact - OKITO Jean-Pierre Kalala :

In memoriam Dr Didier Mudjir Balanda

Le 27 septembre 2012, Didier Mudjir Balanda de son nom complet est décédé. Ce triste jour un collègue et un homme de valeurs nous a quitté. La neurochirurgie congolaise et africaine sont endeuillées.

Né le 26 février 1968 à Kinshasa, Didier fait ses études primaires et secondaires à Kinshasa. Il entreprend ensuite des études de médecine à l'Université de Kinshasa où il sort diplômé en 1995. Résident en chirurgie à la Clinique Ngaliema entre 1995 et 2002, il entre en contact avec la neurochirurgie pour laquelle il montre un intérêt et des aptitudes certaines.

Il se marie avec une consœur, le Dr Rose Tambwe. De leur union naissent trois enfants : Amina, Titine, et David. Didier Mudjir est admis en 2002 au CHU de Rabat dans l'Hôpital des Spécialités dans le Service du Professeur Abdelsham El Kamlichi où il suivra une formation complète en neurochirurgie. Pendant cette formation, il bénéficiera de la première bourse africaine de la WFNS (Fédération mondiale des sociétés de neurochirugie) et aura l'occasion de séjourner à Charlottesville en Virgine (USA) En octobre 2007, il reçoit son diplôme et sa certification de neurochirurgien. Il gardera toujours un contact actif et enrichissant avec « la maison », l'Hôpital des Spécialités à Rabat et le Pr El Kamlichi.

En 2007, Didier Mudjir rentre à Kinshasa, exerce à la Clinique Ngaliema et reprend avec succès le service de Neurochirurgie. Etant à l'époque l'un des deux seuls neurochirurgiens pour le pays entier, il est

consultant dans différents centres hospitaliers. Il prend une part active à différents activités de la WFNS, la AFNS et la PAANS.

D'un point de vue humain, le Dr Mudjir Balanda était un homme droit, toujours disponible pour aider son prochain et particulièrement lorsque celui-ci se trouvait être un patient. Didier était très apprécié par ses collègues pour sa gentillesse.

Le microcosme neurochirurgical africain perd un de ses jeunes membres très prometteur. Que sa famille et ses patients trouvent ici nos sincères condoléances et encouragements pour la perte de cet être cher et attachant.

Pr Jean-Pierre Kalala Okito

OBITUARY / NECROLOGIE
Pr. ADEBAYO A. OLUMIDE

Pan African Association of Neurological Sciences (PAANS) [1]

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E-Mail Contact - Pan African Association of Neurological Sciences (PAANS) :

The Pan African Association of Neurological Sciences is sad to inform the passing on of Professor Adebayo A. Olumide who was past president of the PAANS and past second vice president of WFNS.

He died on Friday 19th October 2012.

May his Soul have perfect repose.

INFORMATIONS
PAANS NAIROBI DECEMBER 2012
Pan African Association of Neurological Sciences (PAANS) [1] 1. E-Mail Contact - Pan African Association of Neurological Sciences (PAANS) :

Report of the local organising committee document