

Constraints in the neurosurgical management of pituitary tumours in an African developing country: a 5-year observational study from Benin Republic

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Abstract

Introduction: Benin Republic, a very low-income sub-Saharan African developing country, has a severely resource-constrained health system. There is hardly any data available on the pattern of pituitary tumour in this country

Methods: A single surgeon, hospital-based retrospective analysis of the pattern, presentation and clinical / surgical course of a prospective cohort of pituitary tumours seen over a 5-year period is presented

Results: There were 38 cases, 20 (52.6%) females; 27% of all brain tumours seen. They were macroadenomas in 97. 4%, and greater than 4cm in 63.2%. They occurred mainly (86.8%) in people aged 15 to 59 years. Delayed neurosurgical presentation, mean 5.16years (range 1-23years) was the rule in 94.7% %; and, visual and endocrinological dysfunction the two most prominent symptomatology. Due to severe logistic constraints, neuroimaging evaluation was possible with cranial CT only in about 90% of the cases. Also only 9 cases (23.7%) did eventually receive the planned neurosurgical operative treatment, in 5 cases of which even this surgical treatment was only facilitated by some foreign neurosurgical missions.

Conclusions: Pituitary adenomas represent a sizeable proportion of brain tumours in Benin Republic. National health care resources in this low income African country for their optimal clinical / radiological evaluation, and surgical treatment, are grossly inadequate; indeed, almost non-existent.

Keywords: Pituitary adenomas, hospital management, Benin Republic.

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Introduction

The Republic of Benin is a small, low-income developing country in sub-Saharan West Africa. The country's

population is about 11 million. Her vital economic statistics like the Gross National Income (GNI) qualify her among the low income countries of the world, and are even much less than the sub-Sahara African average in many respects. [1] The health system, is therefore much less than optimal [2]. Hence, majority of the Benin population face several difficulties in their efforts to obtain appropriate medical care. For instance, there is only one established department of neurosurgery located in the country's military hospital, and there are only 6 neurosurgeons in the whole country. These difficult situations lead to delayed neurosurgical consultations and hospitalizations in many instances. As a result, when brain tumours are diagnosed in Benin, the common characteristics are that they are voluminous in size, and are a source of various handicaps at presentation. This phenomenon has also been described to a less severe extent in Nigeria [3, 4].

There is paucity of literature on the epidemiologic features of brain tumours in general, and sellar/pituitary tumours in particular, in Benin. Thus, the major aim of this study is to present the clinical, and, a brief epidemiological characterization of sellar lesions deemed to be pituitary tumours seen in our practice over a time period. We also set out to evaluate local options for clinical and radiological diagnosis, and also the clinical and surgical care for these tumours for the Benin populations. It is hoped that this would lead to the formulation of appropriate multidisciplinary strategies for addressing this much-neglected health issues affecting our rural and local populations, majority of whom are living in poverty.

Materials and method

This series is a retrospective analysis of our neurosurgical / clinical data base. The data were gathered in the Republic of Benin by the principal author (HG) in his neurosurgical practice/referral base spanning several hospital departments and clinics: the Military Hospital, Benin (Departments of Neurosurgery and Ophthalmology); the University Hospital, Cotonou, Benin (Departments of Surgery, Radiology, Endocrinology, Ophthalmology and Psychiatry); and the 'Clinique la Lumiere', a private health facility, Cotonou, Benin.

All the patients were primarily seen by HG or referred for his consultation. All of them were registered consecutively and prospectively in an on-going database which include the patients' socio-demographic information; history and examination records, and copies of their cranial computed

tomography (CT) scanning or magnetic resonance imaging (MRI) when available. This study spanned a period of 5 years from September 2006 to 2011.

All patients received radiological imaging consisting of cranial CT or MRI as the case may be. Only cases in which the lesions primarily originated within the sellar were considered as most likely pituitary tumours. In all CT and MRI scans, the maximal diameter of the lesion was reported in the coronal plane as seen in the post-contrast imaging studies. The main clinical symptomatology of the cases was captured, as well as the findings of additional clinical evaluations like fundoscopy and visual field perimetry. In all patients, endocrinological studies were systematically performed at the appropriate diurnal time periods to document the existence of imbalance in certain hormones like prolactin, cortisol, and adrenocorticotrophic hormone (ACTH).

All patients personally paid in full for their medical and surgical treatment in the Benin's out-of-pocket, privately funded health financing system. Sometimes people in the Benin public civil services are sponsored by the government (through the Ministry of Health) in the expenses related to surgery and hospitalization, when such services are available in public hospitals. All medical/surgical treatments not available in public hospitals have to be paid for directly by the patients or their relations.

Results

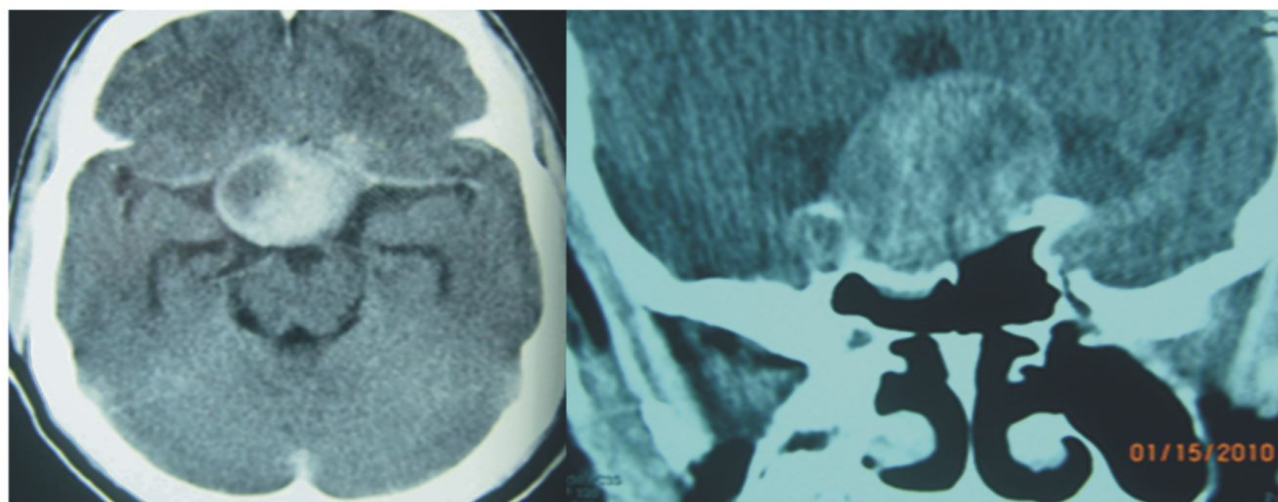
During this 5-year period of study, data from 38 patients presenting with tumours originating within the sellar were collected, as shown in table 1. Only those lesions presumed to be pituitary adenomas were recruited for this study. Other parasellar lesions were not considered as such. During the same period, about 140 brain tumours were managed in the unit, meaning that sellar lesions suggestive of pituitary adenomas accounted for 27.14 % of total brain tumours in our unit. The average age of the patients was 40.9 years (range 2 to 75 years). Pituitary tumours presented mainly (87%) amongst subjects in the prime of life, aged 15 to 59 years, in this study.

Clinical symptoms/Presentation

Before neurosurgical evaluation, majority of the patients (36, 94.73%) had initially presented with various symptoms to several other clinical specialists, including ophthalmologists (57.89%), gynecologists and endocrinologists (26.31%) and psychiatrists (5.26%). The duration of these presentations ranged from 1 to

Table 1: Pituitary tumors in the Republic of Benin: age and gender distribution of the patients

| Years | <20 | 20 - 30 | 30 - 40 | 40 - 50 | 50 - 60 | >60 | Total |
|--------------------|------|---------|---------|---------|---------|------|-------|
| Male | 1 | 3 | 7 | 3 | 3 | 1 | 18 |
| Female | 1 | 2 | 2 | 3 | 11 | 1 | 20 |
| Total | 2 | 5 | 9 | 6 | 14 | 2 | 38 |
| % of total (38) | 5.26 | 13.15 | 23.68 | 15.78 | 36.84 | 5.26 | 100 |

**Fig.1:** Cranial CT scanning, axial slice, and coronal reconstruction demonstrating a typical case of pituitary adenoma in this study.

23 years with an average of 5.16 years. Significant, incapacitating visual disorders (47.35%) were the most frequent symptoms presented. Endocrine disorders followed with 26.31 %, and several syndromes of intracranial hypertension were encountered in 18.42% of cases. Motor deficits (2 cases) and pituitary apoplexy (1 case) were very rare in our series. Six patients (15.78 %) were eventually lost to follow up in the course of this observational study; 15 of the remaining 32 patients (46.87%) experienced worsening of their symptoms while waiting for surgical care. This included blindness in 7 cases (21.87 %); occurrence or worsening of endocrine disorders in 4 (12.5 %); and development of symptoms of intracranial hypertension in 2 (6.25 %) one of which had a psychiatric presentation. In this last case, the patient presented with decline in visual acuity and delirium alternating with episodes of cognitive impairment. Three patients (7.89%) died whilst still being prepared for definitive treatment in the course of this study, respectively, at 7th, 15th and 21th months. All those deaths were associated with clinical evidence of increased intracranial pressure.

Patients and tumour size, figure 1

In our series, majority (96%) of the pituitary adenomas were giant lesions extending well above and beyond the sellar, figure 1. The mean lesion size was 4.9 centimeters, ranging from 0.2 to 10.6 cm. Only one patient (2.63%) presented with a tumour less than 1cm; 24 (63%) actually had lesions greater than 4cm. Tumours larger than 4 cm were likely more frequent in men (13 of 18 cases) than women (11 of 20 cases), table 2. This showed a statistically significant relation between tumour size and the patient's gender, Pearson's $\chi^2 5.14$, $p=0.023$.

Endocrinological and imaging findings

Due to several severe logistic constraints, the various hormonal assessments including the serum prolactin levels in this study subjects could only be performed abroad. Patients' blood specimens had to be sent out of the country to be analyzed. In effect, only 17 patients could perform blood prolactin level test. Ten patients (9 operated cases, 1 waiting for surgery) had a prolactin

Table 2: Pituitary tumors in the Republic of Benin: pattern of tumour sizes in males and females

| Imaging study in 38 cases | | Male= N(%) | Female= N(%) | Total |
|---------------------------|-----|-------------|--------------|-------|
| Type of Exam | MRI | 3 (7.89) | 1 (2.63) | 4 |
| | CT | 15 (39.47) | 19 (50) | 34 |
| Tumour size (cm) | <4 | 5 (13.15) | 9 (23.68) | 14 |
| | >4 | 13 (34.21)* | 11 (28.94) | 24 |

*Pearson's $\chi^2 = 5.14$; $p = 0.023$

Table 3: Pituitary tumors in the Republic of Benin: serum prolactin levels and response to medical treatment in some of the patients.

| Patients | First assessment (ng/ml) | Follow-up (ng/ml) | Remarks |
|----------|--------------------------|-------------------|---------------|
| 1 | 2945 | 107 | Good response |
| 2 | 49.5 | 606.7 | No response |
| 3 | 23.61 | 21 | unchanged |
| 4 | 143 | 28.3 | Good response |
| 5 | 76 | 200 | No Response |
| 6 | 3678 | 47 | Good response |
| 7 | 194 | 27 | Good response |
| 8 | 87 | 52 | Good response |

level ranging from 4.45 to 23.61 ng/ml (laboratory normal ranging from 5 to 35 ng/ml). The 7 remaining had their levels ranging from 49.5 to 3678 ng/ml of measurements. In 6 (85.7%) of these cases of hyperprolactinaemia the tumour was presumed to be prolactinomas because the prolactin blood level was markedly raised, ranging from 231.6 to 3678 ng/ml but no other endocrinological test could be performed to

assess disturbance in the other hypophyseal function, table 3. Only the 2 patients that had their surgical operations abroad, in Europe (France and Italia), received complete endocrinological investigations including serum Cortisol and ACTH. A hypersecretion was noted in both ACTH and cortisol with respect to the circadian rhythm. None of them showed Cushing's symptoms clinically. Only 4 (10.4%) patients had MRI diagnosis of their tumours; cranial CT scanning was used to confirm the diagnosis in most, 34 (89.6 %), of the cases.

Treatment, Medical

Six (85.71%) of the seven patients with confirmed significantly-high-enough levels of serum prolactin for a diagnosis of prolactinoma were kept under bromocriptine, table 3. The duration of this therapy was 21 days to 2 months. In all cases, a decreased level was noted. Good responses were noted in 5 patients (71.42 %), with normalization of prolactin level. In the 2 remaining cases, there was significant fall in the hormonal level. Even given the slightly increased levels (23.61 and 36.78) in two patients, there were apparent clinical symptoms of hypersecretion. These also

Table 4: Pituitary tumors in the Republic of Benin: surgical history of those patients operated

| | Age, sex | Tumor size | Place of surgery | Surgical approach | Follow up |
|---|----------|------------|------------------|-------------------|-------------------------|
| 1 | 18, M | 4.85 | Morocco | Endoscopic | Steroid supplementation |
| 2 | 34, M | 10.64 | Benin | Micro/Trsph* | Recurrence |
| 3 | 38, M | 6.02 | Cot d'Ivoire | Micro/Trsph | Recurrence |
| 4 | 73, F | 2.9 | Benin | Micro/Trsph | Good outcome- |
| 5 | 47, M | 7.39 | Benin | Micro/Trsph | Good outcome |
| 6 | 45, F | | Burkina F | Micro/Trsph | Tum left in Cav. sinus |
| 7 | 42, F | 5.43 | Benin | Crani/Mic** | Death, Meningitis |
| 8 | 65, F | 5.32 | Italy | Endoscopic | Good outcome |
| 9 | 60, F | 3.33 | France | Endoscopic | Good outcome |

*Microscopic transphenoidal resection

** transcranial / microsurgical resection

appeared to have benefitted from bromocryptine substitution.

Treatment, Surgical

Of all the 38 patients with the diagnosis of pituitary tumour in this study, only 9 (23.7%) ultimately received surgical treatment of their lesions. None of the 9 patients selected for surgery however showed high level of prolactin. Even so, 4 of these surgical operations (44.4%) were only via surgical missions by some foreigners. The rest of the patients simply could not afford the cost of care. The 4 patients were operated at home, in Benin Republic, for clinical diagnosis of pituitary tumours as part of an operative charity work. The charity mission was led by the Neurological Hospital of Lyon, and took place in 2006 in the Military Teaching Hospital, with the support of both the Health and Defense Ministries in Cotonou, Benin Republic: 3 cases by transphenoidal approach using operative microscope, and one by open cranial approach because of significant supra sellar extension. The surgical histories of the remaining 5 patients are included in brief in table 4.

Another patient was operated by a similar French operative mission conducted in April, 2011 in Burkina Faso (five years later). Finally, 4 other patients got funding from various non-governmental financial / organizational supports or their own families to procure surgical treatment abroad. This took place in France, Italy, Ivory Coast and Morocco, respectively. There were 2 cases (22.22 %) of tumour recurrence after microscopic transphenoidal approach each in Cotonou and Abidjan. Unfortunately, redo surgery has not been possible, to date, for logistic reasons in these cases.

In all, this means that the majority of Beninese (29 cases, 76.31 %) presenting with pituitary adenoma in this study are still home bound in Benin Republic unable as yet to receive the surgical treatment needed. This is for reasons of lack of equipment and other infrastructural and staff support.

Discussion

Our work reviewed 38 patients presenting with sellar tumours, clinically presumed to be pituitary adenomas among a total of 140 brain tumours during a 5-year period in Benin Republic. This means that these tumours represented 27.14% of brain tumours in this study population. Our findings are higher than those reported by El Mahdi [5] in 1996 in a North African series. Also in Cameroon, 2 cases of gonadotropin secreting adenomas were reported by Nouedoui [6].

In this series adults (94.73 %) have higher incidence of pituitary tumours than children. Similar conclusions were made by Arendt *et al* [7] in whose series, 80.2 % were adults versus 19.8 % children. Mori *et al* [8] reported 87.2 % of adults versus 12.97 % of children. Furthermore, there is only a slight female preponderance, 52.6 %, in this study population. This is in contrast to results of Cottier *et al* [9] for instance which has 81.13 % female versus 18.86 % male differential proportions. And yet another distinct contrast is the report of Mahdi *et al* [5] which had male to female proportions of 55.15 % versus 44.85%. However, the latter also found a higher incidence of the female gender among their study population aged 20 to 40 years.

Visual disorders (47.35%) were the most frequent symptoms in this study subjects, a similar proportion to that of a retrospective study conducted in Nigeria [10] in which visual symptoms were dominant (43%) and visual field defects were present in 47.1% of patients.

The average tumor diameter measured within our patients was 4.9 centimeters, ranging from 0.2 to 10.64 centimeters. In fact, 97.37% were macro adenomas. In a report from Cameroon only 24 of 36 patients had imaging diagnosis of their pituitary tumours; only 4 of these 24 (16.67%) had macroprolactinomas, the rest were microadenomas. [11] In France, Cottier *et al* [9] reported on a series of 21 pituitary adenomas invading the cavernous sinus. Three cases (14.28 %) were micro and 18 (85.71 %) macro adenomas. On the other hand, in Canada, Kucharczyk *et al* [12] reported 13 cases (72.22 %) of micro adenomas in a series of 18 patients. And in the United States of America, Li-Ng *et al* [13] underlined an average of only 35 % macro adenomas among the pituitary tumors reported. These results from literature therefore show the stark reality of the preponderance of macro-adenomas in our study; and may explain the inherent challenges to be expected in the peculiar character of the pituitary adenomas collected in Benin Republic.

In our series, the clinical diagnosis of pituitary tumours was established by the CT scan in about 90% and by the MRI in only about 10 % of the cases. As already underlined by other workers, [14, 15, 16] CT scan and MRI remain the practical modalities of diagnosis of pituitary adenomas in the current era. Both investigations are either expensive or unavailable in Benin Republic. These account for the usual difficulties of diagnosis of intracranial lesions in this region; lead to delayed medical care, and thus to severe morbidity

related to the clinical presentation of pituitary adenomas. In our series, this delay in diagnosis ranged from 1 to 23 years with an average of 5.16 years. Hence many of the patients presented with major handicaps with 39.47 % of them with symptoms running from total blindness to cognitive impairment.

Of the 7 patients with laboratory evidence of hyperprolactinaemia, 6 (85.71%) showed markedly high blood levels of prolactin. This may suggest a possible high prevalence of prolactinoma in Benin. The preponderance of prolactin adenoma was also reported by Cottier (47.61%) on a series of 21 hormonally active adenoma patients [9]. Davis *et al* (1987) reported 64 % in their own series with an average serum prolactin level of 817ng /ml; 8 % also displayed an ACTH blood level higher than 600ng /ml [14].

There are some limitations that deserve mentioning in this report. Diagnosis of these sellar tumours as pituitary adenomas could be histologically confirmed in only the 9 patients that were eventually operated. Perhaps some of the other sellar lesions were not pituitary tumours histogenetically. This might explain the unusually high frequency of pituitary tumors constituting 27.14% of intracranial tumours reported in this study. Further, hormonal characterization of these lesions was also grossly inadequate as a result of the severe logistic challenges of our practice environment. Indeed, this was the same reason, severe logistic (support personnel and infrastructural) constraints, that operative intervention for these sellar lesions could not be performed for these patients at home in Benin Republic.

All said this report shows that only 9 of a total of 38 patients diagnosed with possible pituitary adenomas eventually received the desired operative treatment in this series: 5 by foreign missions, 4 others in surrounding African countries or Europe. The 29 remaining patients (76.31 %) are still in expectation of surgical care. Here then is another demonstration of the stark reality of the significant global inequalities in access to critical health care needs in the current era.

Conclusion

This work shows the hospital frequency of pituitary adenomas in a cohort of patients from Benin Republic. It specifies problems regarding delayed diagnostic and therapeutic issues leading to voluminous tumors. Pituitary adenomas represent a sizeable proportion of brain tumors in Benin Republic. National health care resources in this low income African country for their

optimal clinical / radiological evaluation, and surgical treatment, are grossly inadequate; indeed, almost non-existent. There is a crying need for improving the nation's health care delivery in general, and the neurosurgical service in particular [4].

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