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Prolactin Adenomas in Senegal: Epidemiological, Diagnostic and Therapeutic Aspects of 89 Cases

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Abstract

Introduction: In Senegal, there is very little data on prolactinomas despite their negative impact on couples fertility. **Patients and methods:** This was a multicentre, retrospective, descriptive, analytical study conducted from 1 January 2008 to 31 December 2022 in the neurosurgery departments of the Fann and Principal hospitals and the endocrinology department of the Abass Ndao Hospital. **Results:** We included 89 patients, representing a prevalence of 36.7% among all cases of pituitary adenoma. The mean age was 35.6 ± 10 years and the sex ratio was 0.34. The mean time to consultation was 27.1 ± 29 months. Clinical symptoms were dominated by gonadotropic disorders represented by galactorrhoea (71 cases, 79.8%), amenorrhoea (61 cases, 68.5%), and infertility in the couple (31 cases, 34.8%). Fifty-seven (58) patients presented with a tumour syndrome (65.2%, including 57 cases of headache (64%), 34 cases of visual disorders (38.2%) and 8 patients with a dysmorphic syndrome (8.9%). Imaging revealed a macroadenoma in 68.5% (61 cases) and extension of the adenoma in 11 patients (12.4%). The hormonal profile was isolated lactotropic hypersecretion (80 cases, 89.9%) and mixed in 9 cases (including concomitant secretion of GH in 8 cases and ACTH in 1 case). All patients had initially benefited from dopaminergic agonist-based medical treatment. Pituitary surgery was effective in 45 patients (50.6%), including 44 cases by transsphenoidal approach. Postoperative incidents included transient diabetes insipidus (77.7%) and cerebrospinal fluid leakage (20%). We noted 7 cases (7.9%) of death presenting with a tumour syndrome (100%), a macro-adenoma (85.7%), having undergone pituitary surgery (42.9%). The factors significantly associated with prolactinoma were young age ($p < 0.001$), female sex ($p < 0.001$), long delay

in consultation ($p < 0.001$) and a microadenoma ($p < 0.001$). **Conclusion**: This series also demonstrates the impact of prolactin adenomas on reproductive function. Delayed diagnosis explains the predominance of macroadenomas, which are a source of pre- and post-operative complications.

Keywords

Prolactinoma, Fertility Disorders, Tumour Syndrome, Pituitary Adenomas

1. Introduction

Pituitary prolactin adenomas are benign tumours caused by the proliferation of lactotropic cells of the anterior pituitary gland [1]. They account for 60% of pituitary adenomas and 40% - 75% of secreting adenomas, but account for only 15% of causes of elevatedprolactin [2]. Theyaccount for 10% to 25% of intracranial tumours, with an incidence of 2 to 5 new cases/100,000 and an estimated prevalence of more than 300 cases per million. Diagnosis is generally made between the ages of 20 and 50 [3] [4]. Dopamine agonists remain the reference medical treatment, with efficacy of around 90% in terms of both tumour volume and secretory syndrome [4]. In Sub-Saharan Africa, particularly in Senegal, studies of pituitary adenomas were mostly limited to general aspects of pituitary adenomatous pathology. In the case of prolactinoma, the last Senegalese series dates back to 1989 and reported 7 observations [5]. To better illustrate this entity among pituitary adenomas, the aim was to study the epidemiological, clinical and therapeutic profile of prolactinomas in Senegal.

2. Patients and Methods

This was a multicentre, retrospective, descriptive, analytical study conducted from 1 January 2008 to 31 December 2022, *i.e.* 14 years. The study setting was the neurosurgery departments of the Fann National University Hospital and the Dakar Principal Hospital, and the endocrinology department of the Abass Ndao Hospital. Our study focused on patients with pituitary prolactin adenoma confirmed on clinical, morphological and biological data and followed up in the different departments. We excluded all cases with incomplete investigations. The data were collected using a data processing form filled in on the basis of a complete clinical examination (direct questioning by telephone if necessary) and completed from the patients' files in the archives of the neurosurgery and endocrinology departments. A data sheet was established to collect the essential data for our study from each patient. The sample size was calculated by the Schwartz formula. We carried out an overall analysis of the various epidemiological, clinical and diagnostic aspects, as well as the therapeutic and evolutionary modalities within our study population. The items chosen for the questionnaire were based on the specific and non-specific clinical manifestations of prolactinomas, the

hormonal profile and the various morphological aspects of the pituitary gland. Other investigations were carried out according to the profile. Post-operative evaluation was based on clinical examination (looking for visual signs, carotid wound, epistaxis, empty sella turcica syndrome, cerebrospinal fluid leakage, transient diabetes insipidus, post-operative pituitary insufficiency, secondary hyponatremia), prolactin dosage and tumour size on imaging. The data entry mask and statistical analysis were carried out using Microsoft Excel software. Thus, qualitative variables were described by frequency tables, bar charts, and pie charts. Quantitative variables were described by their positional (mean, median and mode) and dispersion (standard deviation, extremes) parameters.

All data provided in this study are anonymous. The work was carried out with respect to confidentiality.

Patients consent was sought for the taking and use of personal images.

3. Results

3.1. Epidemiological Data

During the study period, 89 patients met the inclusion criteria, representing a prevalence of 36.7% among all cases of pituitary adenoma. Our study included 66 (74.1%) women, giving a sex ratio (M/F) of 0.34. The mean age of our patients was 35.6 ± 10 years, with extremes of 17 and 60 years. We found 2 cases of diabetes mellitus (2.3%), all carrying a mixed adenoma (GH + Prolactin). Hypertensive subjects accounted for 7.9% (7 cases, including 5 patients with a prolactinoma and 2 patients with a mixed adenoma).

3.2. Clinical Data

The mean delay of consultation was 27.1 ± 29 months, with extremes of 1 and 250 months. Clinical symptoms were dominated by gonadotropic disorders, which were present in all patients (100%). These included galactorrhoea in 71 patients (79.8%), menstrual cycle disorders such as amenorrhoea in 61 patients (68.5%), spaniomenorrhoea in 5 patients (5.6%) and infertility in 31 patients (34.8%). Fifty-seven (58) patients presented with a tumour syndrome (65.2%). Among them, we noted 57 cases of headache (64%), 1 case of pituitary apoplexy (0.11%), 32 cases of visual acuity disorders (36%) and 11 cases of visual field disorders (12.4%). A dysmorphic syndrome was found in 6 patients (6.7%). **Table 1** shows the distribution according to epidemiological and clinical data.

3.3. Biological Data

Among the 89 patients, hormonal investigations were in favour of isolated hyperprolactinaemia in 80 patients (89.9%). Nine (9) patients (10.1%) had mixed hypersecretion, including concomitant hypersecretion of growth hormone (GH) in 8 cases and ACTH in 01 patient (**Table 2**). We found no signs of associated hormonal hypersecretion in favour of an anteropituitary insufficiency syndrome.

Table 1. Distribution of patients according to epidemiological and clinical data.

Parameters studied	Results
Epidemiological data	
Mean age	35.6 ± 10 ans
Sex ratio	0.34
Clinical data	
Mean delay of consultation	27.1 ± 29 mois
Tumour syndrom	58 (65.2%)
Headache	57 (64%)
Visual acuity disorders	32 (36%)
Visual field disorders	11 (12.4%)
Pituitary apoplexy	1 (0.11%)
Gonadotrophic syndrom	88 (100%)
Galactorrhoea	71 (79.8%)
Amenorrhoea	61 (68.5%)
Spaniomenorrhoea	5 (5.6%)
Infertility in the couple	30 (34.8%)
Dysmorphic syndrom	6 (6.7%)

Table 2. Distribution of patients according of the hormonal and morphological profile.

Hormonology	Cases	(%)
Hormonal profile		
Isolated hyperprolactinemia	80	89.9%
Mixed hypersecretion (GH + Prolactine)	8	8.9%
Mixtes hypersecretion (ACTH + Prolactine)	1	1.2%
Morphological profile		
Macroadenoma	61	68.5%
Microadenoma	28	31.5%
Tumour expansion	11	12.4%

3.4. Morphological Data

All patients had undergone pituitary imaging. Thirty-eight patients (42.7%) had undergone computed tomography (CT) and sixty-seven patients (75.3%) magnetic resonance imaging (MRI). Imaging revealed a macroadenoma in 68.5% (61 patients). The adenoma had spread in 11 patients (12.4%). **Table 2** shows the distribution of patients according to hormonal and morphological profile.

3.5. Final Diagnosis

In the end, we found 89 cases of prolactin adenomas, including 80 cases of iso-

lated secretion, 08 cases of mixed secretion associated with acromegaly and 01 case of mixed secretion associated with Cushing's disease. Macroadenomas were found in 68.5% of cases, microadenomas in 31.5% and extensive adenomas in 12.4%. In our series, the factors most significantly associated with prolactinoma were young age ($p < 0.001$), female sex ($p < 0.001$), a long delay in consultation ($p < 0.001$) and a microadenoma ($p < 0.001$).

3.6. Therapeutic and Evolutionary Data

All patients had initially received medical treatment. This was mainly Cabergoline in 79 cases (88.8%) and Bromocriptine in 8 cases (8.9%). Table 3 shows the treatment of the patients. Of our patients, half had undergone surgery, in 45 cases (50.6%). The transsphenoidal approach was the most commonly used (97.8%), in 44 cases, and one patient underwent surgery via the upper approach (2.2%). Immediate post-operative complications included transient diabetes insipidus (35 cases, 77.8%) and cerebrospinal fluid leakage (9 cases, 20%). We noted 7 cases (7.9%) of death. The average age of the patients was 41.2 years. These were patients with 100% tumour syndrome, one case of mixed secretion (GH + prolactin), 6 cases of macroadenomas (85.7%), 03 cases of transsphenoidal surgery and 4 patients who did not undergo surgery. Of the 82 patients still alive, mid-term evaluation was carried out in terms of hormones in 70 patients (85.4%), morphology in 63 patients (76.8%) and ophthalmology in 82 patients (100%). Hormone secretion had normalised in 64 cases (78%). Imaging revealed no pituitary adenoma in 49 patients (59.8%). Of these, only 17 patients had undergone pituitary surgery. In terms of ophthalmology, an improvement in visual acuity was noted in 72 patients (87.8%).

4. Discussion

4.1. Epidemiological Data

This was a study of 89 cases of prolactinoma collected over 14 years, with a prevalence of 36.7%. Several studies have reported a predominance of prolactinomas among pituitary adenomas [2] [3] [6] [7] [8] [9] [10]. The prevalence was 56.26% in Cameroon [11] and 69.5% in Côte d'Ivoire [12]. Our figures for the

Table 3. Distribution of patients according to treatment data.

Treatment received	Case	Percentage
Medical treatment	**89**	**100%**
Cabergoline 0.5 mg 1 cp/semaine	79	88.8%
Bromocriptine 2.5 ng 1 cp/jour	8	8.9%
Quinagolide 50 µg/jour	2	2.3%
Surgical treatment	**45**	**50.6%**
By transsphenoïdal route	44	97.8%
By the upper route	1	2.2%

mean age of onset of the disease are close to the third decade reported in Pakistan [13] and Africa [14] respectively. As already widely illustrated by scientific data [13] [14], the female sex was more representative in our series. This predominance was high, approaching 70% in most series [15] [16]. This female predominance is thought to be due to hormonal fluctuations. Indeed, it has been shown that oestrogen is involved in the development of prolactinomas [17] [18]. These results further indicate that prolactin adenomas are particularly common in young women.

4.2. Clinical Data

In our study, the symptomatology was dominated by the amenorrhoea-galactorrhoea syndrome. This syndrome appears to be the main reason for discovery. It has been reported to be between 60% and 80% in studies carried out in France [19]. The proportion of tumour syndrome is partly explained by the high frequency of macroadenomas. However, macroadenomas appear to be more frequent in males [20]. These macroadenomas partly reflect a delay in consultation. In fact, the literature agrees on an average delay of 18 months in diagnosis in subjects with prolactinomas [1] [2] [11] [14]. In 2010, Fernandez *et al.* [2] reported that the delay in diagnosis was more pronounced in males because of the long insidious nature of the symptoms. In our study, all cases of microadenoma were found in women. In addition, the factors most significantly associated with prolactinoma were young age ($p < 0.001$), female sex ($p < 0.001$), a long delay in consultation ($p < 0.001$) and a microadenoma ($p < 0.001$). However and according to Nishioka *et al.* [21] in Japan, the high proportion of macroadenomas was rather related to a high rate of cells with high proliferativé activity.

4.3. Treatment

As in our study, Kars *et al.* [22] in the Netherlands initially treated all their patients with dopamine antagonists. Of these, 35% required additional surgical treatment, after an average duration of 1.2 years [22]. Cabergoline remains the first-line drug [14] [23]. However, surgery is sometimes essential [14] [22] [23]. Consequently, management requires a personalised, multidisciplinary approach, taking into account each patient's individual state of health and response to previous treatment. Under medical treatment with dopaminergic agonists, our results are similar to those of Irfan *et al.* [23], who found a normalisation of prolactin levels in 73.2% and a reduction of more than 50% in tumour volume in 45.8% after two years. In the study by Kars *et al.* [22] in the Netherlands, prolactin normalised in 85% of patients and tumour volume was reduced in 35%; in a series evaluating the impact of medical treatment on prolactin macroadenomas, 80% of patients reported normalisation of prolactin, 87% a significant reduction in tumour volume and 68% an improvement in visual field abnormalities [24]. This reduction in tumour volume was close to 80% [25], and even 100% in 12% and 45% of cases [20]. The results of these studies highlight the efficacy of med-

ical treatment with Cabergoline in normalising prolactin and significantly reducing tumour size. In addition, the results of this study highlight the need for long-term monitoring of patients treated for macroprolactinomas in order to detect recurrence, regrowth of the adenoma and other complications associated with treatment. It is important to note that patients of childbearing age have regained their fertility. This recovery of fertility was observed in the majority (81%) of treated patients, contributing to an improvement in their quality of life. The results show that medical treatment not only had a positive impact on patients' health, but also on their ability to start a family. This underlines the importance of appropriate treatment and ongoing medical monitoring in these cases.

4.4. Limit

The limitations of the study were mainly based on the fact that clinical records were sometimes incomplete, requiring additional information to be obtained from patients. In some cases, certain paraclinical examinations requested, such as a follow-up MRI, could not be carried out systematically due to a lack of financial resources.

5. Conclusion

Prolactinomas are the most common pituitary tumours. The gonadotropic and tumour repercussions appear to be high. This series is broadly similar to the characteristics reported in the literature in terms of epidemiological, clinical, paraclinical and therapeutic parameters. The delay in diagnosis explains the predominance of macroadenomas, which are a source of pre- and post-operative complications. They require multidisciplinary management.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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