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Neurosurgical Aspects of Growth Hormone Pituitary Adenomas at Fann Teaching Hospital

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Abstract

Introduction: Somatotropic adenomas are benign pituitary tumors characterized by increased GH and IGF1 levels. This study aims to describe the demographic, therapeutic, clinical, and evolutionary aspects of patients with somatotropic adenoma, along with a review of the literature. **Patients and Method:** This retrospective study was conducted in the neurosurgery department of the Fann National University Hospital Center over six years, from 2016 to 2022, covering 18 cases of acromegaly related to a GH adenoma. Sociodemographic, clinical, paraclinical, therapeutic, and evolutionary parameters were studied. **Results:** The average age was 42.8 years, with a sex ratio of 2, and an average diagnosis time of 5.27 years. Clinical diagnosis was suggested by dysmorphic and tumoral syndromes, then confirmed by biological data and imaging. We found one microadenoma, 11 macroadenomas, and six giant pituitary adenomas. All patients underwent transsphenoidal surgery. Complications were mainly transient diabetes insipidus. Postoperative assessments showed 13 total excisions, three residuals, 10 visual improvements, seven stable visual statuses, and 10 cases of hormonal remission. **Conclusion:** Acromegaly is a clinical manifestation of GH adenomas, which remain rare. We collected 18 cases of somatotropic adenoma, all operated on with good clinical, radiological, and hormonal outcomes.

Keywords

Acromegaly, Pituitary Adenoma, GH, Senegal

1. Introduction

GH adenomas (somatotropic) are pituitary tumours with immunohistochemical expression of growth hormone (GH), in which GH and IGF1 levels are usually

high or slightly high [1]. The disease is characterized by clinical, biological, and radiological signs associated with chronic and uncontrollable hypersecretion of GH, usually due to a pituitary adenoma [2]. Excess GH during childhood, before the closure of the epiphyseal growth plates, is rare and causes pituitary gigantism, a serious condition that recent data suggest may have a genetic basis [3]. The prevalence in the general population is estimated at 6 - 12.5 per 100,000 [4] [5]. The average age at diagnosis is 40 years, with a female predominance, although some authors report an equal distribution between sexes [6].

Symptoms that develop gradually often lead to a diagnostic delay. The characteristic dysmorphic syndrome allows us to suggest the diagnosis [7]. The most common complications—rheumatological, cardiovascular, respiratory, and metabolic—contribute to the seriousness of the disease [8] [9].

The treatment is both medical and surgical, with the trans-sphenoidal endonasal endoscopic approach being preferred. In Dakar, the same surgical technique is used in our centres, and additional treatment with conventional radiotherapy is exceptional. The main objective is to describe the neurosurgical aspects of GH pituitary adenomas at Fann University Hospital.

2. Patients and Method

This was a retrospective, descriptive study conducted in the Neurosurgery Department of the Fann University Hospital Center in Dakar. We analyzed, over a period of six years (from October 1, 2016, to July 30, 2022), the medical files of 18 patients, their treatment methods, and the results obtained.

This study included the records of all patients over 25 years of age who had been treated for GH pituitary adenoma during the study period. Patients who had presented with acromegaly, whose records were usable and complete, and finally, we included all patients who had undergone surgery for GH pituitary adenoma in our department.

Several variables were studied:

Quantitative: age, sex, dates of entry and exit, consultation times, length of hospitalization, wake-up time.

Qualitative: profession, laterality, provenance; comorbidities: diabetes, hypertension, familial; circumstances of discovery: tumor syndrome, visual disturbance, pituitary apoplexy, signs of hypersecretion, incidental findings; general examination; clinical examination; assessment: hormonal, ophthalmological, and neuroradiological; medical treatment before and after surgery; route used: endonasal trans-sphenoidal; quality of excision; complications; postoperative follow-up; histological type; postoperative control assessment.

2.1. Procedure and Operating Technique

Patient under general anaesthetic with oro-tracheal intubation, in dorsal decubitus position, head resting either on a round headrest fixed by an adhesive strip, or Mayfield. Oropharyngeal packing. Billot under the popliteal fossae. Strict asepsis

of the nasal cavities and the right parumbilical wall. Sterile draping.

Introduction of the free-handed 0 degree endoscope into the right nasal cavity.

Lateral dislocation of the middle turbinate allowed access to the sphenoid ostium.

The opening of the sphenoid sinus was sometimes preceded by coagulation of the posterior nasal artery, a branch of the sphenopalatine artery, which ran under the sphenoid ostium to vascularise the nasal septum.

Hemostasis of the mucosa at the lateral edge of the ostium was performed with bipolar forceps to prevent postoperative epistaxis.

We performed a sphenoidotomy after locating the carotid arteries using Doppler.

The sellar floor was opened with scissors and the dura was opened in X to visualise the tumour, which was either soft on aspiration or hard and yellowish but did not respond to aspiration.

The tumour was then progressively removed with ring curettes.

We curetted and then used forceps to take samples for pathology.

Intrasellar curettage lateral then upwards. Descent of the sellar diaphragm showed complete exeresis.

Haemostasis was checked and was more often satisfactory at the end of the procedure. Filling with surgical or reconstruction with abdominal fat.

Dry, sterile dressing in the form of a packing.

All the forms were completed with the explicit consent of the patients obtained by telephone and in person for the new patients, who provided the necessary additional information. In addition to the postgraduate medical student, the research team included a neurosurgeon sub-specialised in endoscopy, who confirmed or invalidated the diagnostic hypotheses put forward.

2.2. Data Collection

Data entry and analysis were conducted using Epi Info version 7 software, while tables and figures were created with Excel 2007 software. Qualitative variables were expressed as numbers and percentages, and quantitative variables as averages. For comparisons, we used the Chi-square test and non-parametric correlation tests. The analysis was considered significant with a $P \leq 0.05$. The study was submitted for approval to the ethics committee, and confidentiality was maintained.

3. Results

In this retrospective study, we compiled the data on a total of 18 cases of somatotropic adenoma who underwent medical and surgical treatment at our centre.

3.1. Sociodemographic Data

In our series, the average age was 42.8 years, ranging from 25 to 69 years. At the end of the study, the male population (12 cases) was the largest, with a sex ratio of

2 in favor of males. More than two-thirds of our patients were already at the stage of complications at the time of diagnosis, mainly represented by high blood pressure (HBP) in 27% of cases.

3.2. Clinical Data

The diagnostic delay in this study averaged 5.27 years (range: 1 to 12 years).

The tumor syndrome was primarily indicated by headaches (9 cases), which were the main symptom revealing the disease in this study. Intracranial hypertension (ICH) syndrome (2 cases) was also a reason for consultation. While headaches were the most common presenting sign, ICH syndrome often appeared with other symptoms. Visual disturbances were noted in 9 cases, including four with blurred vision, bilateral blindness, and unilateral left blindness. Dysmorphic syndrome was observed in all patients (Figure 1). Decreased libido was found in five cases, with or without galactorrhea (3 cases) and three cases of gynecomastia. There were also two cases of snoring and two cases of arthralgia. Carpal tunnel syndrome was found in one patient, and there was one case of mental disorder.

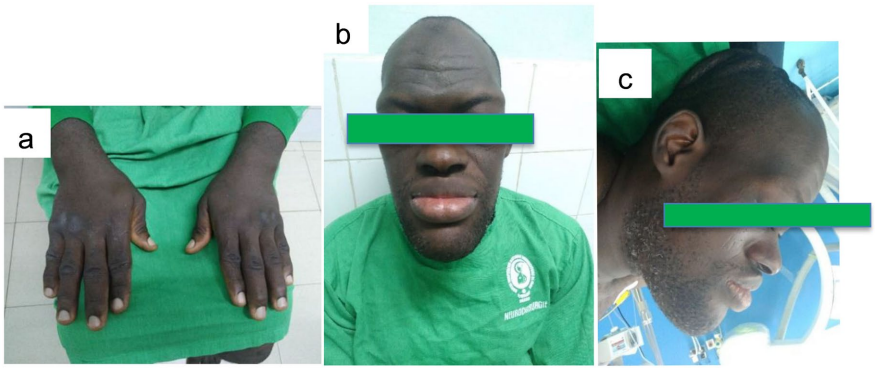

Figure 1. (a, b and c) Acromegaloid dysmorphic syndrome: a: thickening of the bony reliefs of the hand; (b and c) front and side views showing thickening of the bony reliefs of the face with prognatism.

3.3. Biological Data

On the hormonal level, hypercortisolemia was found in one patient, and hyperprolactinemia in five patients. GH levels were elevated in all patients. IGF-1 levels were elevated in 17 patients but showed no correlation with GH levels. The IGF-1 level was within the normal range in one patient, a woman, but she had an elevated plasma GH level. In this study, the most common association was GH-PRL, which was observed in five cases.

3.4. Ophthalmological Data

In this study, 13 patients experienced a decrease in visual acuity. We recorded that 66% of patient files showed visual field impairment, with 61% having bitemporal hemianopia and 5% having homonymous lateral hemianopia at the time of diagnosis.

3.5. Radiological Data

In this study, 17 patients initially underwent brain CT, while brain MRI was performed on all patients. Seventeen patients had good sinus pneumatization. Eleven cases were macroadenomas, and one case was a microadenoma. Six of the adenomas were giant. Cavernous sinus invasions were found in 15 patients. Knosp Grade IV was the most represented with eight cases, followed by Grades II and III with three cases each (Figure 2(a) and Figure 2(b)).

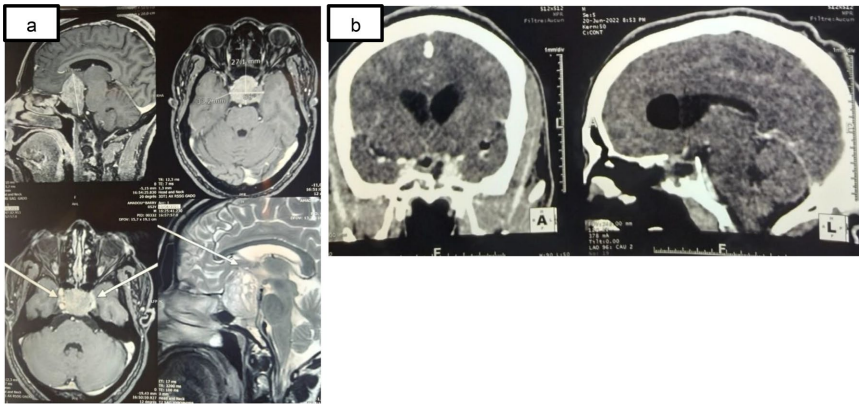

Figure 2. (a) MRI in sagittal T1, and axial, slices after gadolinium injection and sagittal shows a macroadenoma with suprasellar extension compressing the optic chiasma and enveloping the internal carotid arteries on both sides Knosp IV. (b) Cerebral CT scan at 3 months post-operatively.

3.6. Medical-Surgical Treatment

In this series, all patients underwent endoscopic pituitary surgery via a transsphenoidal approach (Figure 3(a) and Figure 3(b); Figure 4). Cabergoline was introduced post-operatively.

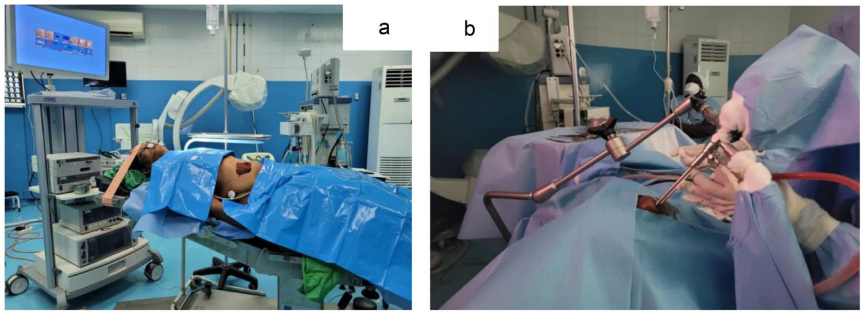

Figure 3. (a and b) Patient in transatlantic position; endoscope and aspirator in place: Images taken from the Neurosurgery Department at Fann.

3.7. Scalable Data

In this study, follow-up imaging was performed on 17 patients. Total radiological excision was observed in 13 patients. Tumor residue persisted in 3 patients, attributed to either the fibrous nature of the adenoma or incomplete excision due to the adenoma's size and invasion.

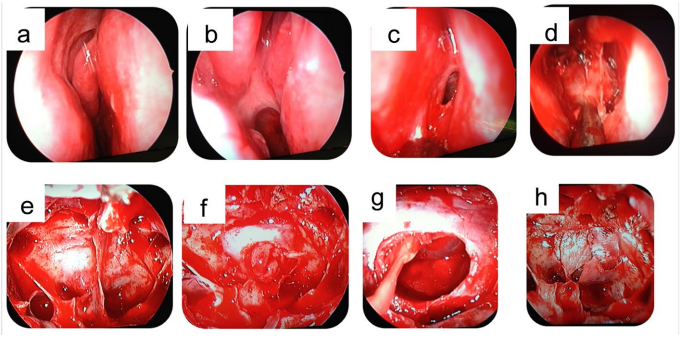

Figure 4. Trans sphenoidal tumor resection: Images taken from the Neurosurgery Department at Fann. Endonasal stage (a, b), locating the sphenoid ostium (c), exposure of the sphenoid rostrum (d). Intraoperative view of the sellar floor after sphenoidotomy: (e), intrasellar curettage (f), end of resection (g), closure of the sellar floor (h).

Ten patients in our study improved their visual function, while seven patients maintained the same visual status.

In our series, we noted a remission of endocrine function in 10 patients; five had normal endocrine function, and two had hormonal elevation.

In follow-up, five patients also achieved normalization of endocrine function; three achieved hormonal remission, and three still had tumor residuals after 3 months. After one year of follow-up, the result remained stationary.

4. Discussion

4.1. Sociodemographic Data: Average Age/Sex Ratio

In our series, the average age was 42.8 years, with a range from 25 to 69 years, consistent with findings in the literature [10]-[13].

Tyler C *et al.*, in two recent works, found the average age to be 48.9 years in 2020 [14] and 40 years in 2021 [15]. This confirms the hypothesis that pituitary adenomas generally develop in young adults during their peak economic (fourth to sixth decade) and reproductive years. The fact that the majority of patients are actively working has significant economic consequences due to absenteeism from work, resulting from the duration of consultations and/or hospitalizations.

At the end of the study, the male population (12) was the largest. We found a sex ratio of 2 in favor of males. This result was comparable to those reported in the literature, which mentioned a male predominance [16]-[19]. However, some authors have reported a similar frequency in both sexes [20]-[22].

Clinical data

The diagnostic delay in this study was, on average, 5.27 years (range: 1 to 12 years). Some authors found a delay of up to 8 - 10 years [23] [24]. The main reason for this delay is primarily the slow progression of pituitary adenomas and the lack of specificity of clinical symptoms.

4.2. Circumstances of Discovery

Headache was the most frequent reason for consultation in this series. It was the

second most common reason, according to Benbow [25], at 20.5% and constituted 74% of consultations according to F. Z. Kaidi [26]. In this study, there were nine cases of visual disturbances, including four with visual blur, bilateral blindness, and unilateral left blindness. In the literature, visual disturbances were the most frequent reason for consultation [17]-[27], representing 74% of discovery circumstances according to Karppinen [28], 54% according to Benbow [25], and 35.6% according to Pennacchietti [17]. This tumor syndrome showed the development of the adenoma pushing against the optic chiasm. Dysmorphic syndrome or acrofacial dysmorphia characterizes this condition and was found in all our patients, consistent with literature data [17]-[25]. Decreased libido was found in five cases, with or without galactorrhea (3 cases), and three cases of gynecomastia. We also found two cases of snoring, two cases of arthralgia, and two cases of incidental discovery. Carpal syndrome was found in one patient, and there was one case of mental disorder. Several authors made similar observations [29]-[33]. Regarding other neurological signs, a neurological deficit was found in three patients, possibly due to tumor extension and delayed consultation.

4.3. Biological Data

On the hormonal level, hypercortisolemia was found in one patient, and hyperprolactinemia in five patients. GH levels were elevated in all patients. IGF-1 levels were elevated in 17 patients but without any correlation with GH levels. The IGF-1 level was within the normal range in one patient, a woman, but she had an elevated plasma GH level. In accordance with the literature [33]-[35], the most common association in this study was GH-PRL, with five cases.

4.4. Ophthalmological Data

In this study, 13 patients had a decreased visual acuity (DVA), which is consistent with literature data [36] [37], and 68.5% of cases had bitemporal hemianopia according to Turner [38]. This aligns with our results, where 66% of patients experienced visual field impairment, including 61% with bitemporal hemianopia and 5% with homonymous lateral hemianopia at the time of diagnosis.

4.5. Radiological Data

In this study, 17 patients initially underwent brain CT, while brain MRI was performed on all patients. Seventeen patients had good sinus pneumatization. We found 11 cases of macroadenomas and one case of microadenoma. Six of the adenomas were giant. This frequency could be explained by the slow and insidious nature of the clinical symptoms. Cavernous sinus invasions were found in 15 patients. Knosp Grade IV was the most common, with eight cases, followed by Grades II and III, with three cases each. This can be attributed to the predominance of pituitary macroadenomas responsible for the invasion of the cavernous sinus in this series. Similar observations have been made in the literature [39] [47].

4.6. Therapeutic Data

4.6.1. Medical Treatment

Cabergoline is a treatment option for patients with mild acromegaly, moderately elevated IGF-I levels, and associated prolactin secretion.

In this study, cabergoline-based treatment was used preoperatively in seven patients. Recent studies have led to similar conclusions [40] [41]. Moreover, it has been debated whether preoperative treatment with somatostatin could benefit the postsurgical remission rate in newly diagnosed acromegaly [42] [43]. In our series, no patient received somatostatin preoperatively or post-operatively. Work by A. Hassani *et al.*, published on September 30, 2020 [13], and Fleseriu M. *et al.*, published in 2021 [44], highlighted the use of somatostatin and dopaminergic analogues.

4.6.2. Surgical Treatment

Transsphenoidal excision of the pituitary adenoma (PA) was the treatment of choice for acromegaly. The average duration of transsphenoidal surgery in this study was 50 minutes, depending on whether the adenoma was a microadenoma, macroadenoma, or giant adenoma. These results align with literature indicating that the endoscopic transsphenoidal procedure lasts on average 30 to 60 minutes [45] [46]. In this series, all patients underwent endoscopic pituitary surgery via a transsphenoidal approach. The sellar floor was lysed by the adenoma in 15 patients. Total excision was achieved in 13 cases. Hyponatremia was observed in four patients. Gabriel Zada *et al.* found similar results in their work [17]. All patients received prevention for immediate postoperative cortisol insufficiency with 100 mg of hydrocortisone succinate during premedication.

Thyrotropic insufficiency was treated with thyroxine or LT4 (Levothyrox) orally at a dose of 100 µg/day [46]. In this study, we noted a case of postoperative anterior pituitary insufficiency in a patient with thyrotropic insufficiency, showing good progress under hormone replacement therapy. In Foch's series [47], postoperative anterior pituitary insufficiency was reported in 3.8% of patients, 1.92% according to Berker [48], 3.1% according to G. Frank [49], and 1.9% according to F. Wang [50]. Two cases of CSF leak were observed in this study population. A study at Reims University Hospital [51] on 337 pituitary adenomas operated on via the trans-sphenoidal endonasal route found that 61 patients (17%) experienced a CSF leak intraoperatively, and 11 patients (3.1% of those operated) had postoperative rhinorrhea. We noted a case of meningitis in a patient who showed good progress with antibiotic treatment. The Foch Hospital series [47] reported a 1.24% incidence of meningitis, 2% in the A. Gondim series [37], 0.95% in the F.X Roux series [52], 1.65% in the J. Torales series [39], and no cases of postoperative meningitis in Karppinen's series [28]. The occurrence of postoperative epistaxis was noted in two patients. The transient occurrence of diabetes insipidus in the postoperative period is estimated at 10% to 60% in the literature. The risk of permanent diabetes insipidus is rare (0.6%) [53]. Careful monitoring of diuresis, fluid intake, urinary osmolarity, and serum sodium levels within 48

hours postoperatively allowed for early diagnosis and appropriate treatment. Diabetes insipidus was found in 14 patients in this study; all cases were reversible within 48 hours. Literature data found 12% transient diabetes insipidus and 1.4% definitive diabetes insipidus according to the Foch hospital series [53] [54], and 10.4% transient diabetes insipidus and 0.95% definitive diabetes insipidus according to Roux [52]. In the literature, cases of death after endoscopic surgery for pituitary adenoma are rare. In this study, one patient died.

4.6.3. Scalable Data

Total excision was observed in 13 patients. Tumor residue persisted in 3 patients, linked to the fibrous nature of the adenoma or incomplete excision due to the size and invasion of the adenoma. Moussa Baldé [55] noted a rate of tumor residue on postoperative MRI in 46% of cases, with a 12% recurrence rate, progression of postoperative residual tumor volume in 10%, and radiological cure in 46% of cases.

A meta-analysis conducted by a team in Arizona across 10 institutions involving 371 patients found a biological remission rate over 10 years of 59% - 69% [56]. The results confirm the effectiveness of surgery and complementary treatment with cabergoline in controlling acromegaly. In follow-up, five patients achieved normalization of endocrine function; three patients achieved hormonal remission, and three patients still had tumor residuals after three months. After one year of follow-up, the result remained stationary.

A follow-up study averaging 5 years post-operation would provide more convincing results.

5. Conclusion

Somatotropic adenoma is a rare but benign endocrine tumor, manifesting as a dysmorphic acromegaloid syndrome in all our patients. Despite its distinct clinical characteristics, it is not well-known in Senegal. We documented 18 cases of somatotropic adenoma, all treated with an endonasal endoscopic approach, showing good clinical, radiological, and hormonal outcomes after a 1-year postoperative follow-up.

Conflicts of Interest

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

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Abbreviations

DVA: Decreased visual acuity
NUHC: National University Hospital Center
GH: Growth hormone
HBP: High blood pressure
ICH: Intracranial hypertension
MRI: Magnetic resonance imaging
CSF: Cerebrospinal fluid
CT: Computed tomography scan
PA: Pituitary adenoma