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# Epidemiological, Clinical and Therapeutic Profiles of Acromegaly in Senegal: About 25 Cases

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## Abstract

**Introduction:** Acromegaly is diagnosed on the basis of elevated IGF1 and GH levels. Management is primarily by pituitary surgery. In Senegal, the few studies of acromegaly have been based on descriptions of isolated cases. The aim was to study aspects of acromegaly through a national multicenter registry. **Methodology:** This was a multicenter, retrospective study conducted from January 1er 2008 to December 31 2022 in the Dakar neurosurgery departments and the endocrinology department of the Abass Ndao hospital. It focused on confirmed cases of acromegaly followed up in our respective departments. **Results:** 25 cases were included, with a mean age of 42.5 ± 12 years and a sex ratio of 1.5. The main circumstances of discovery were a tumor syndrome (100%), craniofacial dysmorphia (36%), diabetes mellitus (44%), arterial hypertension (40%), decreased visual acuity (68%), photophobia (68%). Gigantism was found in 52%, and the main signs of dysmorphic syndrome were prognathism (100%), protruding cheekbones (100%), thickened lips (100%), macroglossia (100%), enlarged extremities (100%), dysphonia (92%), pneumatization of the sinuses (92%), marked wrinkles (92%). Mean plasma IGF-1 level was 610.7 ± 2 ng/ml and GH 61.3 ng/ml. Hyperprolactinemia > 100

ng/ml was found in 36%. Macroadenomas were found in 80% of cases, isolated acromegaly in 75% and mixed secretion in 25%. The proportion of patients who had undergone pituitary surgery was 96%, including 30% with postoperative transient diabetes insipidus. There was one case of post-operative death, related to pulmonary embolism. **Conclusion:** In our practice, the diagnosis of acromegaly remains late in view of the symptoms and frequency of macroadenomas. In the absence of somatostatin analogues, surgery was the treatment of choice, despite some complications.

## Keywords

Acromegaly, Clinical Profile, Surgery, Senegal

## 1. Introduction

Acromegaly refers to the clinical, biological and radiological signs associated with chronic, unchecked hypersecretion of growth hormone (GH), usually by a pituitary adenoma. When GH hypersecretion precedes growth plate fusion, it leads to gigantism [1]. Worldwide prevalence is estimated at 60 cases per million inhabitants, with an annual incidence of 3 to 4 new cases per million [2]. In Europe, the annual prevalence of the disease is 30 - 70 cases per million [3]. In Africa, rare cases are reported in the literature [4]. It accounted for 8.68% of pituitary adenomas in Senegal [5]. The average age of onset of acromegaly was 32 years, while the average age at diagnosis was 42 years, *i.e.* an average diagnostic delay of 10 years. The pathology more frequently affects women, and is most often a pure somatotropic pituitary adenoma (60%) or mixed adenomas [6].

It is responsible for a progressive symptomatology. Acromegaly, revealed by acral and facial dysmorphia (92.5%) and a pituitary tumor syndrome (57.5%), also has numerous metabolic, endocrine and cardiac repercussions that condition prognosis [6]. Diagnosis is based on elevated serum concentrations of IGF1 (Insulin-like Growth Factor 1) and Growth Hormon (GH) [7]-[9]. The management of GH adenomas is primarily based on pituitary surgery. Medical treatment, mainly with somatostatin analogues, is indicated as a second-line treatment, especially in the absence of postoperative disease control [8]. In Senegal, the few works on acromegaly have been based on descriptions of isolated cases or within the overall context of pituitary adenomas. This was the motivation for this multicenter study, the aim of which was to investigate aspects of acromegaly in Senegal.

## 2. Patients and Methods

This was a multicenter, retrospective, descriptive study, conducted from January 1er 2008 to December 31 2022 in the neurosurgery departments of the Fann University Hospital and the Dakar Principal Hospital, and in the endocrinology department of the Abass Ndao Hospital. Our study focused on patients with acromegaly confirmed on clinical, hormonal and radiographic data, and who had been

followed up in the various departments. Files that were incomplete in terms of positive diagnosis of acromegaly were not included. The data required for the study were collected from the patients' files using a variable data processing form in the archives of the neurosurgery departments (Fann and Hospital Principal de Dakar) and the endocrinology consultation at the Abass Ndao Hospital. Direct questioning and/or telephone calls were used to complete the data on a case-by-case basis.

Arterial hypertension (AH) was classified according to the World Health Organization grading system [10]. Body mass index (BMI) was based on the International Obesity Task Force classification [11]. Diabetes mellitus was defined according to the American Diabetes Association (ADA) [12]. Acromegaly was diagnosed according to international criteria [7]-[9]. The necessary information was collected identically for all patients. These were:

- Socio-demographic data: age, gender, origin, background and terrain;
- Clinical data: consultation time, anthropometric data, complete examination of all systems, with emphasis on tumor syndrome (headaches, dizziness, ringing in the ears and visual disturbances), endocrine clinical signs of hypersecretion or hyposecretion, neurological and ophthalmological examination (visual acuity, fundus, visual field). Paraclinical examinations were used to confirm the adenoma, assess its size or volume, and specify the type of pituitary secretion.

Pituitary hormone assessments and biology were carried out in specialized laboratories. These included basic exploration of the pituitary axis, including prolactinemia (norms: 3.46 - 19.4 ng/ml), ACTH (morning norms 5 - 60 ng/L), cortisolemia (norms: 37 - 194 ng/ml), 24-hour urinary cortisol (norms: 28 - 138 nmol/24 h), plasma GH and IGF1 (age-dependent norms), FSH (ovulatory phase, sex and age-dependent norms), LH (ovulatory phase, sex and agedependent norms), testosterone (male norms: 8.7 - 34.7 nmol/l), estrogen (norms according to ovulatory phase, sex and age), TSHus (norms: 0.35 - 4.94 μIU/ml), free T4 (norms: 9 - 19 pmol/l). The main morphological investigations were pituitary computed tomography (CT) and magnetic resonance imaging (MRI). Other investigations were performed according to profile. Histology of the surgical specimen was also studied in cases of pituitary surgery. Other investigations were performed according to profile.

- Therapeutic and evolutionary data: medical treatment (specific treatments and complications of the disease), surgical technique (technique used, quality of excision, intraoperative complications), and histology. Pituitary radiotherapy is not available in Senegal. 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), hormone dosage and assessment of tumour size on imaging. Post-operative treatment was also taken into account.

The analysis was carried out using the following software: Excel 2016 and R

version 4.1.1. In the descriptive analysis, qualitative variables were described by frequency tables. Quantitative variables were described by their position (mean) and dispersion (standard deviation, extremes) parameters. For bivariate analysis, the Chi-square test$^2$ or the Fisher test was used for proportion comparisons. A difference or relationship is observed if $p < 0.05$. Word processing was used.

## 3. Results

### 3.1. Epidemiological Data

A total of 25 cases of acromegaly were recorded. The mean age of the patients was 42.5 ± 12 years, with extremes of 25 and 69 years. There were 10 females and 15 males, giving a sex ratio of 1.5. Our patients were housewives (7 cases, 28%), manual workers (6 cases, 24%), civil servants (5 cases, 20%), shopkeepers (4 cases, 16%) and students (3 cases, 12%). Approximately 48% of our patients came from the country's capital, Dakar (12 cases), 33% from other regions of Senegal (8 cases) and 20% from neighbouring countries such as Guinea, Gambia and Mauritania (5 cases). In our series, 80% of patients were married (20 cases) and the average number of children per patient was 4.3. Only 4 married patients had no children.

Table 1 shows the distribution according to socio-demographic characteristics.

Table 1. Breakdown by socio-demographic characteristics.

| Socio-demographic data | Values |
|---|---|
| Total workforce | 25 cases |
| Average age (extremes) | 42.5 ± 12 years (25 - 69) |
| Men | 15 cases (60%) |
| Sex ratio (M/F) | 1.5 |
| **Profession** | |
| Household | 7 cases (28%) |
| Workers | 6 cases (24%) |
| Civil servants | 5 cases (20%) |
| Retailers | 4 cases (16%) |
| Students | 3 cases (12%) |
| **Provenance** | |
| Senegal | 20 cases (80%) |
| Neighboring countries | 5 cases (20%) |
| **Family status** | |
| Married | 20 cases (80%) |
| Average number of children | 4.3 children |

### 3.2. Clinical Data

#### 3.2.1. Circumstances of Discovery

The main circumstances of discovery were craniofacial dysmorphia (9 cases, 36%), diabetes mellitus (11 cases, 44%) and arterial hypertension (10 cases, 40%).

One patient was previously treated for Behçet's disease (4%) and two others for goiter (8%).

### 3.2.2. Tumor Syndrome

On examination, all patients presented at least one sign related to the tumor syndrome. These included chronic headache in 22 cases (88%), ringing in the ears in 21 cases (84%) and vertigo in 10 cases (40%). In terms of ophthalmology, we found reduced visual acuity in 17 cases (68%), photophobia in 17 cases (68%) and nystagmus in 01 cases (4%).

### 3.2.3. Secretory Syndrome

It was present in all patients. On average, weight was 96 ± 12 kg (extremes 75 and 120 kg), height 180 ± 13 cm (extremes 153 and 209 cm) and body mass index (BMI) 29.6 ± 4.6 kg/m$^2$ (extremes 22.8 and 41.7 kg/m$^2$). According to BMI, obesity was present in 10 cases (40%), overweight in 13 (52%). Arterial hypertension was present in 10 patients (40%). Gigantism was present in 13 patients (52%).

Among our patients, 24 cases (96%) had at least one organomegaly. These included 24 cases of macroglossia (96%), 2 cases of goiter (8%). There was no cardiomegaly, hepatomegaly or splenomegaly. The main signs of dysmorphic syndrome were prognathism (100%), protruding cheekbones (100%), thickened lips (100%), macroglossia (100%), enlarged extremities (100%), dysphonia (92%), sinus pneumatization (92%), marked wrinkles (92%). Other clinical signs related to prolactin hypersecretion were found. These included galactorrhea (7 cases, 28%), gynecomastia (5 cases, 20%), decreased libido and erectile dysfunction (7 cases, 28%), amenorrhea (3 cases, 12%). Table 2 shows the distribution according to pituitary clinical syndromes.

Table 2. Distribution of patients by pituitary clinical syndromes.

| Symptoms of secretory syndrome | Workforce | Percentage (%) |
|---|---|---|
| **Dysmorphic syndrome** | | |
| Prognathism | 25 | 100% |
| Prominent cheekbones | 25 | 100% |
| Thick lips | 25 | 100% |
| Nose thickening | 25 | 100% |
| Macroglossia | 25 | 100% |
| Widening the ends | 25 | 100% |
| Marked wrinkles | 23 | 92% |
| Sinus pneumatization | 23 | 92% |
| Dysphonia | 23 | 92% |
| Nocturnal snoring | 20 | 80% |
| Skin thickening | 16 | 64% |
| Physical asthenia | 14 | 56% |

**Continued**

| | | |
|---|---|---|
| Paresthesia of the extremities | 14 | 56% |
| Osteoarticular pain | 14 | 56% |
| Profuse sweating | 12 | 48% |
| Sternum projection | 11 | 44% |
| Hypoacusis | 11 | 44% |
| Hirsutism | 10 | 40% |
| Occipital protuberance | 8 | 32% |
| Mechanical lumbago | 8 | 32% |
| **Gonadal syndrome** | | |
| Galactorrhea | 7 | 28% |
| Erectile and libido disorders | 7 | 28% |
| Gynecomastia | 5 | 20% |
| Amenorrhea | 3 | 12% |
| **Tumor syndrome** | | |
| Headaches | 22 | 88% |
| Ringing in the ears | 19 | 76% |
| Photophobia | 17 | 68% |
| Visual blur | 17 | 68% |
| Vertigo | 10 | 40% |
| Palpebral edema | 1 | 4% |
| Nystagmus | 1 | 4% |

## 3.3. Paraclinical Data

### 3.3.1. Biological Data

The various growth hormones were increased in all patients. On average, plasma IGF-1 levels were 610.7 ± 218 ng/ml (extremes 263 and 1079) and GH 61.3 ng/ml (extremes 7 and 150). Hyperprolactinemia > 100 ng/ml was found in 09 patients (36%). Other hormonal abnormalities were corticotropic insufficiency in 3 cases (12%), thyrotropic insufficiency in 04 cases (16%) and gonadotropic insufficiency in 06 cases (24%). Phosphocalcic and ionic tests were normal in all our patients.

### 3.3.2. Morphological Data

Magnetic resonance imaging was performed in all patients. There were 20 cases of macroadenoma (80%), 5 cases of microadenoma (20%), 12 cases of extension (48%). This extension was cavernous (4 cases, 16%), chiasmatic (2 cases, 8%), chiasmo-cavernous (6 cases, 24%). The extension concerned only pituitary macroadenomas, where the mean GH level was 68.8 ng/ml and IGF-1 608.6 ng/ml. Abdominal and pelvic ultrasound was performed in 19 patients, including a single case of prostatic hypertrophy. Cardiac ultrasound in 18 patients revealed 4 cases of hypertrophic cardiomyopathy and one case of type 1 diastolic dysfunction (see

Table 3).

### 3.4. Final Diagnosis

The proportion of patients with isolated acromegaly was 75% (15 subjects). Nevertheless, 25% or 5 cases of mixed adenomas were found (see Table 3).

Table 3. Distribution according to morphological, hormonal and therapeutic data.

| Features | Number | Percentage (%) |
|---|---|---|
| **Morphological characteristics of the adenoma** | | |
| Macroadenoma | 20 | 80% |
| Microadenoma | 5 | 20% |
| Extension | 12 | 48% |
| **Secretory characteristics of the adenoma** | | |
| Single-secreting adenoma (GH alone) | 16 | 64% |
| Bis-secreting adenoma (GH + Prolactin) | 9 | 36% |
| Anteropituitary insufficiency | 11 | 44% |
| **Therapeutic data** | | |
| Cabergoline 0.5 mg/week | 25 | 100% |
| Trans-sphenoidal surgery | 24 | 96 |

### 3.5. Therapeutic Data and Evolution

All patients had received medical treatment with Cabergoline (Dostinex®) at an initial dose of 0.5 mg per week. Other medical treatments included antidiabetics and antihypertensives. Somatostatin analogues and GH receptor antagonists were not available in Senegal (see Table 3).

The proportion of patients who had undergone pituitary surgery was 96% (24 cases). This was exclusively trans-sphenoidal surgery. None of our patients underwent radiotherapy. Of the patients who underwent surgery, 30% (6 patients) developed transient diabetes insipidus postoperatively. Other post-operative incidents included epistaxis or rhinorrhea in 5 cases (20.8%), meningitis and pulmonary embolism in 01 cases each. One case of post-operative death was related to pulmonary embolism.

## 4. Discussion

### 4.1. Epidemiological Data

Epidemiological studies presented acromegaly as a rare pathology, with a prevalence ranging from 20 to 80 cases per million inhabitants [13]. In Africa, in the absence of national registries, its frequency depends on the number of cases reported from one series to another [14]-[20]. Because of its insidious nature, diagnosis is often made with considerable delay (4 to 10 years or more). In our series, acromegalia was discovered some 04 years later than the first symptoms. This long

delay in diagnosis is directly responsible for the frequency of complications noted in various series, particularly in Africa [18] [21]. In the study by Maione *et al.* [13], the delay in diagnosis was 6.6 years. The mean age of our patients at the time of acromegaly diagnosis (42.5 ± 12 years) was comparable to that of international reviews. Moreover, age at diagnosis was significantly higher in women than in men in all the studies reported [13] [16].

### 4.2. Clinical and Morphological Data

In Africa, the few cases of acromegaly reported in the literature describe highly advanced forms, as evidenced by complications, notably metabolic [18]. In our population, acromegaly was revealed by a dysmorphic syndrome and/or a pituitary tumor syndrome in all cases. The prevalence of clinical signs varied from one series to another, depending on how early the diagnosis was made [16] [22]. The more chronic and severe the GH excess, the more severe the signs [7].

The disease also has numerous somatic, metabolic, endocrine and cardiac repercussions, all of which affect prognosis. The majority of patients in our series (70%) had already developed complications at the time of diagnosis. These were mainly diabetes mellitus (45%) and hypertension (50%). According to the literature, the incidence of hyperglycemia correlated with the rate of GH secretion and the duration of the condition [23]. The predominance of diabetes and hypertension among the main comorbidities was previously reported among the 16,000 patients from the 19 national registries. In these registries, the prevalence of comorbidities varied from one series to another [13]. According to Anagnostis *et al.* [24], other morbidities during follow-up were myocardial hypertrophy (50%), colon polyps (55%), thyroid nodules (74%) and an adrenal mass (18%).

Pituitary magnetic resonance imaging remains the gold standard. Pituitary adenomas were found in 95% of cases, and pituitary hyperplasia in 5%. We report a predominance of macroadenomas. In the 19 national acromegaly registries reported by Maione *et al.* [13] and the South African series by Elbueishi *et al.* [16], macroadenomas accounted for 75% and 92.5% of cases respectively. 4.3. Therapeutic data.

#### 4.2.1. Medical Treatment

In the systematic review by Maione *et al.* [13], which included 16,000 patients drawn from 19 national registries, first-line medical treatment was administered in an average of 24% of cases. Most patients were treated with somatostatin analogues, followed by dopaminergic agonists and finally pegvisomant. In our series, in the absence of somatostatin analogues and pegvisomant, 44% of patients had initially benefited from dopaminergic agonists. In a Belgian study of 64 patients treated with Cabergoline (Dostinex), normalization of IGF1 was achieved in 39% of patients with mixed adenomas and moderately elevated initial GH levels [25]. Depending on the study, the efficacy of somatostatin analogues on hormonal control was 6474% in the first few months [26]. A time effect was suggested. Thus, during follow-up (84 months in the study by Cozzi *et al.* [27] and 18 years in the

study by Maiza *et al.* [28]), IGF-1 concentration would continue to fall while the same dose of somatostatin analogues was continued. It should be noted that the efficacy of this treatment varies from study to study, probably due to differences in treatment duration, patient selection and the existence or absence of a history of surgery or radiotherapy. Finally, the expression of receptor subtypes by the tumor probably also plays a role [13].

GH antagonists are the medical treatment with the fastest and most consistent effect on symptoms. In clinical trials, after 12 weeks of treatment, the percentage of patients normalized reached 90% [29] [30]. Unfortunately, this drug is not yet available in Senegal.

#### 4.2.2. Surgical Treatment

Given the unavailability of somatostatin analogues in Senegal, the proportion of our patients operated on was 96%. Elsewhere, the weighted mean percentage of cases operated on was 80.4%, and was relatively stable across countries (ranging from 67% to 96.3%) [13] [16]. The surgical success rate alone has not changed over time, indicating stability in neurosurgical performance, despite the introduction of new techniques [31] [32]. This is also linked to the persistence of a high prevalence of macroadenomas at diagnosis, which is a major predictor of surgical outcome [13]. Intraoperative complications.

In our series, 04 patients presented with transient diabetes insipidus. Shah *et al.* [33] reported a rate of 7.6% transient diabetes insipidus and 3.8% definite diabetes insipidus in the endoscopic surgery group, compared with 20% transient diabetes insipidus and 7.2% definite diabetes insipidus in the microscopic surgery group. Other incidents were mainly bleeding (6 cases), cerebrospinal fluid leakage (5 cases), rhinorrhea (4 cases) and epistaxis (4 cases). Two cases of death were recorded, one by pulmonary embolism and the other by pituitary apoplexy.

According to Zhu *et al.* [34], this rate was observed in 4.8% of pituitary macroadenomas.

## 5. Conclusion

This original study in sub-Saharan Africa has highlighted cases of acromegaly whose main revealing mode is the dysmorphic syndrome and the tumoral syndrome. Macroadenomas are the main morphological forms. Most patients who underwent surgery had a favourable outcome, with hormonal remission, although complications such as transient diabetes insipidus did occur.

## Conflicts of Interest

The authors have nothing to disclose.

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