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Type 2 Diabetes Revealing a Mixed GH (Acromegaly) and Prolactin Adenoma: A Case Report of the Internal Medicine Department of the Gabriel Touré University Hospital, Bamako, Mali

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Abstract **Case Report**

Introduction: Pituitary adenomas are benign, well-differentiated tumours that usually grow slowly over several years and are developed monoclonally from anteropituitary endocrine cells. We report a case of mixed GH and prolactin adenoma diagnosed in the Internal Medicine Department of the Gabriel Touré University Hospital, Bamako, Mali. ***Observation:*** The patient was a 36-year-old man with a 4-year history of type 2 diabetes mellitus who had consulted a specialist for headache, polyuro-polydipsic syndrome, decreased libido and erectile dysfunction. On clinical examination, a tumour syndrome was noted with headache and visual blur. The biology revealed a GH hypersecretion syndrome (IGF1) which was elevated to 561.9 µg/ml (VN=116-353) and prolactin elevated to 463.3 µIU/ml (VN: 24-324) and diabetes. Pituitary MRI revealed a pituitary macroadenoma. Our patient was treated with Dostinex 0.5mg/week with a gradual increase in dose and insulin. He was also referred to neurosurgery, where he is awaiting removal of the adenoma after glycaemic control and hormone normalisation. The evolution was marked by the disappearance of headaches, improvement in vision, GH and prolactin hypersecretion syndrome and glycaemic control. ***Conclusion:*** In sub-Saharan Africa, the problems posed by pituitary adenomatous pathologies are complex, due to the limited biological and morphological investigation facilities and the rarity of specialised surgical facilities.

Keywords: pituitary adenoma, tumour syndrome, hypersecretion syndrome, Internal Medecin, Gabriel Touré University Hospital.

1. INTRODUCTION

Benign pituitary adenomas are well-differentiated tumors, usually growing slowly over several years, developed monoclonally from anterior pituitary endocrine cells [1]. They represent 10 to 15% of intracranial tumors. We distinguish between microadenomas with a diameter less than 10mm and macroadenomas with a diameter greater than 10mm [2]. Adenomas can be non-secreting, revealed by the tumor syndrome possibly associated with signs of hypopituitarism, or secreting such as prolactinomas (the most common, cause the classic amenorrhea-galactorrhea syndrome); somatotropic adenomas (responsible for acromegaly); corticotropic adenomas (lead to Cushing's disease) and thyrotropic adenomas (which are rarer, lead to hyperthyroidism) [1]. Pituitary adenomas with mixed secretion of Growth Hormone (GH) and prolactin are exceptional [3]. In sub-Saharan Africa, the problems posed by these pituitary adenomatous pathologies are complex; they are due to the precariousness of biological and morphological investigation facilities and the scarcity of specialised surgical facilities [4]. We report a case of mixed GH and prolactin adenoma diagnosed in the Internal Medicine Department of the Gabriel Touré University Hospital in Bamako, Mali.

2. OBSERVATION

A 36-year-old male patient, farmer living in Dioila, a region on the periphery of the capital, with a history of type 2 diabetes for the past 04 years, consulted our internal medicine department on 12/02/2022 for headache and polyuro-polydipsic syndrome, decreased libido and erectile dysfunction.

The disease began 15 years ago, with frontal headaches that radiated to the orbit, interpreted several times as malaria, and the patient being treated by his family and friends as "a man who was too pitiful". The progressive morphological changes included facial deformity, enlarged hands and feet, leading to changes in shoe size and blurred vision. Polyuria was also noted. The association of a decrease in libido and erectile dysfunction that had led to several years without having children, the family decided to consult.

The parameters at entry were: weight 100 kg for a height of 186 cm (BMI=28.90 $^{kg/m2}$). Blood pressure was 130/80 mmHg.

Physical examination revealed a clear dysmorphic syndrome:

- Face: rounded forehead, hypertrophy of the nose and lips, prognathism of the dental arches (Photo 1)
- Thorax: bilateral gynaecomastia without galactorrhoea
- Upper limbs: drum-rod shaped fingers (Photo 2)
- Lower limbs: enlarged feet with a large foot pad

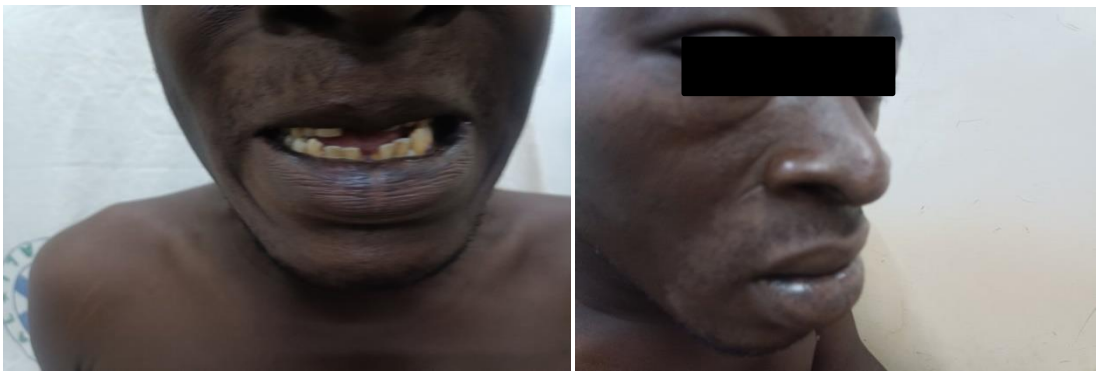

Photo 1: Facial dysmorphia

Photo 2: Doigts en « baguette de tambour »

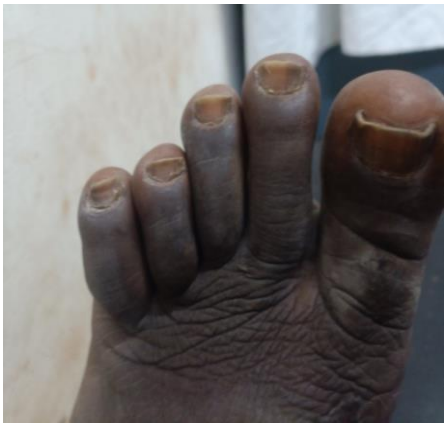

Photo 3: Hypertrophy of the toes

Biological Tests

15/02/2022: Prolactin 2nd Generation=463.3µUI/ml (NV: 24-324) Blood glucose= 2.43g/l (0.7-1.10)

21/05/2022: HbA1c=11.10% (VN=4-6) Blood glucose= 2g/l (0.7-1.10); **Prolactin 2nd Generation=12**.18ng/ml (VN=1.5-19.0); **2nd Generation Testosterone=2**.18nmol/l (VN=8.33-30.19); **IGF1=561.9 µg/ml** (VN=116-353)

27/09/2022: HbA1c=9,90% (VN=4-6); **TSH (us)**=1,3734Mui/l (VN=0,35-4,94) ; **Cortisol 08h=** 135,2nmol/l (VN= 101,2-535,7) ; **Microalbuminuria 24h** =691.8mg/24h (VN=0-30)

Testosterone 2nd Generation= 5.48nmol/l (VN=8.33-30.19) ; **Prolactin 2nd Generation=**38.54ng/ml (VN=1.5-19.0) ; Serum **LH=2**.29Mui/ml (VN=1.1-7.0); Serum **FSH=** 3.6Mui/ml (VN=0.95-11.95); **17 Serum Beta Oestradiol** = 11.00 pg/ml (VN < 62).

Imaging:

Pituitary MRI: showed enlargement of the sella turcica by an **intra-sellar mass** with superior-anterior and infra-sellar extension filling the sphenoidal sinuses. It measured 49 mm in anteroposterior diameter, 28 mm in height and 23 mm in transverse diameter, concluding in a pituitary macroadenoma. **(10/10/2022**)

Cardiac Doppler ultrasound on **31/10/2022**: Normal

Abdomino-pelvic ultrasound on **14/10/2022**: Homogeneous hepato-spleno-nephromegaly with no focal lesions.

3. DISCUSSION

Some limitations of our study:

The absence of certain investigations, such as campimetry and colonoscopy, due to a lack of financial resources, and the late completion of other investigations. The dates on which certain tests were carried out in relation to the date of admission bear witness to this.

Depending on their morphological (size, tumour extension) and functional characteristics, pituitary adenomas may present with one or more of the elements of the symptomatic triad:

- **Tumour syndrome**, with its clinical and radiological manifestations;
- **Hypersecretion syndrome** of one or more anteropituitary hormones;
- **Hyposecretion syndrome**: hormonal deficit affecting one or more of the pituitary hormone lineages, with its clinical and biological manifestations [5].

Tumour Syndrome

1 - Clinical

Headaches are typically frontal or orbital, frequently radiating to the vertex. They are non-specific and non-pulsatile, and are generally soothed by the usual analgesics. They are present even in cases of microadenomas, due to tension in the sellar diaphragm [1]. This was the case of our patient, his headaches had been present for several years, and in other authors [6, 7], where they had been present for several weeks to several months.

Visual field reductions (Goldmann campimetry) are only observed in cases of macroadenoma with suprasellar extension reaching the optic pathways. Because of the distribution of nerve fibres in the chiasma, the temporal field on each side is the first to be affected. The intensity of the damage increases with the degree of compression: exclusion of the blind spot, flattening of the isopters, superior temporal quadranopsia, then temporal hemianopsia, culminating in blindness [5]. In our patient, as in those of H.G. MONABEKA [6] in Congo and M.P. NTYONGA-PONO [7] in Gabon, there was a decrease in visual acuity.

2 - Neuroradiology

The only contributory morphological investigations are pituitary computed tomography (CT) or magnetic resonance imaging (MRI). Magnetic resonance imaging has proved its superiority in both micro-adenomas (sensitivity limit: around 2 mm) and macro-adenomas. However, CT can be used for reasons of accessibility or to better explore the bony framework. A rounded intraparenchymal signal anomaly may be observed in up to 10% of control subjects ("pituitary incidentalomas") and should therefore only be interpreted in the light of the clinical and biological context [5].

In our case, pituitary MRI showed a macroadenoma measuring 49 mm in anteroposterior diameter, 28 mm in height and 23 mm in transverse diameter, unlike the Congolese and Gabonese series [6, 7] where MRI or CT scans were not available. Ophthalmological examination using the fundus and Goldman's kinetic campimetry, which shows visual field abnormalities, helps in the diagnosis. Our patient did not benefit from Goldman's kinetic campimetry, although it has been performed in patients of other authors [6, 7].

A plain radiograph of the skull, even one centred on the sella turcica, is not sufficiently sensitive and should not be used for diagnostic purposes [5].

Hypersecretion Syndrome:

***A. GH hypersecretion* (Acromegaly)**

1 - Clinical features:

Acromegaly or "singular non-congenital hypertrophy of the upper, lower and cephalic extremities", first described by Pierre Marie in 1886 [8], is a rare condition with an estimated prevalence of between 40 and 60 per million population and an incidence of between 3 and 4 new cases per million per year [9]. It is due to hypersecretion of growth hormone

(GH), most often from a pituitary adenoma and more rarely from a hypothalamic or ectopic tumour producing GH or CHRH (somatoliberin) [10, 11].

The clinical presentation associated with chronic hypersecretion of GH (growth hormone) is characterised by the progressive onset of morphological changes: prognathism, enlargement of the hands and feet necessitating changes in shoe size, and thickening of the features, particularly the nose and lips [5]. In this case, the clinical signs, characterised mainly by the dysmorphic syndrome, are in line with the data in the literature [12, 13] and confirmed by other African authors [6, 7]. Acromegaly is a disease of young adults. The age of our patient, 36, is close to that of patients in the Congolese series (three men aged 36, 40 and 42 and two women: one aged 43 and the other aged 61) and the Gabonese series (one man aged 45) [6, 7].

Complications of the disease are also frequent: diabetes, arterial hypertension, cardiomyopathy, gonadotropic deficiency, visual disorders, etc. In our case, it was a case of type 2 diabetes mellitus, probably secondary to acromegaly, which had only been diagnosed after 5 to 6 years. Insidious symptoms and slow progression make the condition difficult to detect in its early stages. It often goes undetected for many years. This confirms the long latency of the condition, which takes an average of 9.2 years to diagnose [14].

2 - Biology:

The diagnosis of acromegaly is based on the presence of an elevated plasma concentration of GH, which cannot be controlled by induced oral hyperglycaemia. The diagnosis is confirmed by an increase in the concentration of *insulin-like growth factor-1*(IGF-1), the main GH-dependent growth factor, with reference to age-dependent norms. [15]. In our case, IGF1 was elevated to 561.9 µg/ml (VN=116-353). Acromegaly is most often induced by a benign tumour of the pituitary gland which causes hypersecretion of growth hormone. In the Gabonese series [7], GH (measured abroad) was 38.50 ng/ml (N < 7).

The evaluation of the repercussions of acromegaly (cardiac ultrasound, search for sleep apnoea, colonoscopy, etc.) was completed by an assessment of other pituitary functions, in search of associated anteropituitary insufficiency linked to compression, by the tumour, of the normal pituitary gland or pituitary stalk [8]. Baseline cortisol, TSH (us), FSH and LH were all normal in our patient as in the Gabonese series [7].

B. Prolactin hypersecretion

1 - Clinical:

The endocrine repercussions of hyperprolactinaemia manifest early on in premenopausal women in the form of cycle disorders (oligospaniomenorrhoea, amenorrhoea), galactorrhoea, sexual disorders (reduced libido, vaginal dryness, dyspareunia), and sometimes only in the form of infertility due to anovulation with preservation of cycles. The mechanism by which gonadal function is impaired is inhibition of the release of hypothalamic LHRH (luteinizing hormone releasing hormone) induced by excess prolactin. In post-menopausal women, galactorrhoea is rare, and it is the tumour syndrome that is indicative [1].

The symptoms in men, which lead to diagnosis later than in young women, include sexual problems (reduced libido, erectile dysfunction, erectile impotence), reduced facial or somatic hair growth and rarely gynaecomastia or even galactorrhoea [5]. Our patient presented clinically with erectile dysfunction and reduced libido. As for the patient in the Gabonese series [7], he had consulted for secondary sterility which had been evolving for some twenty years.

2 - Biology:

GH hypersecretion is very often associated with hypersecretion of the hormone prolactin, which controls mammary gland growth, milk secretion and fertility. Prolactinemia in our patient was high at 463.3µUI/ml (VN: 24-324) in contrast to the patient in Gabon [7] and 2/5 patients in Congo [6] where it was normal. In 1/5 patients in Congo, it was 20ng/ml.

Treatment:

Treatment is based on medical, surgical and radiotherapeutic means. By acting on D2-type receptors, dopaminergic agonists (bromocriptine or Parlodel, lisuride or Dopergine, quinagolide or Norprolac, cabergoline or Dostinex) make it possible in the majority of cases of prolactinoma to restore normal sexual and reproductive function, normalise prolactin levels and reduce tumour volume without, however, causing the adenomatous cells to disappear. They can reduce GH levels in less than 20% of acromegalic patients [5].

In general, transsphenoidal surgery remains the first choice of treatment, but is effective in 60-70% of cases [16, 17], with failures being treated by radiotherapy [18] and/or medical therapy.

When surgical treatment has failed to cure GH hypersecretion, medical treatment using cabergoline and, above all, somatostatin analogues is proposed, followed, if these drugs are not sufficiently effective (possibly combined), by the GH antagonist (Pegvisomant) [15].

Our patient was treated with Dostinex 0.5mg/week with a progressive increase in dose for GH and prolactin hypersecretion syndrome. To treat hyperglycaemia, he was prescribed insulin. The patient also benefited from a neurosurgical opinion and is awaiting removal of the adenoma after glycaemic control and normalisation of hormones, as was the case in the Congo and Gabon [6, 7].

As a last resort, radiotherapy (fractionated conventional radiotherapy or a single gamma-knife session) completes the therapeutic armoury and brings the disease under control in almost all cases [15].

Evolution:

Tumour syndrome: resolution of headaches and improvement in vision.

GH and prolactin hypersecretion syndrome: regression of prolactinemia after 7 months on DOSTINEX 0.5 mg to 38.54 µIU/ml on 27/09/2022 compared with 463.3 µIU/ml (VN: 24-324) on 15/02/2022.

For diabetes: improvement in glycaemic control (HbA1c of 9.90% on 27/09/2022 compared with 11.10% on 21/05/2022) on insulin. Maintain insulin therapy.

4. CONCLUSION

The management of pituitary adenomas requires multidisciplinary collaboration involving endocrinologists, gynaecologists and neurosurgeons.

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