



## Pituitary Incidentalomas: A Tunisian Experience

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### Abstract

**Background:** Pituitary Incidentalomas (PI) are pituitary lesions that are unexpectedly discovered on brain imaging conducted in order to explore symptoms un-suggestive of a pituitary disease.

The aim of our study is to describe the clinical, biochemical and radiological characteristics of PI and to detail the therapeutic and evolutive modalities.

**Methods:** This is a descriptive retrospective study conducted at the Endocrinology-Diabetology Department of the Hedi Chaker University Hospital in Sfax-Tunisia, after collecting medical records of 12 patients with PIs between January 2000 and December 2020. We included patients with PI who underwent adequate biochemical evaluation and we excluded patients who were not explored.

**Results:** We collected the data of 12 adult patients (8 men and 4 women). The mean age of our study group was 46.2 years [18 to 75 years]. The diagnosis of PI was established following a brain MRI in 8 patients and CT scan in 4 cases, of which 3 had then MRI. All PIs in our series were pituitary adenomas. Radiological and biochemical investigations concluded that nine of our patients had non-functional pituitary adenomas including 2 microadenomas while the remaining three were prolactinomas. Headache was the most common revealing circumstance of PI, found in 5 cases. In our study, three of our patients reported sexual complaints. Clinical hypothyroidism without goiter was found in 4 patients while one patient presented thyrotoxicosis with two palpable thyroid nodules. The clinical examination revealed no acromegalic nor cushingoid features in all patients. Hormonal assessment confirmed a gonadotropic and corticotropic insufficiency in three male patients. As for serum prolactin, it was elevated in four patients. Visual acuity assessment was reported in only 10 patients. It was normal in 2 patients, while 8 patients had a decreased Visual Acuity (VA). Prolactinoma were treated with an average dose of 3 mg per day of bromocriptine. Post-surgical complications were noted in 3 cases. Gonadotropic was the most common complication found in all three cases while corticotropic and thyrotrophic insufficiency and diabetes insipidus were noted in one case. Our series included one case of post-operative purulent meningitis.

**Conclusion:** Pi is a frequent finding that should be taken seriously since it can be a life-threatening tumor and therefore a careful clinical examination, hormonal, radiological, ophthalmological assessment is crucial in order to dictate the appropriate management of the lesion.

**Keywords:** Thyrotoxicosis; Hypothyroidism; Hyperthyroidism; Diabetes insipidus

### Abbreviations

PI: Pituitary Incidentaloma; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; VA: Visual Acuity; CD: Corticotrope Deficiency; ACTH: Adrenocorticotrophic Hormone; TSH: Thyroid Stimulating Hormone; IGF: Insulin Growth Factor; GH: Growth Hormone; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; NFPA: Non-Functional Pituitary Adenoma; PS: Pituitary Stalk; PRL: Prolactin; SFE: French Society of Endocrinology; OC: Optic Chiasm; DA: Dopaminergic Agonist; DI: Diabetes Insipidus; SIADH: Syndrome of Inappropriate Antidiuretic Hormone Secretion

### Introduction

Pituitary Incidentalomas (PI) are pituitary lesions that are unexpectedly discovered on brain imaging conducted in order to explore symptoms un-suggestive of a pituitary disease [1]. There are mainly two types of PI: Micro-incidentomas (<10 mm) and macro-incidentomas ( $\geq 10$  mm) [2]. They can be either functional or nonfunctional.

The aim of our study is to describe the clinical, biochemical and radiological characteristics of PI and to detail the therapeutic and evolutive modalities.

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Received Date: 18 Feb 2022

Accepted Date: 25 Mar 2022

Published Date: 13 Apr 2022

#### Citation:

Hadjkacem F, Ben Bnina M, Trimeche O, Frikha H, Charfi N, Mnif M, et al. Pituitary Incidentalomas: A Tunisian Experience. *Ann Clin Diabetes Endocrinol.* 2022; 5(1): 1025.

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## Methods

This is a descriptive retrospective study conducted at the Endocrinology-Diabetology department of the Hedi Chaker University Hospital in Sfax-Tunisia, after collecting medical records of 12 patients with PIs between January 2000 and December 2020. We included patients with PI who underwent adequate biochemical evaluation and we excluded patients who were not explored. Clinical and paraclinical data were extracted from medical files and for each patient, a pre-established information sheet has been made to collect demographic and socioeconomic data as well as personal and family health history. Our clinical evaluation was based on reasons of consultation and on clinical presentation. All patients had brain imaging: MRI or tomography both done at the Radiology Department of Hedi Chaker Hospital or Habib Bourguiba Hospital in Sfax and most of them had visual field test. Both static and dynamic hormonal testing were carried out at the laboratory of biochemistry at Habib Bourguiba Hospital in Sfax.

### Dynamic hormonal evaluation

Dynamic tests were performed in order to identify or rule out hypopituitarism and/or hormonal hypersecretion.

The diagnosis of a Corticotrope Deficiency (CD) was made based on a low morning serum cortisol (<50 µg/L) associated with a normal or low Adrenocorticotropic Hormone (ACTH). A morning cortisol value over 180 µg/L ruled out cortisol deficiency. For intermediate cortisol levels between 50 and 180 µg/L, the 1 µg ACTH stimulation test was needed and the diagnosis of CD was established based on stimulated serum cortisol level under 180 µg/L assessed after 30 min or 60 min of ACTH injection. Although Insulin hypoglycemia test is rarely used, it is considered the gold standard for the diagnosis of adrenal insufficiency. A cortisol peak level above 180 µg/L (500 nmol/L) after hypoglycemia obtained by intravenous insulin injection of 0.1 IU/kg dismissed corticotrophin deficiency.

A corticotroph adenoma was diagnosed based on an ACTH level greater than 15 pg/ml to 20 pg/ml and an autonomic secretion of cortisol identified with standard 2-day dexamethasone suppression test.

Central hypothyroidism was defined as an abnormally normal or low Thyroid-Stimulating Hormone (TSH) associated with low free Thyroxine (fT4). Increased or normal TSH levels with high thyrotropin serum level was suggestive of a TSH-producing incidentaloma. Unsuppressed GH levels after a 75 g oral glucose tolerance test (a threshold of GH at the time of nadir higher than 0.4 µg/l or 1.2 mUI/l) and high Insulin-like Growth Factor (IGF)-1 level made the diagnosis of Growth Hormone (GH) secreting adenoma. If the GH level was lower than 0.4 µg (<1.2 µmol/l) and the IGF-1 level was normal, acromegaly was ruled out. Low estradiol levels in premenopausal women or low testosterone levels in men with inappropriately normal or low gonadotropins: Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) provided confirmation of central hypogonadism.

Hyperprolactinemia is defined as a prolactin level above 25 ng/ml. A prolactin level greater than 500 ng/ml is in favor of the diagnosis of a macroprolactinoma. Although a prolactin level above 250 ng/ml is indicative of a prolactinoma, it could be imputable to some drugs and therefore their implication in elevating prolactin level should be determined. The diagnosis of Non-Functional Pituitary Adenoma (NFPA) was made after excluding hormonal hypersecretion (with

the exception of gonadotropins). When surgery was indicated, it was performed at the Neurosurgery Department of the Habib Bourguiba University Hospital in Sfax or at the National Institute of Neurology Mongi Ben Hmida in Tunis. The anatomopathological study was carried out in the majority of cases at the anatomic pathology laboratory of the Habib Bourguiba University Hospital in Sfax. Statistical analyses were performed using SPSS version 20 Windows.

## Results

### General characteristics of the study population

We collected the data of 12 adult patients (8 men and 4 women), Sex ratio was 2. The mean age of our study group was 46.2 years (between 18 and 75 years). Two of our patients were above 65 years. Medical history showed hypertension in four of our patients, type 2 diabetes treated with oral anti diabetic drugs in one patient and Down syndrome with mild mental retardation in one patient. Only one of our female patients had menopause.

### Clinical study

Headache was the most common revealing circumstance of PI, which was found in 5 cases. It was incidentally discovered on an MRI performed while controlling a hemorrhagic stroke, post-surgical neuroma, and while exploring a Cavum tumor and an atypical seizure in one case each. The search for a brain thrombophlebitis in a context of facial staphylococcal infection led to the discovery of the PI in another case and it was loss of consciousness and head trauma that led to the discovery of the PI in the two remaining cases. In our study, three of our patients reported erectile dysfunction, with only one patient having in addition to his erectile dysfunction a loss of libido. The clinical examination revealed no acromegalic nor cushingoid features, signs of hypothyroidism without goiter in 4 patients and signs of hyperthyroidism with two palpable thyroid nodules in one case.

### Radiographic study

The diagnosis of PI was established following a brain MRI in 8 patients and CT scan in 4 cases of which 3 had then MRI. All PIs in our series were pituitary adenomas. Our data revealed:

- Two microadenomas measuring 7 mm and 9 mm respectively.
- Ten macroadenomas with an average size of 24 mm (extremes ranging from 12 mm to 51 mm). Among these, there were two giant PI with a size of 42 mm and 51 mm respectively. Two of the PI of our series were abutting the optic chiasm while the compression of the latter was found in a suprasellar PI in 2 of our patients. An invasion of the opto-chiasmatic tank and the compression of the third ventricle was noted in only one case. Two patients had macroadenomas with lateral extension to the cavernous sinuses without encasing the carotid artery. The Pituitary Stalk (PS) was median in 5 cases, pushed back in 4 other patients and ascended in the last case.

### Hormonal assessment

Thyroid function was normal in 7 cases with an average FT4

**Table 1:** Cases with impaired thyroid function.

FT4	TSH	Diagnostic
26.1 pmol/ml	0.8 µUI/ml	Central hyperthyroidism
4.4 pmol/ml	>100 µUI/ml	Primary hypothyroidism
7.53 pmol/ml	2.24 µUI/ml	Thyrotropic insufficiency
5.4 pmol/ml	0.95 µUI/ml	Thyrotropic insufficiency
12.55 pmol/l	4.61 µUI/ml	Subclinical hypothyroidism

**Table 2:** Overview of discovery circumstances in literature and in our study.

Studies	Headache	Visual disturbances	Neurological Signs	Others
Our study	44.44%	22.22%	22.22%	22.22%
Eteves et al.	33.80%	3%	14%	49.20%
Anagnostis et al. [8]	43%	3%	16%	38%

**Table 3:** Immunohistochemical studies of operated pituitary adenomas.

Study	Immuno negative	FSH/LH	PRL	GH	ACTH	Mixed secretion
Arafah et al.	32%	28.50%	14.20%	16.30%	0%	8%
Day et al. [26]	31%	23%	0%	15%	31%	0%

of 11.96 pmol/ml and an average TSH of 1.98  $\mu$ UI/ml (Table 1). Impairment of the thyroid axis was noted in 5 cases (Table 2). Three male patients had gonadotropic insufficiency with an average testosterone level of 1.23 ng/ml (1-1.5), an average LH level of 1.43 ng/ml (0.48-2.1) and an average FSH level of 5.43 ng/ml (1.1-10.4). The average prolactin level of our patients was 309.43 ng/ml with extremes ranging from 14.7 ng/ml to 1917 ng/ml. Four patients had elevated serum prolactin resulting from pituitary stalk effect with an average of 37.08 ng/ml (extremes ranging from 32.6 ng/ml to 42 ng/ml).

The mean morning serum cortisol level (8H) was 119.33 ng/ml (11-201.7). One patient had a low cortisol level (11 ng/ml) and low ACTH level at 6 pmol/l which is indicative of CD. For this patient, 1  $\mu$ g ACTH stimulation test was performed (T0: 11, T30: 153, T60: 175 ng/ml). CD was also found in a second patient with ACTH 8 pg/ml, 1  $\mu$ g ACTH stimulation test was therefore performed (T0=75, T30=130 and T60=140 ng/ml) as well as insulin hypoglycemia test which revealed a serum cortisol of 123.8 ng/ml. Based on low cortisol level (96.3 ng/ml) and low cortisol stimulated with 1  $\mu$ g ACTH (152.4 ng/ml) a third patient was diagnosed with CD. Unfortunately, the ACTH level was unknown. As for the rest of patients, they had a normal adrenal function. Nine patients had GH and IGF1 measurements and were normal with a mean GH and IGF1 level of 193.11  $\mu$ g/L (97-308) and 0.24  $\mu$ g/L (0.1-0.35), respectively. Our radiological and biochemical investigations concluded that nine out of twelve of our patients had non-functional pituitary adenomas including 2 microadenomas and three out of the twelve PI were prolactinomas.

### Visual repercussion of the pituitary incidentaloma

Visual acuity assessment was reported in only 10 patients. It was normal in 2 patients, while 8 patients had a decreased Visual Acuity (VA). Six of our patients had a visual field test and it was abnormal in 4 cases: Unilateral isopter contraction in one case and bilateral abnormalities in 3 cases. Fundus was enrolled in 11 patients and abnormal results were found in 3 patients who had respectively bilateral papillitis, stage II papillary edema in the left eye and bilateral papillary edema. Because of the cataract, fundus was impossible in only one case.

### Therapeutic management

Bromocriptine was taken by 3 patients having a prolactinoma with an average dose of 3 mg per day. Hydrocortisone replacement dose at 20 mg was giving to three patients with CD. Two of our patients suffering from thyrotrophic insufficiency were giving L-thyroxine 100  $\mu$ g per day. Five of our patients were referred to surgery, three with non-functional macroadenoma and one who had a prolactinoma with optic nerve compression. Pituitary apoplexy with visual disturbance of a nonfunctional macroadenoma was the cause of referral to surgery

in the last case. Patients who had surgical removal of their tumors had systematic perioperative and postoperative coverage with intravenous hydrocortisone. The transsphenoidal resection was the technique of choice.

### Monitoring and evolution

Patients with incidentalomas who do not met criteria for surgical tumor removal had received both clinical and paraclinical follow-up, it was the case for 2 microadenomas and 3 macroadenomas. For microadenomas, clinical, biochemical (PRL, LH, FSH, TSH, FT4) and radiological monitoring were performed yearly and the results were unchanged. For macroadenomas, the clinical and biochemical follow-up, in 3 of the cases was normal during the first 2 control visits and on follow-up MRI scans, no adenoma enlargement was found. In our series, there was only one prolactinoma who had a regular clinical and biochemical follow-up. The patient's prolactin level was normalized after 3 months of treatment with a 5 mg per day Bromocriptine and no hypopituitarism was found during follow-up. He did not however have an MRI scan during his follow up. Tumor removal was complete in 4 cases and partial in the fifth. Post-surgical complications were noted in 3 cases. The first had definitive central insipidus diabetes, corticotropic and gonadotropic insufficiency treated with desmopressin, hydrocortisone and testosterone enanthate, respectively. The second had purulent meningitis treated with antibiotics, gonadotropic and thyrotrophic insufficiency treated with L-thyroxine and testosterone enanthate and the third patient had a gonadotropic deficiency.

## Discussion

### Epidemiological data

The incidence of PIs is estimated to be 24.4/100,000 habitants and its prevalence is about 1.62% of brain tumors [2-5]. Our study collected the data of 12 patients diagnosed with PI, over a period of 21 years, which corresponds to an estimated incidence of 0.57 cases/year. The average age of diagnosis according to Vaninetti et al. [6], Imran et al. [4] and Anagnostis et al. [7], is 53.7, 55 and 53 years respectively. The sex ratio according to these same three studies is estimated at 0.83, 0.92 and 1.65 respectively. And therefore, our results are consistent with the literature regarding the epidemiological characteristics of PIs.

### Clinical data

The circumstances of discovery of PI were headaches, visual and/or neurological disorders (Table 3). Headaches are described in more than 70% of macro-adenomas in the literature [8,9] explained by the mass effect. Otherwise, visual impairment is related to the pituitary mass effect on the optic pathways and the result is an upper temporal quadrantanopia or, at a later stage, a bitemporal hemianopsia.

## Biological assessment of pituitary incidentalomas

Screening for a pituitary hypersecretion is recommended in all patients with PI with a minimal endocrine panel: Prolactin (PRL) and IGF1 [2,10]. However, it is not systematic to screen for glucocorticoid excess in asymptomatic people. Prolactinomas are the main feature of functional macro-adenomas in our study. In literature, the prevalence of prolactinoma varies from 8.6% to 11.94% depending on the study [11,12]. Although silent somatotrophic tumors are rare, a screening for GH excess is recommended. In a prospective study, 1 in 11 macroadenomas had high IGF1, consisting with a subclinical excess of GH [13]. The PRL measurement was conducted in all of our patients, but an IGF1 measurement was only done for only three patients. None of our patients were screened for Cushing disease because they didn't show any signs of glucocorticoid excess. Several studies report that microadenomas cause rarely hypopituitarism [14,15]. Our 2 patients with a micro-PI had no hypopituitarism, whereas macroadenomas are more likely to cause hypopituitarism (85%) due to its possible compression of the hypothalamus, the pituitary stalk and the pituitary gland itself [16,17]. The majority of PIs are Non-Functional Pituitary Adenomas (NFPA): According to Anagnostis et al. [7] 77% of the PIs studied were NFPA and according to the Day et al. [18] study 50 % of PIs were NFPA, which is consisting with our study, 9 out of 12 PIs were NFPA which are mostly gonadotrophic adenomas, secreting FSH, LH or alpha sub-unit but can also be silent adenomas.

## Ophthalmological examination

The French Society of Endocrinology and the Endocrine Society recommend an ophthalmological examination in PI abutting the Optic Chiasm (OC). Nevertheless, the French Society of Endocrinology (SFE) does not recommend this evaluation if the pituitary incidentaloma is a microadenoma. Ophthalmological assessment consists of the measurement of visual acuity, pupil examination, fundus, examination of the oculomotor nerves by the Hess Lancaster test and the visual field by the Goldmann method [2] and so an ophthalmological examination was required in our ten patients with macroadenomas. There is no consequence to a PI abutting the anterior visual pathways. We found a patient who had a normal visual acuity even though he had a macro-adenoma filling the opto-chiasmatic tank without compression of the OC. Two other patients with similar MRI lesions had decrease in visual acuity explained in those cases by the macular field damage.

The visual field defects seen in PI are usually asymmetrical. First affecting the upper and then the lower temporal quadrants, which results in bitemporal hemianopsia, then the lower and superior nasal quadrants. The bitemporal hemianopsia scotoma is one of the most frequent defects of the visual field found in literature with a prevalence of 5.55% to 33%. This latter visual complication was observed in one patient (8.3%). According to Day et al. [18] 22% of PIs studied had visual disorders: 40% had a bitemporal hemianopsia, 30% had quadrantanopia, 20% had overall impairment, and 10% had scotoma.

## Morphological study: Hypothalamic-pituitary imaging

Findings from our study showed that macro adenomas are majoritarian with a prevalence of 83%, of which 0.16% are giant prolactinomas. According to literature, giant prolactinomas represent 0.5% to 4.4% of all pituitary tumors [19,20,17]. The extension of adenomas generally occurs in the suprasellar region. It results in a compression of the optic chiasm and/or of the third ventricle with different degrees that can generate hydrocephalus in the case of

voluminous PIs. However, micro-PIs are almost always intrasellar and rarely cause visual field alteration. According to the Iglesias et al. [19] study, 86.4% of PIs had shown suprasellar extension with chiasm compression observed in 73.7% of patients. In our case, two patients with macroadenomas had suprasellar extension resulting in chiasm compression. As for the infra-sellar extension, it causes remodeling of the floor Sella or in more severe cases, an invasion of the sphenoidal sinus, which was not found in our series. Laterosellar extension is characterized by the invasion of the cavernous sinus which can alter the prognosis and thus the management of the PIs. In literature, cavernous sinus invasion was found in 6% to 10% of cases [21]. Our study found similar results with 2 patients suffering from the cavernous sinus invasion.

## Management

**Medical treatment:** Replacement therapy should be instituted for patients suffering from hypopituitarism.

Corticotrope deficiency should be treated with hydrocortisone at a dose of 20 mg in the morning with an additional dose of 5 mg to 10 mg in the middle of the afternoon [22]. It was the case for 3 of our study subjects. L thyroxine is the treatment of choice for Central hypothyroidism. Given the accelerated degradation of cortisol by thyroid hormones which can result in a considerable risk of acute adrenal insufficiency, it's first essential to substitute the corticotrophic axis and then the thyrotrophic axis. As for growth hormone deficiency, the treatment with GH remains controversial in older adults, unlike in younger subjects [23,24]. The substitutive dose is based on age, sex and body weight. The initial dose is low and will subsequently be adapted to height, bone age and serum IGF1 [25]. In premenopausal women, adequate hormonal replacement therapy should be instituted if gonadotrophic insufficiency is confirmed [26]. Men should benefit from a testosterone substitution, in order to improve libido, treat erectile dysfunction, stimulate erythropoiesis, optimize muscle mass and bone density. It's generally administered with an intramuscular injection every 4 weeks [22]. Three of our patients had gonadotrophic insufficiency, two of which were treated with Enanthate testosterone. Dopaminergic Agonists (DA) are the curative treatment for most of prolactinomas. It lowers secretion and thus tumor volume through D2-like receptors. Since its efficiency and tolerability, Cabergoline is currently the recommended DA when treating prolactinoma [27]. Conversely, in our study Bromocriptine was prescribed in the three cases of macro prolactinoma, only because it's more affordable than Cabergoline.

**Surgical treatment:** According to the Endocrine Society, surgery is indicated when PI is complicated with visual field deficit, neurological or visual abnormalities, compression of optic nerve or the chiasm, pituitary apoplexy with visual impairment, functional adenomas other than prolactinomas, disabling headaches and hypopituitarism [28]. It is also indicated in case of pregnancy desire with a tumor near the optic chiasm. As for secreting PIs, some experts recommend medical treatment in the absence of visual or neurological damage in order to reduce tumor size and normalize hormonal secretion [28-30]. In our study, the surgical treatment was indicated in 5 cases: 3 non-functional macro-PIs and 1 prolactinoma with optic nerve compression. The fifth patient had invalidating headaches due to an apoplexy of macroadenoma. Since it's a minimally invasive technique, the endoscopic endonasal transsphenoidal surgery is the actual recommended surgical approach for PI. And thus, it was the surgical approach chosen in our 5 patients who underwent pituitary surgery.

Among our five operated patients, the histopathological examination was done in only 3 patients. The anatomopathological study provided confirmation of the adenoma nature of the pituitary lesions with no signs of malignancy. As for the immunohistochemical study, it was conducted in 2 of our patients, showing a GH and prolactin secreting adenoma in one case and a GH- secreting adenoma in the other one. According to the SFE, immunonegative pituitary adenomas do not exceed 1%. They are gonadotropic in 35% and silent in 8% of operated PI.

### Monitoring and evolution of pituitary incidentalomas

**Non-operated patients:** The increase in size, even in the case of macro-PI, is not systematic. On average, 89% of microadenomas and 75% of macroadenomas remain stable after two to eight years of follow-up [10].

Therapeutic abstention with close follow-up was indicated in 5 cases in our series. For non-functional microadenomas, the SFE doesn't recommend any radiological or hormonal monitoring if the size of the adenoma is less than or equal to 5 mm. MRI scan is indicated 6 months after the initial scan if it's a macroincidentaloma and after 1 year in case of a micro incidentaloma. In patients whose incidentaloma doesn't change in size, it's recommended to perform an MRI every year when it's a macroincidentaloma and every 1 to 2 years if it's a microincidentaloma, according to the ES. In our series, MRI monitoring objectified a stable aspect of the 2 micro-PI joining the studies [10,31,32]. Visual field was indicated in one of the two patients who had a microadenoma close to the optic chiasm and it was normal. If the macroadenoma is abutting the optic Chiasm, MRI and an ophthalmological assessment including visual field exam and measurement of visual acuity, must be performed at six months. Otherwise, it is necessary to perform a clinical and biochemical evaluation of hypopituitarism and an MRI yearly. In our study, monitoring of macroadenomas was indicated in 3 cases. In two cases morphological and hormonal follow-up showed no change, the other patient didn't proceed with the follow-up.

**Outcomes of the operated patients:** Several complications can be observed following the pituitary surgery. For instance, postoperative cerebrospinal fluid-leaking rhinorrhea is the most common complication of the trans-sphenoidal approach, and could lead to meningitis. This complication was found in 0.9% and in 1.5% to 4.2% of cases according to Roux et al. [33], and to a multicentric study Ciric et al. respectively [34]. Purulent meningitis was seen in only one of our operated patients. Central Diabetes Insipidus (DI) is another possible complication of pituitary surgery. A triphasic response is often noted, characterized by three consecutive phases: DI lasting 5 to 7 days, followed by second phases which can last 2 to 4 days, of inappropriate Antidiuresis (SIADH) due to uncontrolled AVP release from the degenerated nerve endings in the posterior pituitary gland. The third phase consists of the recurrence of DI, which is often permanent, due to depleted AVP deposits and insufficient secreting neurons [35]. Following the transsphenoidal pituitary surgery, the prevalence of transient and definitive CID ranges from 2% to 30% according to the studies [36,37]. Definitive central insipid diabetes was found in only one of our cases. Post operative hematoma at operation site is the most devastating complication of pituitary surgery. Carotid artery wound is noted in 0.4% of cases [38]. In our series, only one case of intraoperative hemorrhage was noted due to a lesion of the carotid artery. Mortality is noted in less than 0.6% according to literature. Meningitis, which was a major cause of death, has become rare since

the use of antibiotic prophylaxis. The major risk of death remains when removing large tumors invading the floor of the 3<sup>rd</sup> ventricle [39]. There were no deaths in our study. Pituitary adenomas require regular and long-term monitoring to detect early complications or possible tumor recurrence [36,37]. This has not been possible for all our patients because of socio-economic difficulties.

According to Diop et al. [40], 78% of patients were relieved after surgery from headaches. It was the case for 2 of our followed cases. The hormonal assessment should be performed 3 months after the operation and repeated if the patient had clinical signs suggestive of hypopituitarism or has a persistent hypopituitarism [40]. The resolution of one or more hormonal deficiencies after pituitary surgery can be expected in 35% to 50% of patients, with a resolution of hyperprolactinemia noted in more than two-thirds of patients [41]. Surgery can also induce one or more pituitary axis deficiencies in 2% to 15% [41]. Among our 5 operated patients, 2 patients had partial postoperative hypopituitarism. Pituitary stalk hyperprolactinemia has disappeared in all of our operated patients. Ideally, post-operative MRIs should be performed at least 3 to 6 months after surgery to assess the post operative tumor. A second MRI will be performed, in all cases, one year after the surgery. These two MRIs will serve as a reference for further follow-up. If there is no tumor residue, very long-term radiological monitoring is necessary. The MRI will be repeated every year for 5 years, then at 7, 10 and 15 years after surgery. In case of confirmed or suspected tumor residue on imagery, an MRI will be performed every year for 5 years and then every two to three years if the tumor volume remains stationary. The duration and the interval of follow-up could be redefined on a case-by-case basis, depending on the tumor volume and the distance between the tumor residue and the optical pathways. Particular vigilance is necessary because recurrences most often occur 1 to 5 years after surgery and sometimes later up to more than 10 years after the initial surgery. In our series, only 3 patients had radiological follow-up. For the first two cases, a single MRI control at 6 and 8 months respectively was performed, while for the third one an MRI was conducted immediately following surgery and two MRI were then carried out at a one-year interval. All 3 cases showed no residue tumor or recurrence.

In case of preoperative visual abnormality, a complete ophthalmological assessment with visual acuity, visual field test and fundus examination should be done 3 months after surgery. In the absence of any visual impairment during the first post-operative examination, follow-up may be stopped if there is no tumor residue abutting the optic pathways [41-45]. The ophthalmologic control was performed in 2 patients and had objectified an improvement of their visual function.

### Conclusion

Pi is a frequent finding that should be taking seriously since it can be a life-threatening tumor and therefore a careful clinical examination, hormonal, radiological, ophthalmological assessment is crucial in order to dictate the appropriate management of the lesion.

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