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(CASE REPORT)

Pituitary adenomas in children and adolescents: Diagnostic challenge

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Abstract

Pituitary adenomas have a low incidence in pediatric and adolescent patients, ant they are usually benign and relatively common intracranial tumors, with under- and overexpression of pituitary hormones and local mass effects causing considerable morbidity and increased mortality

We report the observations of three patients who presented visual disorders, an MRI was done objectifying a sellar tumoral process with suspicion of a craniopharyngioma for the 3 cases, a surgical treatment was indicated with rectification of the diagnosis after the anatomopatho-immunohistochemical study, which concluded to a prolactinoma for 1st end 2nd cases which were put under dopamine agonists, and to a somatotropic adenoma for 3rd case which was addressed for revision surgery.

Immunohistochemistry remains the key element in diagnosing pituitary tumors and orientating their management.

The management of pituitary adenomas in pediatric patient's mimic's patterns of management in the adult population end requires a multidisciplinary management.

Keywords: Pediatric pituitary adenomas; Craniopharyngioma; Prolactinoma; somatotropic adenoma; Anatomopatho-immunohistochemical study; Transsphenoidal pituitary surgery

1. Introduction

Pituitary adenomas (PA) are benign well-differentiated tumors, with monoclonal development from the anterior pituitary gland, which can result in serious complications, in particular endocrine, metabolic and visual.

They represent 10%–25% of all intracranial neoplasms and the estimated prevalence rate in the general population is 17%.

Pituitary adenomas are, however, rare in children and adolescents constituting only about 3% or less of all diagnosed intracranial tumors and 5% of all pituitary adenomas (5–9). Due to its rarity and complexity, pediatric pituitary adenoma has been relatively infrequently studied, and recommendations regarding its optimal management are debated.

The aim of the study is to discuss the clinico-radiological and etiological characteristics of pituitary tumors in the pediatric population, with particular interest in the medical and surgical management, and associated adjuvant therapy.

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2. Observation

2.1. 1st case

A 14 years and 5 months old male child, who presented with a left migraine evolving for 5 years with trigeminal neuralgia.

A brain MRI was performed revealing a sellar tumor process measuring 24×32×21mm.

A craniopharyngioma was suspected and the patient was operated in November 2018 by transsphenoidal approach, with simple operative follow-up.

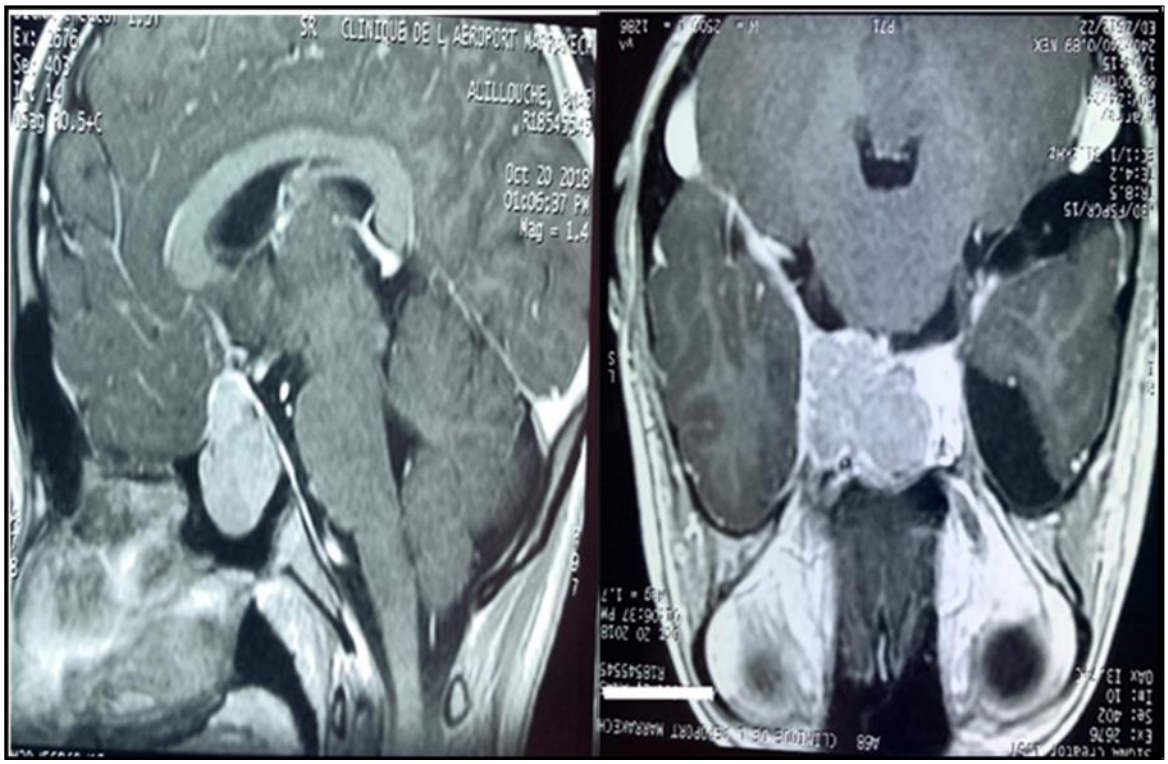

Figure 1 Preoperative sagittal end coronal hypothalamic-pituitary MRI showing a sellar tumor process measuring 24×32×21mm

The anatomo-pathology study was in favor of an immunohistochemical appearance of a pituitary prolactin adenoma with a Ki 67 10%.

The patient was referred to the endocrinology department for complementary management

The clinical examination showed a child with a weight of 39 kg and a height of 1.47 m (-2DS), the Tanner stage was P1G2 (6ml)

The hormonal evaluation showed a hyperprolactinemia at 470ng/ml with FSH: 1,4UI/l LH: 0,9UI/l testo:0,1µg/l, cortisol: 17µg/dl TSH:0,9 UI/l T4: 18pmol/L

The patient was put on cabergoline at a dose of 1 mg/week with a good clinical and biological improvement: disappearance of headache and neuralgia with à Prolactin level of 53 ng/ml.

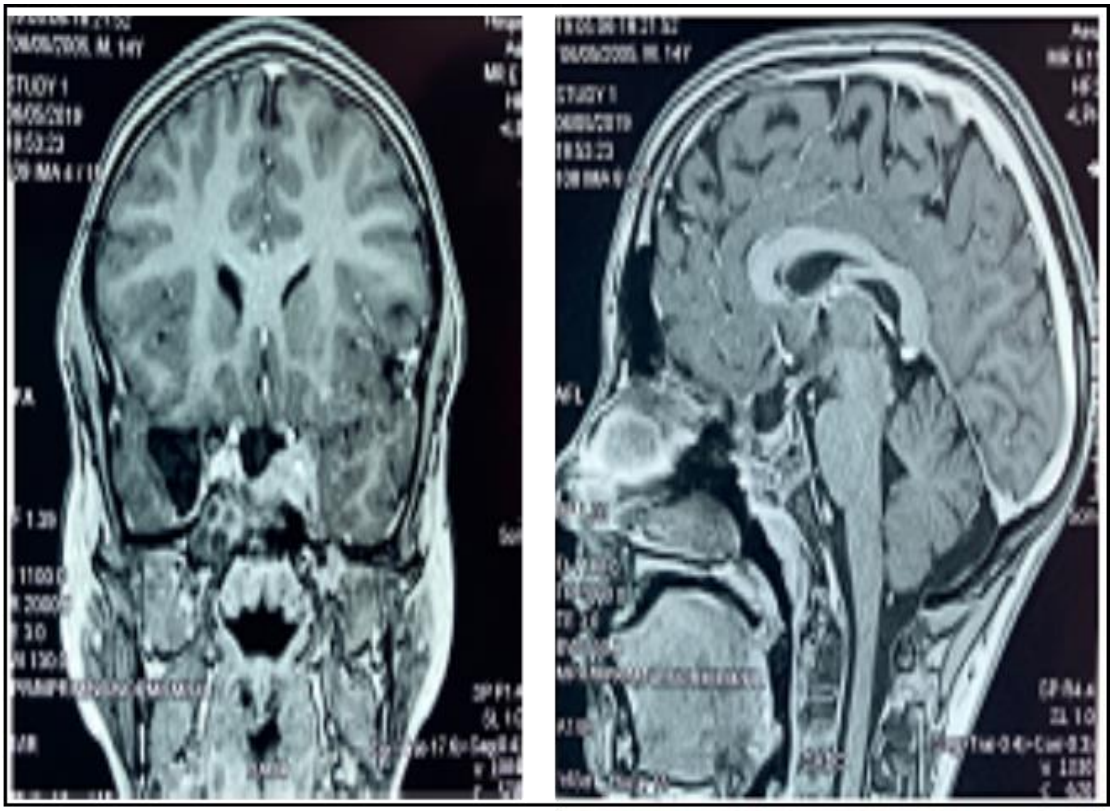

Figure 2 Follow-up coronal end sagittal section MRI showing a pituitary adenoma measuring

2.2. 2nd Case

A 15-year-old adolescent girl presented with loss of vision over a long period of time. Magnetic resonance imaging revealed an expansive sellar and suprasellar mass measuring 48x47x37 mm consisting of cystic and solid components in favor of craniopharyngioma. Patient underwent transsphenoidal surgery for tumor resection. Post operative laboratory findings were in favor of a hyperprolactinemia with prolactin of 600 ng/ml and a thyrotrope deficiency. Histological assessment confirmed diagnosis of prolactinoma. Pituitary MRI control revealed a 20x9x17mm residual macroadenoma. Patient was started on cabergoline resulting in lowering prolactin levels and tumor shrinkage.

2.3. 3rd Case

A 13 year old patient with no particular history was admitted for an abrupt onset HTIC syndrome. Clinical examination revealed a patient with Tanner Stage P1S3, no dysmorphic syndrome, no galactorrhea, no delay or the statural advance. MRI revealed a heterogeneous intra and supra sellar tumor process of 30mm×15 mm in size, containing foci of necrosis exerting a mass effect on the neighboring structures and in particular on the optic nerves and quiasma evoking a craniopharyngioma.

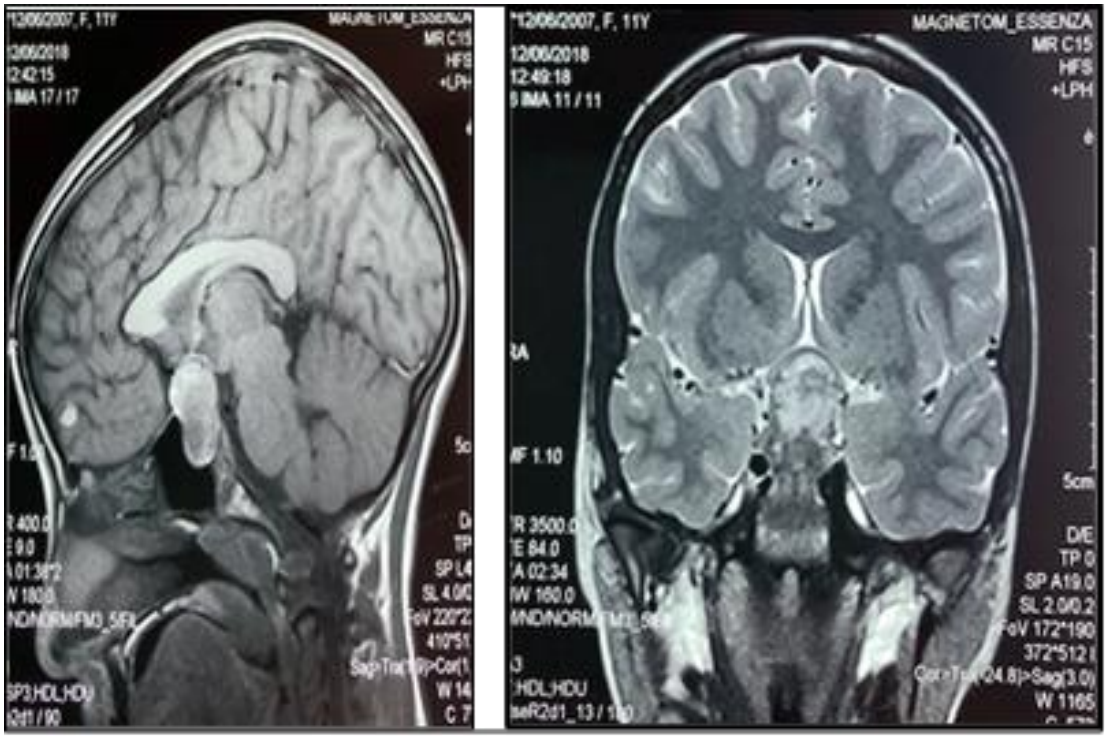

Figure 3 Sagittal end coronal hypothalamic-pituitary MRI showing an intra and supra sellar tumor process of 30mm×15 mm

Initial hormonal workup: T4: 17.1pmol/L; Cortisol: 8.85 mg/dL Prolactin: 10.25 ng/mL, FSH: 2.2 IU/L; LH: 0.1 IU/L; Eostradiol: 8.2 ng/L and on visual field bitemporal hemianopsia.

Partial transsphenoidal pituitary surgery performed in emergency with simple postoperative course and supplemented thyroid-corticotropic deficit.

The anatomopatho-immunohistochemical study concluded to a tumor proliferation with round cells whose morphological aspect first evokes a pituitary adenoma secreting GH with Ki 67 at 1%.

In view of this and the normal initial IGF-1 at 360.1 ng/mL (90-581) a GH braking test under OGTT was performed with a GH nadir at 2.03 ng/mL confirming GH hypersecretion. The Patient was referred for revision surgery.

3. Discussion

Brain tumors are the most common solid tumor type in children, and represent approximately 15–20% of all childhood cancers. Pituitary tumors are rare in the pediatric population with a prevalence of up to 1 case per 1 million children.11 they encompass a diverse group of different tumor types: predominantly comprised of pituitary adenomas and craniopharyngiomas, but also spanning germ cell tumors and others [2,13], with craniopharyngiomas accounting for 80%–90% of tumors in the pituitary fossa.

Pediatric pituitary adenoma (PPA) is a rare disease, its incidence in pediatric and adolescent patients (age < 20 years) is low, accounting for approximately 2.6 to 6.1% of all pituitary tumors and 1% of all intracranial tumors in pediatric and adolescent patients. [4,5].

The overall prevalence of pituitary adenoma may be increased among female children, due to the marked prolactinoma predominance in girls. [4]

Pituitary adenomas (PA) are classified according to the 4th edition of the World Health Organization (WHO) 2017 guidelines by their immunohistochemical labelling, according to the somatotropic (GH), lactotropic (PRL), gonadotropic (FSH/LH), corticotropic (ACTH) or thyrotropic (TSH) contingent. [12,15].

The Associations with genetic syndromes are rare, but potentially an important consideration in younger patients with pituitary adenoma. MEN-1 is the most common such association and has been reported to present with pituitary adenoma in children as young as 5 years. A second important association is the McCune–Albright syndrome, other associations are possible in the carny complex and Familial isolated pituitary adenomas (FIPA) [4,13].

When compared with the adult tumors, pituitary adenomas in children are predominantly comprised of secreting tumors, with prolactin, adrenocorticotropic hormone (ACTH), and growth hormone (GH) secreting tumors being the most frequent, and in turn related to substantial morbidity. [3, 17].

Although most of these tumor types are typically benign, they can cause significant morbidity as they expand due to their proximity to the optic chiasm and compression of the pituitary gland [4],end the patients may present with headaches, visual field defects, and other neurologic symptoms, as well as hormonal deficiencies due to disruption of the hypothalamic-pituitary axis, and may include growth deficiency, symptoms of hypothyroidism or hypoadrenalism, pubertal delay, amenorrhea, and diabetes insipidus. [1, 16].

Clinical manifestation of PPA will vary based on age and sex of the patient, type of adenoma (secreting vs. non secreting), and size of the lesion. [3] Moreover, hormonal symptoms cannot be easily identified in the growing stages of each organ; therefore, apoplexy-related symptoms are frequently found in functional PAs in younger patients. [1, 3].

Corticotropinomas (ACTH-secreting adenomas), better known as Cushing's disease, peak at the onset of puberty with a predilection for female gender [16, 7]. Primary chief complaints include rapid and significant weight gain as well as growth failure. The majority of patients also present with typical adult Cushing syndrome manifestations. Other complications can result from hypercortisolism such as hypertension and glucose intolerance although frank diabetes mellitus is rare [5, 7, 16].

Prolactinomas are the most common pituitary adenomas in older children, with the majority occurring in adolescence with a female preponderance, Clinical presentation varies depending on the age and gender of the child, although growth arrest is typically seen in children and adolescents before epiphyseal fusion is completed. [7, 16].

Females may present with pubertal delay, amenorrhea, and other symptoms of hypogonadism. In males, macroprolactinomas are more frequent; accordingly, males with prolactinomas also have a higher incidence of neurological and ophthalmological abnormalities (cranial nerve compression, headaches, visual loss), growth or pubertal arrest and other pituitary dysfunctions. Which is similar to the case of our observations, with a disease manifestation by nerve compression and headaches in the 1st case, and by visual disorders in the 2nd case. [11, 15].

Since various factors such as neurogenic or mechanical processes can lead to loss of dopaminergic suppression of pituitary lactotrophs resulting in hyperprolactinemia, [5, 16]

In comparison to prolactinomas and corticotropinomas, growth hormone–secreting adenomas are rare in children and are mainly found in males. The manifestation of increased growth is referred to as gigantism if it occurs before the fusion of long bone growth plates or to acromegaly if it presents after. Since somatotropic adenoma are often macroadenomas, headaches and visual disturbances are frequently reported [5, 7, 16]. As in our patient's case, with diagnostic reassessment after the anatomopatho-immunohistochemical study.

Thyrotropinomas is TSH-secreting adenomas end it is rare in children. In addition to general signs of hyperthyroidism, they usually manifest as macroadenomas with symptoms of mass effect including visual defects and headaches [7, 16].

Pituitary apoplexy, consisting of an abrupt onset of infarction and/or hemorrhage of a pituitary adenoma, is rarely seen in children. Case series have reported this occurring in prolactinomas, corticotropinomas, non-functional adenomas and more frequently in macroadenomas. The clinical syndrome generally involves a sudden severe headache and is occasionally accompanied by cranial neuropathies from compression of the cavernous sinus or optic chiasm apparatus. It is critical to identify rapidly this entity due to the possible acute hypopituitarism that requires urgent steroid replacement. Surgical intervention is generally recommended. [1, 16]

The most important initial imaging technique in the localization and characterization of pituitary tumors is pituitary magnetic resonance imaging (MRI) accurate detection and localization of adenomas is an important tool to permit successful treatment. [16].

Most protocols will include thin (1–3 mm) coronal slices through the Sella turcica. Dynamic techniques using quick repeated scans after the injection of intravenous gadolinium contrast show a time dependent pattern that allows better delineation of the lesion from the normal gland [1, 7].

All patients with pituitary tumors should be subjected to endocrinological evaluation, serum PRL measurements should be systematically performed in the presence of any tumor of the sellar region Levels greater than 200–250 ng/mL are generally considered diagnostic of prolactinoma. Levels between 100 and 200 ng/mL could result from a decreased tonic dopaminergic inhibition of PRL if the infundibulum is compressed by a lesion. [5, 7].

GH-secreting adenomas are highly suspected based on clinical features and confirmed by measuring insulin-like growth factor-1. The latter correlates well with general levels of GH secreted in the previous 24–48 h. The oral glucose tolerance test is a useful confirmatory test (75-g glucose load). [7, 16].

While most pituitary adenomas require surgical management, the preferred first-line treatment for prolactinoma is with dopamine agonists due to their most effective and best tolerated in reducing clinical symptoms, prolactin levels and tumor size. 44 In adults, cabergoline is the preferred drug for management of prolactinoma according to a recent consensus statement due to higher efficacy reducing hyperprolactinemia and larger reduction in tumor size, No recommendations have been made on the preferred dopamine agonist in the pediatric population although several studies have shown improved efficacy with cabergoline, with remission achieved in 80–90% of microadenomas and 70% of macroadenomas [5, 8]. Cabergoline should be started at a dose of 0.25-0.5 mg once a week and increased monthly by 0.5 mg twice a week up to a dose of 3.5 mg/week as a mean dose. [5, 17]. Surgery is indicated in case of resistance to medical treatment or the presence or progression of cranial nerve deficits or vision loss due to mass effect and radiotherapy in case of failure of surgery. [5, 7, 17]. Our two patients with prolactinomas were started on cabergoline with a good clinico-biological and radiological improvement.

GH secreting tumors are often large and locally invasive and transsphenoidal pituitary surgery remains the first-line therapy for treating this PPA variant and resulting in biochemical normalization in approximately 70–85% of microadenoma patients and in 50% of macroadenomas. Invasive GH adenomas often require multiple treatment modalities additional to surgery to obtain cure. [3,15] Radiation therapy has a defined role in the management of adult recurrent pituitary adenoma, but the role of radiation in the pediatric population is less clear with many physicians attempting to avoid or postpone radiation therapy after puberty to avoid hypopituitarism and growth delay. Prior to radiation administration, revision surgery or medical management (if not already attempted) should be considered. [3, 5]. Some patients may benefit from medical treatment including cabergoline or octreotide if revision surgery is not successful or not feasible, while some physicians use medical therapy to forestall radiation therapy until after puberty [6, 7].

If revision surgery and medical management are not indicated, radiation therapy for recurrent or progressive disease may be entertained, although its use in the pediatric population is not well studied. [7].

Close collaboration with a pediatric ophthalmologist is recommended in the pre- and post-operative setting to diagnose any unrecognized visual field deficits and to monitor response to therapy. [7].

4. Conclusion

Pediatric pituitary adenomas are a rare entity but may have a remarkable effect on quality or length of life. they should be considered as a differential diagnosis of any tumor of the sellar region. Therefor endocrinological evaluation is necessary, preoperatively as well as postoperatively, in order to detect any pituitary hypersecretion or insufficiency that can be treated quickly to prevent morbidity, without mentioning the role of Pathology and immunohistochemistry study's that remain the key elements in the diagnosis of pituitary tumors and help the decision make on the appropriate management.

Compliance with ethical standards

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Disclosure of conflict of interest:

The authors declare no conflict of interests.

Statement of informed consent:

Informed consent was obtained from all individual participants included in the study

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