Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/14179
DOI URL: http://dx.doi.org/10.21474/IJAR01/14179

RESEARCH ARTICLE

GIANT SILENT CORTICOTROPIC ADENOMA IN AN ADOLESCENT: A CASE REPORT

S.E. N'koua[1], Z. Ait Si Ali[1], S. Rafi[2], G. El Mghari[2] and N. El Ansari[1]

1. Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition.
2. Mohammed VI University Hospitalcenter, Marrakech, Morocco.

Manuscript Info

Manuscript History
Received: 05 December 2021
Final Accepted: 09 January 2022
Published: February 2022

Key words:-
Silent Pituitary Adenoma, Corticotropic Adenoma, Adolescent, Management, Follow-Up

Abstract

Pituitary tumors in children and adolescents are dominated by craniopharyngiomas (80-90%) followed by adenomas. Silent pituitary adenomas in children and adolescents are rare; represent only 4-6% of all adenomas. We present the case of a silent giant corticotropic adenoma revealed by pituitary tumoral syndrome in an adolescent. This is a 17-year-old patient operated for an invasive interstellar and suprasellar mass of 34x63x42 mm revealed by intense headaches, blindness in the left eye and a significant decrease in visual acuity in the right eye evolving for 1 month in a context of growth retardation for 4 years, without signs of associated pituitary hormonal hypersecretion. immunohistochemistry had concluded to a corticotropic adenoma. control hypothalamic-pituitary MRI showed persistence of the sellar and suprasellar mass of 33x31x34 mm. The patient had been referred for revision surgery. Silent adenomas are rare in childhood and adolescence let alone giant corticotropic silent adenomas. They are associated with significant morbidity due to their location, their mass effect and / or their interference with normal pituitary hormonal functions. Surgical treatment remains the first-line treatment. Long-term follow-up remains essential to detect recurrence and to manage the various pituitary deficits.

Introduction:-

Pituitary tumors in children and adolescents are dominated by craniopharyngiomas (80–90%) [1]. Pediatric pituitary adenoma is a rare disease, accounting for approximately 5% of all pituitary adenomas. Compared to adults, pituitary adenoma in children is mainly made up of secreting tumors, prolactin (PRL), adrenocorticotropic hormone (ACTH) and growth hormone (GH) being the most frequently observed. Silent pituitary adenomas in childhood and adolescence are relatively rare let alone giant corticotropic silent adenomas; these tumors represent only 4 to 6% of all adenomas [1,2]. We present the case of an adolescent followed initially for an imagery aspect suitable with a craniopharyngioma, but the immunohistochemistry had concluded to a corticotropicadenoma , thus demonstrating the essential place occupied by immunohistochemistry in the typing of these pituitary tumors on which the therapeutic strategy depends.

Corresponding Author:- S.E. N'koua
Address**:-** Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition.

Observation:-

Patient of 17-year-old whose parents noticed a growth retardation for 4 years, presents for 1 month before, a pituitary tumor syndrome made up of fronto-parietal headaches of progressively increasing intensity with blindness of the left eye and a significant decrease in visual acuity in the right eye. Clinical examination noted severe growth retardation with height at -4 standard deviation score (SDS) and weight less than -3 SDS, puberty delay with Tanner stage at G1P1. Paraclinical exams noted a low IGF1 compared to age, with a bone ageof 12 years for a chronological age of 17 years, the hypophysogram demonstrated a lack of thyreotropic(substituted)and gonadotropic functions, the other pituitary axis functions were normal.

The encephalic MRI described a suprasellarlesionwith polycyclic contours, locally infiltrating, measuring 34x63x42 mm, with filling of optochiasmatic cisterns and repression of the optic chiasma ; MRI aspect was suggestive of a cystic craniopharyngioma.

The patient underwent a decompressive partial resection via transsphenoidal approach with simple postoperative course, He had presented diabetes insipidus treated with Desmopressin. Theanapthomopathological report showed: a monomorphic tumor proliferation, of endocrine architecture organized into lobules, islands and spans of variable size. The fibrous stroma contains many small, thin-walled vascular elements. The immunohistochemistry analysis concluded to a corticotropic pituitary adenoma with a Ki67 index of 3%.

The absence of cortisol hyper-secretion was demonstrated witha normal 1mg dexamethasone suppression testof 0.2 µg/dl and a low 24-hours urinary free cortisol (UFC) <4.37 µg/24h. thePatient reported a regression of headaches and an improved visual acuity.Postoperative hypothalamic-pituitary MRI, performed 8 months after surgery, revealed the persistence of a sellar and suprasellar multi-partitioned tumoral lesion with a predominant cystic component of 33x31x34 mm pushing back the optic chiasm, raising and compressing the floor of the third ventricle without hydrocephalus .

A decision for revision surgery had been indicated with prior ophthalmological expertise.

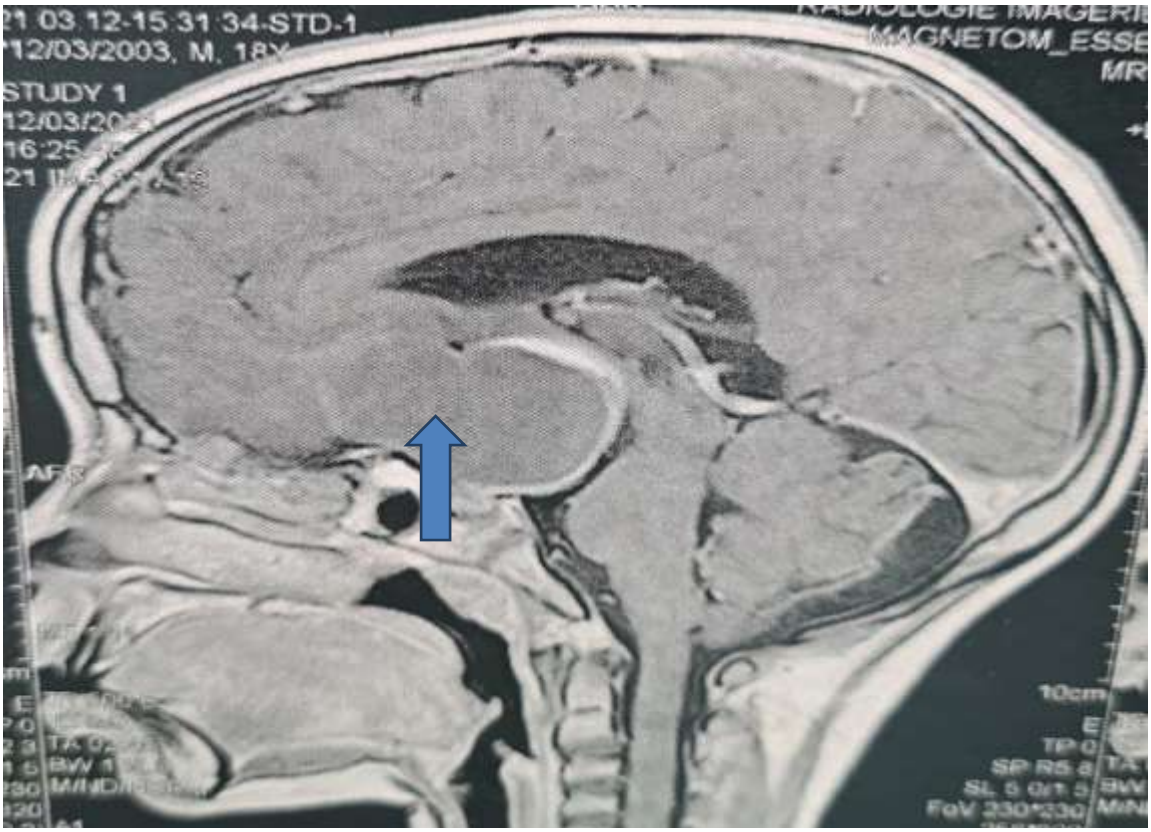

Figure 1:- Preoperative encephalic MRI showing a polycyclic suprasellartumoal lesion.

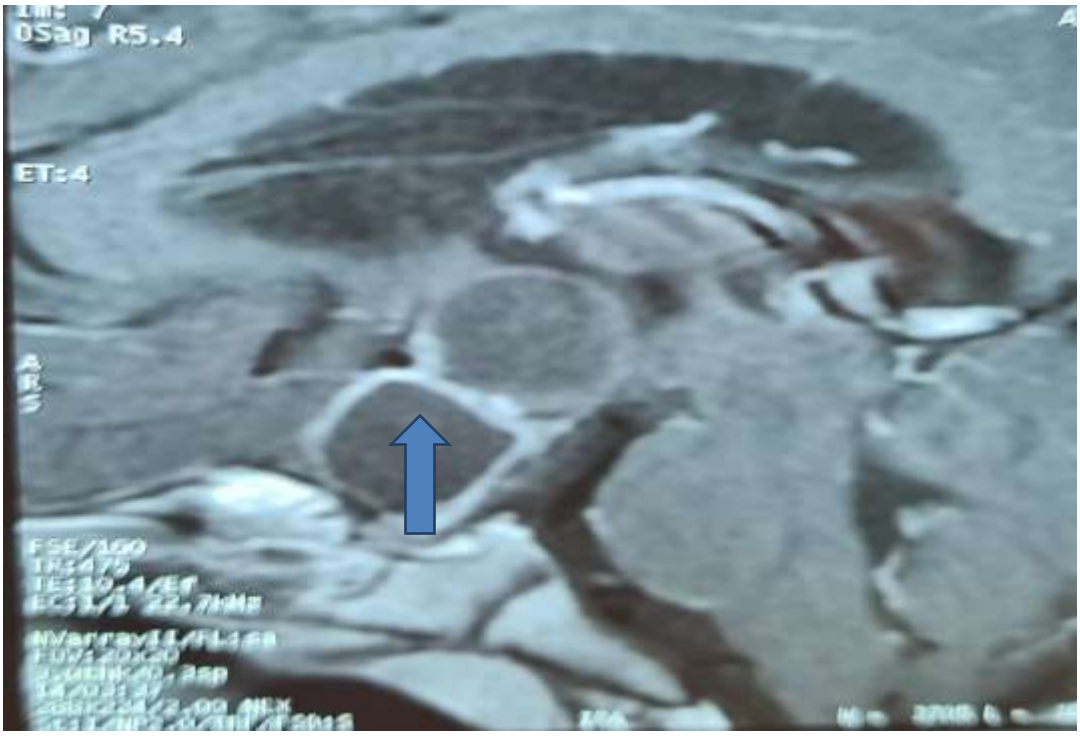

Figure 2:- Postoperative hypothalamic-pituitary MRI showing the persistence of sellar and suprasellar multi-partitioned tumoral lesion.

Discussion:-

Pituitary tumors in children and adolescents are mostly represented by craniopharyngiomas (80 to 90%). Pituitary adenomas are very rare at these ages, even less silent adenomas; their frequency increases in adolescence but they remain relatively rare tumours: about 3% of all intracranial tumors diagnosed in childhood. The majority of these tumors are sporadic, but in children, more common than in adults, they may be part of a genetic disease predisposing to pituitary and other tumors [1,3].

Genetic conditions associated with pituitary tumors include MEN 1 caused by germ-line mutations in menin. Recently, a mutation in the CDKN1B gene (also known as p27/KIP1) was reported to be associated with MEN-like 1 syndrome in a rat model [4]. Genetic defects in one of the protein kinase A (PKA) regulatory subunits (regulatory subunit type 1 alpha, PRKAR1A) cause Carney complex [5]. Inactivating mutations in the gene encoding for the aryl hydrocarbon receptor-interacting protein (AIP) have been found in patients with pituitary tumors (mainly acromegaly) in sporadic and familial forms [6]. Somatic mutations in the adenylatecyclase-stimulating G protein alpha (locus of the GNAS complex, GNAS) are found in McCune-Albright syndrome [7].

Pituitary adenomas (AH) are classified according to the 4th edition of the 2017 World Health Organization (WHO) guidelines by immunohistochemical labeling, according to their contingent :somatotropic (GH), lactotropic (PRL), gonadotropic (FSH/LH), corticotrope (ACTH) or thyrotrope (TSH) [8]. Silent pituitary adenomas are benign tumors arising from adenohypophyseal cells characterized by the absence of evidence of hormonal hypersecretion [9].

Our patient showed no clinical signs of hormonalhypersecretion, immunohistochemistry concluded to a corticotropic adenoma. We made sure of the absence of cortisol hypersecretion by a normal 1mg dexamethasone suppression test and a low 24-hours urinary free cortisol (UFC).

Most silent adenomas arise from gonadotroph cells and often are macroadenomas at diagnosis; they occasionally grow and may present with headaches and visual disturbances, as well as deficient growth and/or pubertal delay. Large adenomas may obstruct the foramen of Monro and cause hydrocephalus, while pituitary adenomas and sellar tumors that impinge on the optic apparatus and/or cavernous sinus can result in cranial nerve palsies, cavernous

sinus syndromes, and/or additional visual disturbances[1]. Nonfunctioning pituitary adenomas may present with GH deficiency (up to 75%), LH/FSH deficiency (~40%), or ACTH and TSH deficiency (~25%)[1].

In general, the natural evolution of non-functional pituitary adenomas (NFPA) presents a significant risk of growth. Indeed, on a study by Dekkers et Al, nine studies evaluated the natural course of non-functional macroadenomas in addition to a study where data from microadenomas and macroadenomas were combined. The follow-up period in these 10 studies ranged from 20 to 85 months. The proportion of patients with growth of the macroadenoma ranged from 7 to 51% [10].

Our patient had growth retardation evolving for 4 years with headaches of increasing intensity, and unilateral blindness with significant decrease in visual acuity in the contralateral eye evolving for 1 month, which can be explained by the growth potential of silent corticotropic adenomas, leading graduallyto growth retardation and thentumoral syndrome with significant visual consequences.

Patients with silent corticotrophadenomas (SCAs) are younger than patients with silent gonadotrophadenomas(SGAs) and true null cell adenomas. In contrast to SGAs, SCAs show a female preponderance, are more frequently giant adenomas, and are more often associated with marked cavernous sinus invasion. The presence of cystic and hemorrhagic components in T2-weighted pituitary MRI sequences in a nonfunctioning pituitaryadenoma (NFPA) might point toward the corticotroph subtype [11].

Our young patient presented a giant adenoma of6cm with cystic components, a feature although described as identifying SCA but difficult to distinguish from craniopharyngioma without anatomopathological and immunohistochemicalanalysis.

To explain the silent attitude of these adenomas, several hypotheses have been put forward, including: 1)-Defective expressionof the prohormoneconvertase 1/3 (PC1/3) involved in the post-translational processing of proopiomelanocortin (POMC) into mature and biologically active ACTH [11,12]. 2)- Cells associated with Cushing disease are suggested to arise from the ACTH-positive cells in the anterior pituitary, and SCAs might arise from the proopiomelanocortin (POMC)-producing cells in the pars intermedia, which, in turn, demonstrates a low ACTH secretory capacity[11]. This localization hypothesis could also explain the high frequency of SGAs. 3)-It has also been proposed that SCAs secrete predominantly high-molecularweight ACTH, which could compete with the normal ACTH (1 to 39 amino acids) at the receptor level[11].4)-Other suggested mechanisms include increased intracellular degradation of ACTH and failure of exocytosis of hormone from the cell membrane[11].

The main aims for treatment of patients with clinically nonfunctioning macroadenomas are the preservation or restoration of visual function and adequate long-term tumor control. Transsphenoidal surgery is the first-line treatment in patients with visual field defects, leading to immediate decompression of the optic nerve.Surgery should preferably be performed by an experienced neurosurgeon because this will enhance the success rate and decrease complication risks [10]. A conservative approach is recommended for macroadenomas that do not reach the optic chiasm with regular monitoring of tumor status and pituitary endocrine functions. However, treatment decisions should be individualized and consider age (surgery may be favored for younger patients due tohigher lifetime probability of tumor growth), pituitary function, and patientpreference [9,10].

According to the recent WHO classification, silent corticotropic tumors (approximately 15% of all NFPAs) and poorly granulated somatotropic tumors (approximately 2% of all NFPAs) are generally more aggressive because they tend to have invasive growth and a high recurrence rate [9, 13]

NFPAs can progress after surgical treatment, with regrowth rates of 15–66% in patients treated with surgery alone and 2–28% in those treated with surgery and radiotherapy. Therefore, long-term radiological monitoring after treatment of NFPAs is recommended [9,14]. However, there are concerns about long-term complications of radiation therapy (eg, hypopituitarism, radiation-induced optic neuropathy, increased risk of cerebrovascular events and secondary brain tumors) [15]. Radiation therapy is usually reserved for cases of incomplete resection with histology showing high proliferative activity and recurrence after repeated surgeries [16]. In patients with an anatomically accessible lesion, surgical revision is generally proposed [2].

Our patient underwent a decompressive resection via transsphenoidal approach, reviewed 8 months after the procedure with hypothalamic-pituitary MRI which revealed the persistence of a sellar and supraselar multi-partitioned tumoral lesion with a predominant cystic component of 33x31x34 mm pushing back the optic chiasm, raising and compressing the floor of the third ventricle without hydrocephalus. Our management had consisted of a surgical revision with ophthalmological expertise.

After surgery for pituitary macroadenomas, hypopituitarism will still be present in a considerable proportion of patients: GH deficiency in approximately 83%; LH/FSH deficiency in about 60%; and TSH and ACTH deficiency in approximately 30% [10].

The patient had kept his replacement therapy for his thyrotropic deficiency.

Conclusion:-

Although silent adenomas are rare during childhood and adolescence, significant morbidity can result from them due to their location, mass effect, and/or interference with normal pituitary hormonal functions. Advances in diagnostic tests, neuroimaging and therapeutic interventions have led to significant improvements in their management. Surgical treatment remains the first-line treatment. long-term follow-up remains essential to detect recurrences and the management of the various pituitary deficits.

References:-

1. Pituitary Tumors in Childhood: an update in their diagnosis, treatment and molecular genetics.
   Margaret F. Keil1,3 and Constantine A. Stratakis.
   Expert Rev Neurother. 2008 Apr; 8(4): 563–574.
2. Pediatric Pituitary Adenoma: Case Series, Review of the Literature, and a Skull Base Treatment Paradigm .Avital Perry,1 Christopher Salvatore Graffeo,1 Christopher Marcellino,1 Bruce E. Pollock,1 Nicholas M. Wetjen,1 and Fredric B. Meyer .
   J NeurolSurg B Skull Base. 2018 Feb; 79(1): 91–114.
3. Clinically nonfunctioning pituitary tumors are monoclonal in origin.
   J M Alexander, B M Biller, H Bikkal, N T Zervas, A Arnold, A Klibanski .
   J Clin Invest. juillet 1990 ; 86(1):336-40.
4. Germ-line mutations in p27Kip1 cause a multiple endocrine neoplasia syndrome in rats and humans.
   Natalia S. Pellegata,*† Leticia Quintanilla-Martinez,* HeideSiggelkow,‡Elenore Samson,* Karin Bink,* Heinz Höfler,*§ Falko Fend,§ JochenGraw,¶ and Michael J. Atkinson.
   ProcNatlAcadSci U S A. 2006 Oct 17; 103(42): 15558–15563.
5. Genetic and histologic studies of somatomammotropic pituitary tumors in patients with the "complex of spotty skin pigmentation, myxomas, endocrine overactivity and schwannomas" (Carney complex).
   Pack SD, Kirschner LS, Pak E, Zhuang Z, Carney JA, StratakisCA .
   J ClinEndocrinolMetab. 2000 Oct; 85(10):3860-5.
6. Aryl hydrocarbon receptor-interacting protein gene mutations in familial isolated pituitary adenomas: analysis in 73 families.
   Daly AF, Vanbellinghen JF, Khoo SK, Jaffrain-Rea ML, Naves LA, Guitelman MA, Murat A, Emy P, Gimenez-Roqueplo AP, Tamburrano G, Raverot G, Barlier A, De Herder W, Penfornis A, Ciccarelli E, Estour B, Lecomte P, Gatta B, Chabre O, Sabaté MI, Bertagna X, Garcia Basavilbaso N, Stalldecker G, Colao A, Ferolla P, Wémeau JL, Caron P, Sadoul JL, Oneto A, Archambeaud F, Calender A, Sinilnikova O, Montañana CF, Cavagnini F, Hana V, Solano A, Delettieres D, Luccio-Camelo DC, Basso A, Rohmer V, Brue T, Bours V, Teh BT, Beckers A
   J ClinEndocrinolMetab. 2007 May; 92(5):1891-6.
7. Characterization of gsp-Mediated Growth Hormone Excess in the Context of McCune-Albright Syndrome.Sunday O.
   Akintoye, Caroline Chebli, Susan Booher, Penelope Feuillan, Harvey Kushner, Derek Leroith, Natasha Cherman, Paolo Bianco, ShlomoWientroub, Pamela GehronRobey .
   The Journal of Clinical Endocrinology & Metabolism, Volume 87, Issue 11, 1 November 2002, Pages 5104–5112
8. How to Classify and Define Pituitary Tumors: Recent Advances and Current Controversies.
   Dai C, Kang J, Liu X, Yao Y, Wang H, Wang R.

Front Endocrinol (Lausanne). 2021 Mar 17;12:604644. doi: 10.3389/fendo.2021.604644. eCollection 2021.PMID: 33815274

9. Non-functioning pituitary adenomas: indications for pituitary surgery and post-surgical management.
   Daniela Esposito,1 Daniel S. Olsson,1 Oskar Ragnarsson,1 Michael Buchfelder,2 Thomas Skoglund,3 and GudmundurJohannsson .
   Pituitary. 2019; 22(4): 422–4344
10. Review Treatment and follow-up of clinically nonfunctioning pituitary macroadenomas.
    Dekkers OM, Pereira AM, Romijn JA.
    J ClinEndocrinolMetab. 2008 Oct; 93(10):3717-26.
11. Clinical and Pathological Aspects of Silent Pituitary Adenomas.
    Juliana Drummond,1 Federico Roncaroli,2 Ashley B Grossman,1 .
    J ClinEndocrinolMetab. Published online 2018 Jul 17
12. Clinical, hormonal and molecular characterization of pituitary ACTH adenomas without (silent corticotroph adenomas) and with Cushing's disease.
    Raverot G, Wierinckx A, Jouanneau E, Auger C, Borson-Chazot F, Lachuer J, Pugeat M, Trouillas J.
    Eur J Endocrinol. 2010 Jul; 163(1):35-43.
13. Review Histopathological classification of non-functioning pituitary neuroendocrine tumors.
    Manojlovic-GacicE, Engström BE, Casar-Borota O.
    Pituitary. 2018 Apr; 21(2):119-129.
14. Can we ever stop imaging in surgically treated and radiotherapy-naive patients with non-functioning pituitary adenoma?
    Reddy R, Cudlip S, Byrne JV, Karavitaki N, WassJA .
    Eur J Endocrinol. 2011 Nov; 165(5):739-44.
15. Review Nonfunctioning pituitary tumors and pituitary incidentalomas.

MolitchME .

EndocrinolMetabClin North Am. 2008 Mar; 37(1):151-71, xi.

16. Review Radiation therapy in the management of pituitary adenomas.
    Loeffler JS, Shih HA
    J ClinEndocrinolMetab. 2011 Jul; 96(7):1992-2003.