Case Report

A rare presentation of craniopharyngioma: Delayed Puberty; A case report and literature review

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ABSTRACT

Background: Craniopharyngiomas are among the most common suprasellar tumors in children and adolescents. Owing to their slow-growing and indolent nature, patients may remain asymptomatic for prolonged periods or may present with visual disturbance or headache. Delayed puberty resulting from hypopituitarism is a recognized clinical feature.

Case Report: We describe a 23-year-old male who presented with short stature and absent pubertal development. His clinical and biochemical evaluation revealed panhypopituitarism. MRI of the brain demonstrated a large suprasellar mass with radiologic features consistent with craniopharyngioma. The patient did not report headache, visual symptoms, or polyuria.

Discussion: Suprasellar masses may present with non-specific or atypical symptoms, and the absence of headache or visual disturbance does not exclude significant underlying pathology. Clinicians should maintain a high index of suspicion for hypopituitarism when evaluating individuals with unexplained short stature.

Conclusion: Early assessment of children and young adults with short stature, particularly when accompanied by lethargy, is essential to avoid delayed diagnosis of significant endocrine or structural abnormalities. For patients who decline surgical management, appropriate hormone replacement therapy can provide meaningful symptomatic improvement.

KEY WORDS: Panhypopituitarism, Craniopharyngioma, Suprasellar tumors, Hypogonadotropic hypogonadism.

INTRODUCTION

Craniopharyngioma is an extra-axial, calcified, cystic, very slow-growing tumor, originating from remnants of the craniopharyngeal duct.[1] It mostly arises from the pituitary stalk and projects into the hypothalamus. Craniopharyngioma constitute 13% of suprasellar tumors and 1-3% of intracranial tumors.[1,2] Craniopharyngioma constitute 5-10% of all tumors and 56% of sellar and suprasellar tumors in children. There are no gender differences in the incidence of craniopharyngioma in all age group.[3] Craniopharyngiomas are infrequently encountered intracranial tumors in clinical practice (0.5%). It is uncommon to see them as a first presentation in the third decade of life, as in our case as it is very slow growing tumor and take years to grow and

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manifest(insidious onset). They are more prevalent in 1st decade and then in 5th decade of life. In existing literature, a bimodal age distribution has been shown, childhood onset at 5-14 years of age and adult onset at 50-74 years of age.[4] They have malignant behavior but benign histology as they have a predilection for invading surrounding structures.[5] Symptoms of craniopharyngioma are gradual in onset and these tumors mostly become symptomatic only when the tumor reaches a size of 3 presenting symptom (55-86%) followed by endocrine dysfunction (66-90%), and visual disturbances cm. Surgery is the mainstay of treatment.[5,6] Among presenting features, headache is the most common (37-68%).[5,6] At the time of presentation, 40% of patients have symptoms associated with hypothyroidism. Approximately 25% patients have signs and symptoms of adrenal failure and 20% have diabetes insipidus. A vast majority of young patients present with short stature and delayed puberty.[7,8]

Approximately 40-70% of patients have optic pathway dysfunction at presentation.[1] Children due to unawareness of visual problems often present with complete and irreversible visual damage. The presentation of optic pathway dysfunction includes papilledema, visual field deficits and even optic nerve atrophy in severe cases. Short stature is seen in 23-45% of patients and 11-18% of patients present with obesity.[7,8]

CASE REPORT

A 23-year-old male, who appeared significantly younger than his chronological age, presented for his first formal medical evaluation in 2016 with complaints of

Table-I: Laboratory Investigations.

Lab parameters	*03/11/2016*	*10/11/2017*	*08/03/2019*	*11/03/2021*	*21/10/2021*	*14/09/2022*	*Normal ranges*
Hemoglobin (g/dl)	12.2				14.5		12.3-16.6
MCV	86.4						78.7-96.3
TLC	8.4						4.8-11.3
Platelets	239						154-443
Vitamin D level (ng/ml)	19.1		23.2				>30ng/ml
TSH (ng/dl)	7.366						0.4-4.0
FT4 (ng/dl)	0.63	1.05	0.95	1.36	1.34	1.34	0.89-1.76
FBS (mg/dl)	81						65-100
Testosterone level (ng/dl)	<2.5	59.02	165	330	20.88	610.1	244-836
LH mIU/ml	< 0.1						1.2-7.8
FSH mIU/ml	< 0.3						1.4-15.4
Prolactin (ng/ml)	12.4						3-14.7
8Am cortisol (ug/dl)	3.7						5.27-22.45
IGF-1 (ng/ml)	20.7	374	540	103	117.9		96.4-227.8
ACTHpg/ml	15.7						
Sodium mmol/l	142	143			145	142	136-145
Potassium mmol/l	4.7	3.9			3.8		3.5-5.1
ALT IU/L	23						
Calcium (mg/dl)	9.8						
Serum Osmolality(mosm/kg)	292						275-300
Urine Osmolality(mosm/kg)	132						50-1400

short stature, lethargy, and easy fatigability. His parents had first noticed growth delay and absence of secondary sexual characteristics at the age of 14 years; however, due to social and personal constraints, medical consultation was delayed in the hope of spontaneous catch-up growth.

On examination, his height was 154 cm and weight 33.1 kg. His blood pressure was 110/70 mmHg. Genital examination showed Tanner stage 0 pubic hair, with both testes located in the scrotum, each measuring approximately 4 mL and soft in consistency. Visual fields were normal to confrontation, and he denied polyuria or polydipsia. Hormonal evaluation revealed hypogonadotropic hypogonadism, secondary hypothyroidism, secondary adrenal insufficiency, and growth hormone deficiency, consistent with panhypopituitarism (Table-I).

MRI of the brain demonstrated a suprasellar mass with radiologic features suggestive of craniopharyngioma (Fig.1). Formal visual field assessment (perimetry) was advised repeatedly; however, the patient declined, citing the absence of visual symptoms.

Following the initial diagnosis in 2016, he was started on hydrocortisone 20 mg/day, levothyroxine 75 µg/day, growth hormone 2 units subcutaneously daily, and testosterone 75 mg intramuscularly monthly. He declined surgical and radiotherapy options. After one year of treatment, improvements were observed in IGF-1, FT4, and testosterone levels. His height increased to 158 cm, reflecting a 4 cm gain over one year, and bone age showed progressive improvement (Table-II). No postural hypotension was noted.

A repeat genital examination in 2019, after 2.5 years of testosterone replacement, showed pubic hair development to Tanner stage 3, and testicular volume increased to 10 mL bilaterally. He remained clinically stable without headaches or visual impairment and was compliant with hydrocortisone and levothyroxine therapy. Due to financial limitations, growth hormone therapy was used intermittently and eventually discontinued, though his IGF-1 levels remained within the reference range. Testosterone replacement was gradually increased to 125 mg monthly to simulate normal pubertal progression while minimizing the risk of premature epiphyseal fusion. Levothyroxine doses were adjusted to maintain free T4 levels in the upper normal range.

Two MRI scans performed six months apart demonstrated a slight reduction in tumor size, from 2.6 × 2.1 × 1.7 cm to 2.5 × 1.8 × 1.3 cm (Table-II; Fig.1 and 2).

The patient is now satisfied with his physical appearance, general health, and sexual function and expresses a desire to marry and start a family. To achieve fertility, testosterone therapy will need to be discontinued, and gonadotropin therapy using human chorionic gonadotropin (hCG) and follicle-stimulating hormone (FSH) will be initiated, with monitoring of testosterone levels and semen analysis every six months, given his prepubertal-onset hypogonadism.

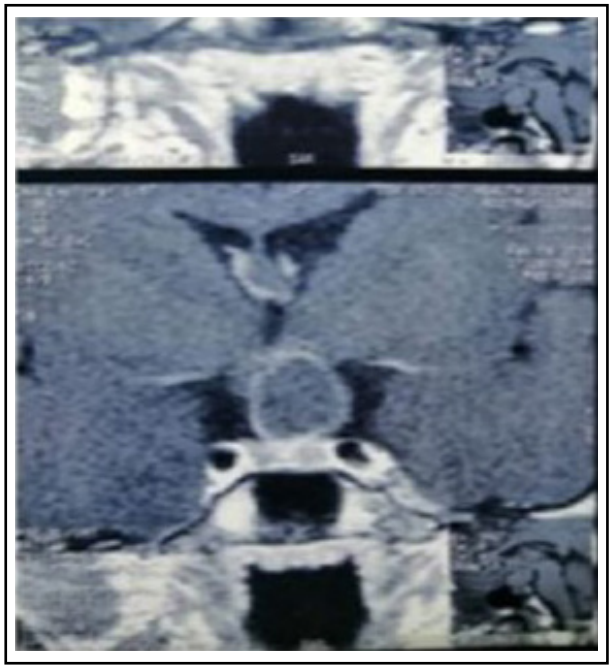

Fig.1: Suprasellar Mass at time of initial Presentation: Well demarcated, slightly lobulated ovoid shaped cystic structure in suprasellar region 2.6x2.1x1.7cm with ring enhancement- appearance suggestive of craniopharyngioma.

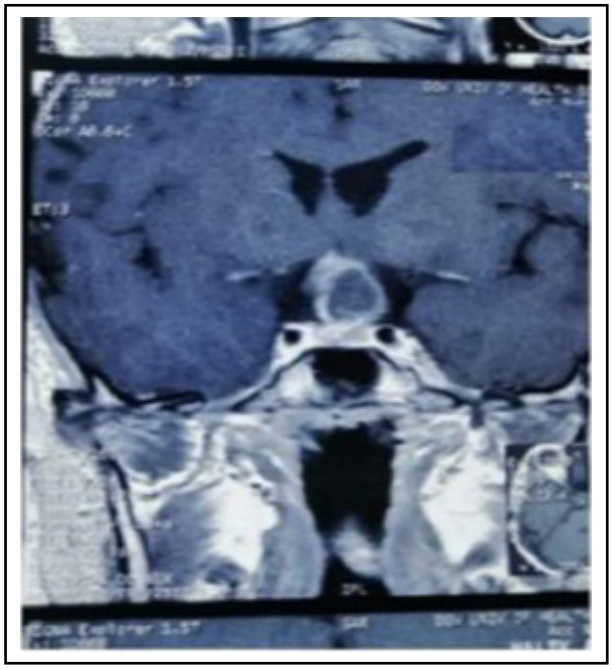

Fig.2: MRI Pituitary showing slight reduction in size of Suprasellar mass: Slight reduction in previously identified solid cum cystic mass in Suprasellar region measuring 2.5x1.8x1.3cm, superiorly compressing optic chiasma.

Table-II: Radiologic Investigations.

MRI brain	8/2/17	20/8/17
	Well demarcated, slightly lobulated ovoid shaped cystic structure in suprasellar region 2.6x2.1x1.7cm with ring enhancement is seen.	Slight reduction in previously identified solid cum cystic mass in suprasellar region measuring 2.5x1.8x1.3cm, superiorly compressing optic chiasma.
Visual fields	Normal to confrontation	Normal to confrontation
Bone age	05/11/2016	24/9/2019
	14-15years (Chronological age = 23yrs)	18 years (Chronological age = 26yrs)

DISCUSSION

This case was interesting as it presented at an unusual age, with no accompanying headache or vision disturbance. The main reason for presentation was short stature accompanied by progressively worsening lethargy. Further work-up revealed panhypopituitarism. Subsequent radiologic investigation revealed a suprasellar mass, likely representing craniopharyngioma. Craniopharyngioma presents as a solitary large cyst or multiple cysts filled with brownish-yellow proteinaceous material. The tumor appears bright due to high amount of cholesterol crystals in it.[1,2,6] The radiologic characteristic of a craniopharyngioma is the presence of a suprasellar calcified cyst. Approximately 70-75%of craniopharyngiomas are cystic and 80-87% are calcified. Calcifications are more frequently seen in children (90%) than in adults (50%).[1] To demonstrate calcifications, CT scan is the most sensitive imaging modality and it has superseded the plain radiograph.[1] The diagnostic workup for craniopharyngioma encompass precontrast and postcontrast CT scans, MRI Pituitary, hormonal profile and neuro-ophthalmologic evaluation with formal visual field assessment perimetry.[4]

Craniopharyngioma has a recurrence rate of 50%. It has 83% to 96% five-year survival and 65% to 100% 10-year survival. It has high morbidity too with majority of patients experiencing sequelae. The most prevalent anatomical location of craniopharyngioma is the sellar/ suprasellar region, with 95% of craniopharyngiomas having a suprasellar component. Craniopharyngiomas due to compression on normal pituitary tissue ultimately result in pituitary deficiencies especially of the anterior pituitary hormones. Due to compression on third ventricle craniopharyngioma can also present with hydrocephalus.

At the time of the initial clinical encounter, about 40 to 87% of patients present with at least one hormonal deficiency.[1] In adults, 40% of patients present with amenorrhea in females and loss of libido and erectile dysfunction in males, secondary to gonadotrophic deficiency.[5] Growth hormone (GH) deficiency is found in 85% of adult patients and these present with weight gain, central obesity, and fatigue. Approximately 25 % of patients are found to have adrenocortical hormone (ACTH) deficiency leading to symptoms of adrenal insufficiency. Hypothyroidism is found in 25% of patients. Vasopressin deficiency, also known as diabetes insipidus, is prevalent in approximately 20% of patients.[4] In this case, there was indeed severe anterior pituitary hormone deficiency but no polyuria even after hydrocortisone replacement. Hydrocortisone is recognized to lead to unmasking of diabetes insipidus as glucocorticosteroids enhance free water clearance. Despite the severe growth hormone deficiency there was no obesity in our patient.

Hormonal deficiency, specifically secondary adrenal insufficiency, and hypothyroidism should be treated with glucocorticoid and thyroid hormone replacement prior to surgical intervention and continued on long term basis if conservative approach to management is adopted. The prognosis is good in young individuals and poor for individuals over the age of 65.

Our patient had very low levels of FSH, LH and testosterone levels (suggestive of secondary hypogonadism). He also had low IGF-1 level and low 8am cortisol level without raised ACTH level suggestive of secondary hypoadrenalism. The panhypopituitarism state in our patient occurred due to the compression of his pituitary gland by the tumor that had remained unaddressed for several years. There was no symptomatic visual loss despite some chiasmal compression. The majority of craniopharyngiomas in adults present with impaired vision. The decrease, albeit small, in size of the lesion on follow-up MRI scan, could be explained by some auto infarction of the mass. This, to our knowledge, is unusual in the case of craniopharyngiomas which are notorious to increase in size even after surgical intervention, often necessitating radio-therapy.[5] The possibility of other differentials such as Rathkes Cleft Cyst, germinoma, pituitary adenoma cannot be excluded. However, the radiologic appearances were more suggestive of craniopharyngioma.

Although clinically doing well following 7 years of diagnosis, without definitive treatment, the patient and family were periodically counselled about immediate hospital referral in case of sudden severe headache, altered consciousness and visual impairment. This is in keeping with the possible occurrence of pituitary apoplexy, a condition that may require immediate surgical intervention (89As regards fertility prospects, gonadadotropin replacement has shown promise in subjects with hypogonadotropic hypogonadism.[9] Majority of patients who developed hypogonadotropic hypogonadism post puberty require induction of spermatogenesis with Injections HCG (human choroinic gonadotrophins).[10] In order to stimulate the Sertoli cells to promote spermatogenesis in the absence of intrinsic FSH activity, either rFSH (recombinant FSH) or human menopausal gonadotropins (HMG) can be used. HMG is a combination of LH and FSH extracted and then purified from the urine of postmenopausal women. These are effective methods to induce spermatogenesis via stimulation of FSH receptors.[11-16]

The patient has been counselled regarding the need for prolonged gonadotropin replacement (like injections human chorionic gonadotropin (HCG) and injections recombinant FSH prior to successful attainment of spermatogenesis-fertility- and the cost implications.

CONCLUSION

Sellar masses such as craniopharyngiomas may present in young individuals with endocrine dysfunction and headache. Surgery is the mainstay of treatment for such tumors especially if they are causing headache and visual symptoms. Once normal serum total testosterone levels are achieved, if spermatogenesis is not induced with HCG alone, rFSH or HMG can be used to enable these men to have children.

List of Abbreviations:

MCV: Mean corpuscular volume
TSH: Thyroid Stimulating Hormone
FT4: Free Thyroxine Levels
FBS: Fasting Blood Sugar
LH: Luteinizing Hormone
FSH: Follicle Stimulating Hormone
ALT: Alanine Transaminase
ACTH: Adrenocorticotropic Hormone
IGF-1: Insulin-Like Growth Factor 1
MRI: Magnetic Resonance Imaging

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Author Contributions:

Dr. Azra Rizwan provided the idea of writing this case report and provided Sabiha Banu all details and workup of the patient, she has reviewed whole case report in detail.
Sabiha Banu wrote case report abstract, introduction and case report part.
Muntazir Mehdi wrote discussion and conclusion parts that were reviewed and modified by Sabiha Banu.

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