Granular Cell Tumor: A Rare Suprasellar Tumor

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ABSTRACT

Introduction: Granular cell tumors of the neurohypophysis are rare, benign neoplasms originating from pituicytes that often pose diagnostic challenges due to their resemblance to other sellar lesions.

Case Presentation: We report the case of a 26-year-old man with a 2-year history of headache, polyuria, and hypopituitarism. Magnetic resonance imaging revealed a 21×23×30 mm suprasellar mass compressing the optic chiasm and hypothalamus. Hormonal evaluation showed hypogonadotropic hypogonadism, central hypothyroidism, and arginine vasopressin deficiency. The patient underwent partial tumor resection. Histopathology confirmed a grade I granular cell tumor, positive for thyroid transcription factor 1, S100, and vimentin.

Discussion: Granular cell tumors are slow-growing lesions with nonspecific clinical and radiologic features. Diagnosis relies on histologic and immunohistochemical findings. Complete resection is often limited by tumor vascularity and proximity to vital structures.

Conclusions: Granular cell tumors should be considered in the differential diagnosis of suprasellar tumors. Early recognition and multidisciplinary management may improve patient outcomes.

INTRODUCTION

Neurohypophysial granular cell tumors (GCTs) are rare, benign neoplasms that belong—together with pituicytoma and spindle cell oncocytoma—to the family of low-grade neoplasms with common immunostaining for thyroid transcription factor 1 (TTF-1).[1,2] These tumors are considered to have a common origin from the pituicytes of the posterior pituitary or infundibulum.[2]

GCTs are slow-growing and cause compressive symptoms over time. They usually present as a solid mass located in the suprasellar region, arising from the infundibulum or, less frequently, from the neurohypophysis.[3] They are composed of polygonal monomorphic cells with abundant granular cytoplasm, which is ultrastructurally filled with lysosomes, without evidence of atypia.[4]

Preoperative diagnosis is often challenging due to similarities with other sellar lesions, such as pituitary adenoma, meningioma, pituicytoma, and spindle cell oncocytoma.[5,6] The prognosis is determined mainly by extent of surgical resection; however, surgical treatment is frequently hampered by factors such as tumor size, proximity to the optic chiasm, and high vascularization, leading to a significant recurrence rate.[7]

The objective of this report is to describe the case of an adult male patient with GCT to highlight its clinical, radiologic, and histopathologic characteristics.

CASE PRESENTATION

A 26-year-old male patient of Peruvian nationality, with no

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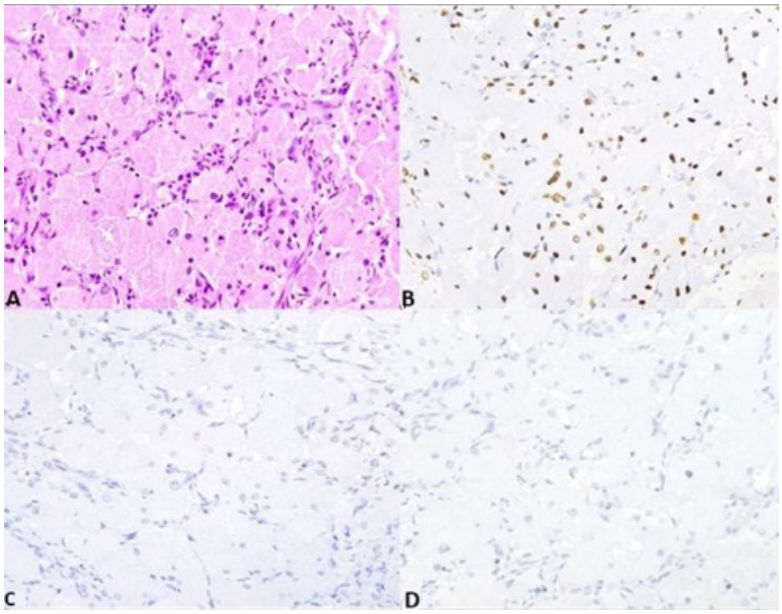
medical history or relevant family history, presented with a 2-year history of oppressive retro-orbital headache with increasing intensity from moderate to severe (pain score 9/10) over the last year. Symptoms were partially relieved by tramadol 50 mg orally once daily and were associated with decreased visual acuity, nausea, and sporadic vomiting. Based on these symptoms, at the recommendation of his private physician, the patient underwent a contrast-enhanced brain magnetic resonance imaging (MRI), which suggested a probable craniopharyngioma.

Given the clinical presentation, the patient was hospitalized in the neuroendocrinology service. Medical history revealed polyuria (5 L/day), polydipsia, nocturia, asthenia, and cold intolerance for 5 months. Physical examination revealed an axillary temperature of 37 °C, heart rate of 80 beats per minute, respiratory rate of 20 breaths per minute, a body mass index of 21 kg/m^2 (eutrophic). Confrontational campimetry showed no abnormalities in the right eye and inferior temporal quadrantanopia in the left eye. The remainder of the examination was unremarkable.

Figure. Photomicrographs of a Suprasellar Tumor at 400× Magnification



(A) Hematoxylin-eosin staining shows eosinophilic polygonal cells with granular cytoplasm, small nuclei, and inconspicuous nucleoli. (B) Immunohistochemistry at 400× shows nuclear positivity for thyroid transcription factor 1. (C) Immunostaining is negative for chromogranin. (D) Immunostaining is negative for synaptophysin.

MRI of the pituitary gland with contrast showed a solid lesion, isointense in T1, T2 and fluid-attenuated inversion recovery (FLAIR), with moderate contrast enhancement and lobulated contours, involving the optic chiasm without extension to the optic nerve or tract. It measured 21 x 23 x 30 mm (transverse x longitudinal x anteroposterior) and occupied part of the interpeduncular and prepontine cistern, affecting structures of the hypothalamic region without involvement of the infundibulum or pituitary gland.

Hormonal testing (Table) revealed an insulin-like growth factor 1 level at the lower limit of normal (116 ng/mL), hypogonadotropic hypogonadism (total testosterone 28 ng/dL; luteinizing hormone 0.66 U/L; follicle-stimulating hormone < 0.66 U/L), central hypothyroidism (thyroid-stimulating hormone [TSH] 2.04 µU/mL, free T4 0.6 ng/dL), normal prolactin (9.5 ng/mL), normal basal cortisol (15 µg/dL), supporting a diagnosis of hypopituitarism. Furthermore, due to the hypernatremia (Na 150 mmol/L) associated with polydipsia and polyuria, arginine vasopressin deficiency (AVP-D) was presumed.

Based on the clinical and radiologic findings, a decision was made to perform a frontotemporal craniotomy using a combined subfrontal, transzygomatic, transsylvian, and translamina terminalis approach for biopsy and limited tumor resection for diagnostic purposes. Hormone replacement therapy was initiated with levothyroxine 100 µg orally once daily and desmopressin intranasally (2 sprays daily). Subsequently, testosterone enanthate 200 mg intramuscularly every 15 days was added, with improvement in symptoms and good tolerance.

Table. Biochemical Tests Requested During Hospitalization and After Surgery

Biochemical Tests	Admission	3 Months Postsurgery	Ref Range
Sodium (mmol/L)	150	132	135 – 150
Potassium (mmol/L)	4.4	4	3.5 – 5.0
Creatinine (mg/dL)	0.6	—	0.7 – 1.3
Alpha-pheoprotein (ng/dL)	< 2	—	1.09 – 8.04
Urine density	1030	1030	1005 – 1030
Prolactin (ng/dl)	9.4	8.9	< 20
Cortisol (µg/dL)	15.4	7.7	5 – 25
FSH (mIU/mL)	< 0.66	—	1.5 – 12.4
Luteinizing hormone (IU/L)	0.63	—	1.8 – 8.6
Total testosterone (ng/dL)	28.5	—	132 – 813
Free thyroxine (ng/dL)	0.6	0.7	0.6 – 1.12
TSH (µIU/mL)	1.5	—	0.4 – 5.5
IGF-1 (ng/mL)	90.1	—	116 – 358

Abbreviations: FSH, follicle-stimulating hormone; TSH, thyroid-stimulating hormone; IGF-1, insulin-like growth factor 1.

Histopathological examination showed neural tissue with focal gliosis and granular cell tumor. Immunohistochemistry revealed a Ki-67 proliferation index of 1%; p53, negative; glial fibrillary acidic protein (GFAP), negative; chromogranin, negative; synap-

tophysin, negative; S100, positive; vimentin, positive; and TTF-1, positive (Figure).

These findings were consistent with suprasellar GCT, World Health Organization grade I. During follow-up 3 months after surgery, the patient presented with sporadic nausea and vomiting and hyponatremia (Na 132 mmol/L) associated with low borderline cortisol (7 µg/dL). These findings suggested adrenal insufficiency, and oral prednisone 5 mg/day was initiated.

Because tumor resection was minimal and primarily diagnostic, the patient is currently awaiting definitive surgery for complete resection and continues outpatient follow-up by the endocrinology service.

DISCUSSION

Granular cell tumors were first described in 1893 by Boyce and Beadles[8] and represent less than 0.5% of all sellar tumors. Most are benign, with a malignant transformation rate of approximately 2%.[9] Fewer than 70 symptomatic cases have been reported in the literature,4 making the present case notable for its florid clinical presentation.

Women are more commonly affected than men (2:1), with peak incidence occurring in the fifth decade of life,[10] However, the present case involves a 26-year-old male patient.

Symptoms associated with GCT include gradual onset of visual disturbances in up to 90% of cases, headache, and endocrine dysfunction (eg, amenorrhea, galactorrhea, infertility, impotence, and weight fluctuations) in approximately 50% of cases. Hormonal disturbances such as hypopituitarism and hyperprolactinemia are frequently observed.[7] In this case, the patient presented primarily with moderate to severe headache accompanied by sporadic nausea, vomiting, visual impairment, and partial hypopituitarism (hypogonadotrophic hypogonadism and central hypothyroidism) with normoprolactinemia.

In addition, due to polyuria (5 L/day), nocturia, and hypernatremia (150 mmol/L), AVP-D was suspected. A water deprivation test was not performed given the clinical context, and copeptin or AVP assays were unavailable.

Radiologic findings are nonspecific and resemble those of other central nervous system lesions, such as meningioma, adenoma, chordoma, or teratoma.[11,12] MRI typically shows an isointense tumor mass on T1 and slightly hypointense on T2, with homogeneous contrast enhancement,[12] consistent with this case.

Definitive diagnosis is typically established by histological examination following surgical excision.[13] In this patient, diagnosis relied on histopathology, as clinical, laboratory and imaging findings were inconclusive.

Histologically, GCTs consist of spindle-shaped and polygonal cells with granular eosinophilic cytoplasm. They are typically positive for certain markers including PAS, S100, CD68, vimentin, and TTF-1, and negative for GFAP and pituitary hormones.[14] These features distinguish them from other oncocytic tumors of the sellar region, such as pituicytoma and spindle-shaped oncocytoma.[14] Expression of TTF-1, S100, and SOX10 supports the diagnosis, which relies on both immunoprofile and cellular morphology.

Surgical removal is the primary treatment, but complete resection is often difficult due to tumor firmness, vascularity, and adherence to adjacent structures.[7] Therefore, partial resection with preservation of adjacent brain structures is more common.[7] In this case, only biopsy and partial resection were performed due to proximity to the optic chiasm and invasion into the third ventricle.

The use of radiotherapy with primary or adjuvant treatment is controversial and not routinely recommended. It may be considered in aggressive, progressive, or inoperable recurrent disease.[15] In this patient, radiotherapy is being considered as further surgery carries a high risk of hypothalamic injury.

However, the diagnosis of AVP-D remains uncertain. Although hypernatremia supports central diabetes insipidus, previously reported elevated urine density values are inconsistent with this diagnosis, as AVP-D typically presents with hypotonic polyuria. The absence of confirmatory testing (water deprivation or copeptin measurement) limits diagnostic certainty.

Prognosis depends largely on surgical excision, and no metastases have been reported to date.[14] An interesting indicator in GCTs is the Ki-67 index; paradoxically, tumors with Ki-67 < 3% have shown growth, whereas higher values remained stable in 1 cohort studied.[12] This patient had a Ki-67 value < 3%, warranting close follow-up due to potential tumor growth.

CONCLUSIONS

Granular cell tumors are a rare but important cause of suprasellar tumors and should be considered in the differential diagnosis of sellar lesions. Early diagnosis, supported by radiologic and immunohistochemical findings, is essential for optimal surgical management. Despite their benign nature, partial resection may be challenging due to proximity to critical structures, increasing the risk of recurrence. Appropriate and timely management may improve patient outcomes.

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