

Sellar and Suprasellar Granular Cell Tumor of Neurohypophysis

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INTRODUCTION

Granular cell tumor (GCT) of neurohypophysis was first reported by Boyce and Beadles in 1983.^[1] In 2016 WHO classification of central nervous system (CNS) tumors, GCT of neurohypophysis was defined as a distinct diagnosis.^[2] Here, we reported two cases of GCT of neurohypophysis misdiagnosed as pituitary adenoma and craniopharyngioma. One of the cases was a very rare fully described neurohypophysial GCT which invaded into the right cavernous sinus [Figure 1a and 1b], indicating that the benign tumor might possess aggressive features.

CASE REPORT

A 37-year-old woman presented with a 3-month history of decreased vision in both eyes. Neuro-ophthalmological evaluation revealed that the patient had slight bitemporal hemianopsia. Hormone levels and biomarkers of gonadotropinoma were within normal ranges. Magnetic resonance imaging (MRI) showed that a solid and uniform lesion located in sellar region with invading into the right cavernous sinus. A right frontobasal craniotomy was performed showing the lesion originated from the pituitary stalk. Pathological examination displayed that tumor was composed of the round or polygonal cells with abundant granular eosinophilic cytoplasm. Immunohistochemistry was positive for neuron-specific enolase and S-100 [Figure 1c] but negative for glial fibrillary acid protein (GFAP). The Ki-67 immunostaining was <1% [Figure 1d]. The diagnosis of GCT of the neurohypophysis was made. Considering the tumor invading into the right cavernous sinus and the residual, fractionated radiotherapy was advised to be performed. The patient remained clinically stable and normal visual field, and the residual tumor showed no enlargement in the next 4-year follow-up.

Another patient was a 66-year-old woman, who was admitted to our department with intermittent dizziness, nausea, and vomiting for about 1 week. Laboratory results, including hormone levels, biochemical examinations, and tumor markers, were within normal limits. MRI showed that a solid and smooth-edged lesion located in the suprasellar region with some hypointensity granules appearing on T2-weighted image (T2-WI) [Figure 1e–1g]. The tumor was approached through the right standard pterional craniotomy, and subtotal resection was achieved. Pathological evaluation revealed that tumor cells with round or irregular-shaped nuclei had abundant cytoplasm and mount of eosinophilic granules [Figure 1h]. Immunohistochemical staining was positive for cluster of differentiation (CD) 68, GFAP, and S-100. The Ki-67 labeling was <1%. The pathological diagnosis was GCT of the neurohypophysis. At the 3-month follow-up examination, the patient had no further complaints of preoperative symptoms and no tumor recurrence.

DISCUSSION

Neurohypophysial GCT originated from the pituitary cells which are modified as gliocytes of ependymal cell lineage located in the neurohypophysis and pituitary stalk. In the 2016 WHO classification of CNS tumors,^[2] neurohypophysial GCT was defined as a low-grade benign tumor. The present

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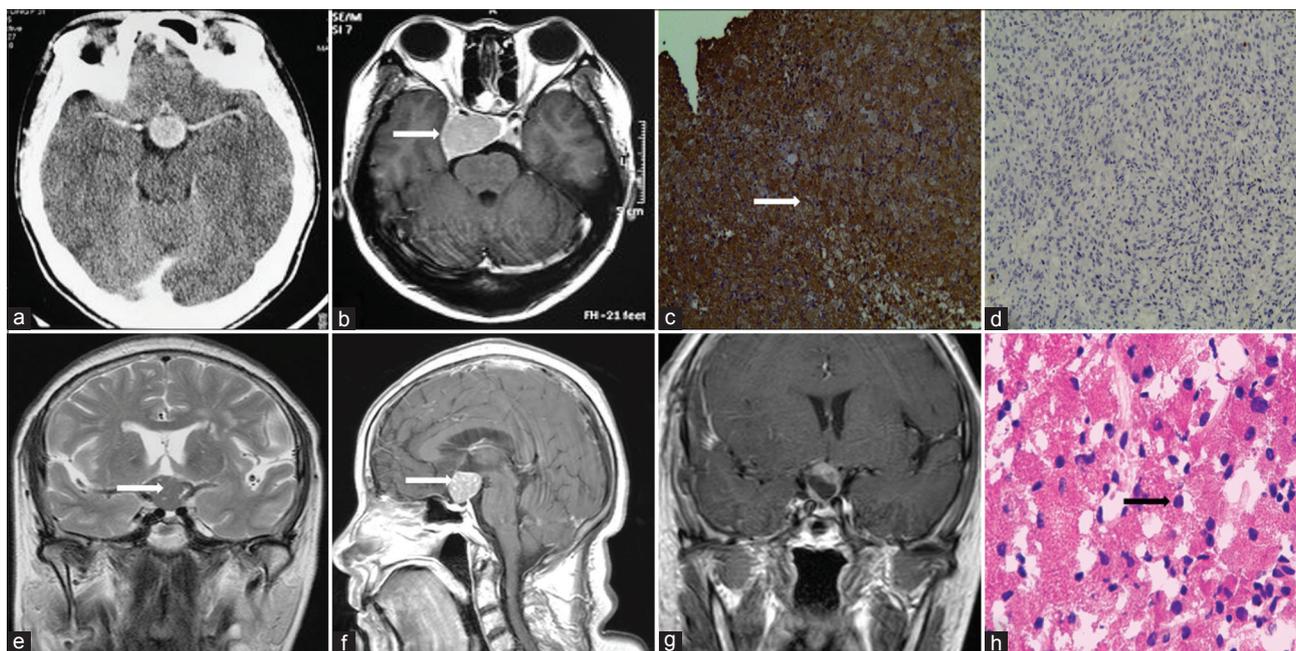


Figure 1: Case 1, (a and b) CT and MRI scans demonstrated the obviously enhancing tumor in intra- and supra-sellar region which infiltrated into the right cavernous sinus (white arrow); (c) Tumor cells were immunohistochemical positive for S-100 (IHC, original magnification $\times 100$, white arrow); (d) The Ki-67 labeling index was less than 1% (IHC, original magnification $\times 100$). Case 2, (e and f) Preoperative MRI scans showed the mass in intra- and supra-sellar region with obvious enhancement and the hypointensity granules on T2-weighted image appeared more enhancement (white arrows); (g) Postoperative MRI scans (3 days later) showed a subtotal resection of the tumor; (h) Tumor cells were composed of round or irregular-shaped nuclei and mount of eosinophilic granules. No significant mitotic figures were identified (haematoxylin and eosin, original magnification $\times 200$, black arrow). CT: Computed telegraph; MRI: Magnetic resonance imaging; IHC: Immunohistochemistry.

case was the first lesion invaded the parasellar region with the lower to 1% Ki-67 staining. GCT developed more commonly in 40–60-year-old patients and has a slight female preponderance. So far, only two cases were reported in pediatric population.

Forty-two percent of symptomatic GCT are suprasellar, and 47% involves both intrasellar and suprasellar compartments. Some authors considered that GCT should be distinguished in the presence of an entirely suprasellar mass with enhancement but should be excluded from the purely intrasellar lesions.^[3] In Case 1, the lesion not only extended the suprasellar region but also invaded the right cavernous sinus, indicating that GCT of neurohypophysis might have the aggressive progress in spite of low Ki-67 index. Herein, we represented the fully described lesion invaded the parasellar region, and an aggressive sellar mass should now include GCT of neurohypophysis in differential diagnosis. Moderate contrast enhancement is typical, and calcification and cystic presentation are extremely rare. MRI scans showed that mass with some hypointense granules appearing on T2-WI is heterogeneous. These sheets might represent the eosinophilic granules in the cytoplasm. GCT should be taken into differential diagnosis because it had a rich vascular supply and a suprasellar location, while the transsphenoidal approach could not meet the purpose of total removal.

GCT of the neurohypophysis revealed immunopositivity for S-100 and GFAP, suggesting that it might originate from Schwann cells as the extracranial GCT. However,

neurohypophysis contained no Schwann cells. Pituicytes, which were specialized glial cells of the posterior pituitary, had five ultrastructural variants: major cells, dark cells, granular cells, ependymal cells, and oncocyctic cells.^[4] Among the five ultrastructural variants, granular pituicytes were observed in neurohypophysis at a high incidence and had similar histological features to GCT.^[5] In addition, thyroid transcription factor-1 (TTF-1) expression in nontumorous pituicytes, pituicytoma, and GCT of neurohypophysis indicated a common pituicyte lineage.^[5] Therefore, GCT of neurohypophysis was identified to arise from granular pituicytes.

Round or polygonal tumor cells had abundant cytoplasm and mount of eosinophilic granules, which were confirmed as lysosomes on electron microscopy, apparently different from neuroendocrine granules. The small-round or irregular-shaped nuclei with prominent nucleoli contain coarse chromatin and show little pleomorphism.^[4] The tumor cells were negative for endocrine markers. GCT was immunopositive for S-100 protein. However, the positive staining of GFAP was controversial though it normally expressed in the pituicytes. The best way to make differential diagnosis between pituicytoma and GCT was that there were no Rosenthal filaments and eosinophilic granules in pituicytoma. Oligodendrocyte transcription factor-2 (Olig2), B-cell lymphoma (Bcl)-2, and CD56 were positive for pituicytoma, whereas GCT was negative for these legends. Most reported cases showed biologically benign. Necrosis, nuclear pleomorphism, high mitotic activity,

high Ki-67 index, high nuclear-cytoplasm (N/C) ratio, and hypervascular density should be included in malignant diagnosis. Currently, microsurgical resection is still the first choice for treatment of neurohypophysial GCT.^[6] Complete resection should be attempted, and there is a high rate of recurrence happened in patients who underwent partial resection. And thus, radiotherapy might be applied in the subtotal-tumor-excised patients.

Neurohypophysial GCT, originating in the neurohypophysis, is a rare, low-grade glial neoplasm and the diagnosis for this disease is still challenging. The histological displays and immunophenotypical characteristics are still the only reliable basis for diagnosis. Surgical resection has been demonstrated an effective treatment approach. Radiotherapy is recommended to the patients undergoing subtotal tumor resection.

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Conflicts of interest

There are no conflicts of interest.

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