



## Case Report

# Clinical features and endoscopic findings of granular cell tumor of the sellar region: A case report and review of the literature

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## ABSTRACT

**Background:** Granular cell tumor (GCT) of the sellar region is a rare tumor of the sellar and suprasellar regions that originate from the neurohypophysis. This tumor is very difficult to differentiate from other pituitary neoplasms, such as pituitary adenoma, pituicytoma, and spindle cell oncocytoma. We report a rare case of GCT arising from the posterior pituitary of the sellar region and suggest a useful indicator for accurate diagnosis and pitfalls for surgical procedures.

**Case Description:** A 42-year-old woman was admitted to our hospital with bitemporal hemianopsia. Neuroimaging showed a large pituitary tumor in the sellar and suprasellar regions with a hypointense part on T2-weighted magnetic resonance imaging, and the enhanced anterior pituitary gland was displaced anteriorly. Laboratory findings showed mild hyperprolactinemia. Subtotal resection of the tumor was achieved using an endoscopic endonasal transsphenoidal approach. Histological findings showed round or polygonal cells with abundant granular eosinophilic cytoplasm staining strongly for thyroid transcription factor 1. The tumor was, therefore, diagnosed as a GCT of the sellar region, belonging to tumors of the posterior pituitary. After surgery, visual impairment and anterior pituitary function were improved. Follow-up neuroimaging after 1 year showed no signs of recurrence.

**Conclusion:** GCT of the sellar region is difficult to diagnose on routine neuroimaging. Therefore, accurate diagnosis requires careful identification of clinical signs, magnetic resonance imaging including hypointensity on T2-weighted imaging, and analysis of combined morphological and immunohistochemical studies.

**Keywords:** Granular cell tumor, Magnetic resonance imaging findings, Neurohypophysis, Pituicyte, Thyroid transcription factor 1

## INTRODUCTION

Granular cell tumor (GCT) of the sellar region is a relatively rare neoplasm originating from the neurohypophysis, including the posterior pituitary and pituitary stalk/infundibulum.<sup>[12]</sup> Pathologically, this tumor arises from the pituicytes, which are modified gliocytes of ependymal

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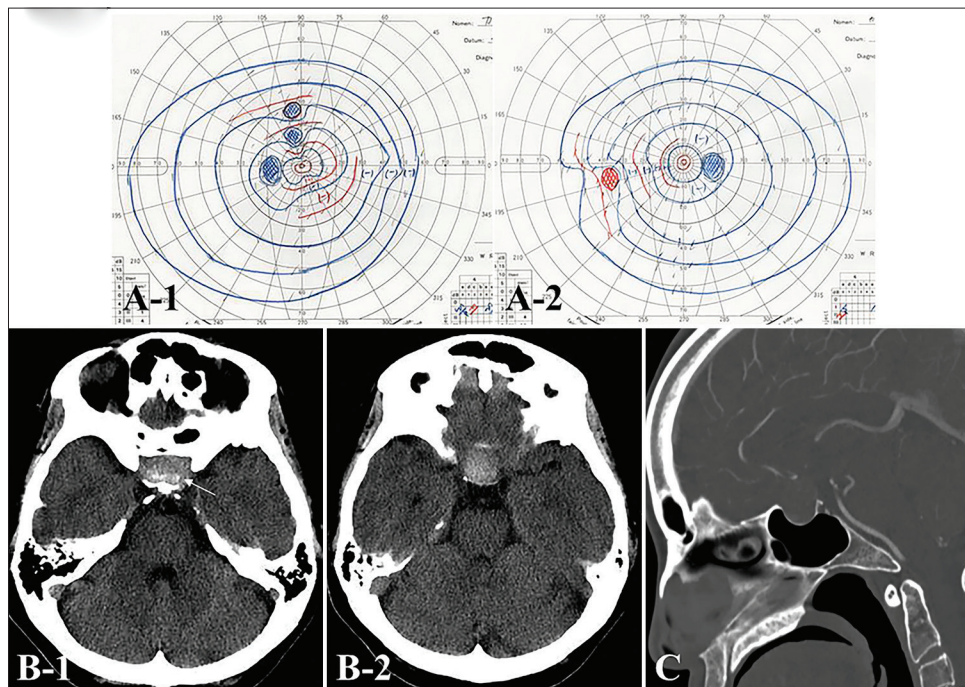
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cell lineage located in the neurohypophysis and pituitary stalk, and the tumor exhibits a preference for the intrasellar and suprasellar regions.<sup>[10,12]</sup> It is difficult to differentiate this tumor from other pituitary tumors, for example, pituitary adenoma, sellar meningioma, germinoma, pituicytoma, and so on, due to the lack of specific radiological findings and its low incidence.<sup>[7,12]</sup> However, this tumor is reported to infiltrate surrounding vital structures, such as the optic chiasm and cavernous sinus, more than other suprasellar tumors.<sup>[12]</sup> These features of GCT make it difficult to safely achieve gross total surgical resection of this tumor.<sup>[7,10,12]</sup> Therefore, it is very important to recognize the characteristic features of GCT, including neuroimaging and pathological findings, and understand the risks of surgical procedures. Here, we report a rare case of GCT of the sellar region resected by endoscopic endonasal transsphenoidal surgery (ETSS), and we suggest useful indicators for the accurate diagnosis of this tumor and pitfalls for the surgical procedure.

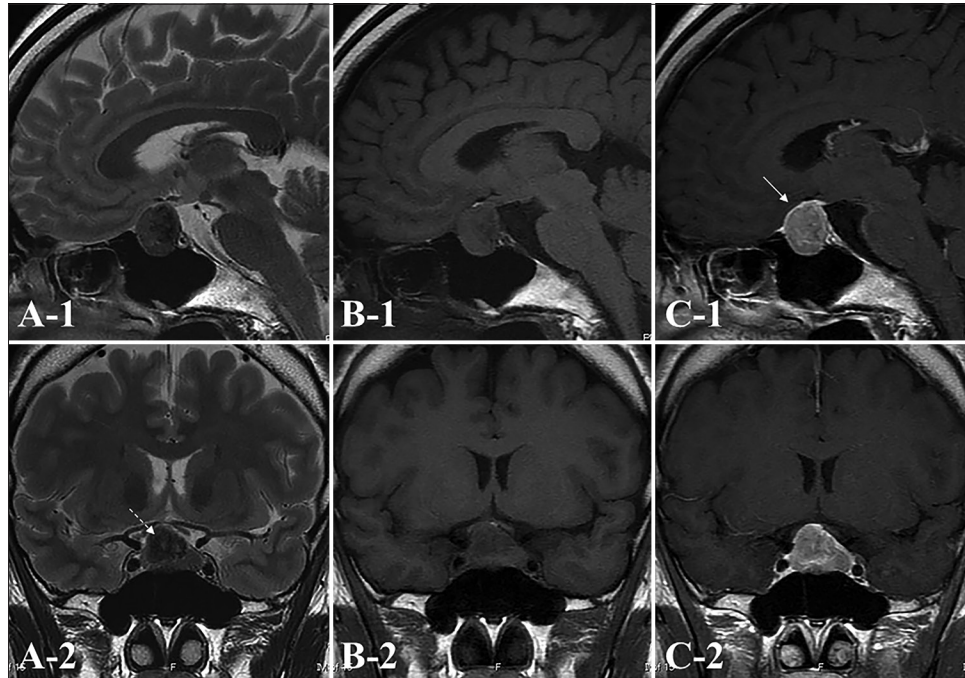
## CASE DESCRIPTION

A 42-year-old woman presented to our department with slight visual deterioration [Figure 1a]. Intracranial computed tomography (CT) showed a high-attenuated mass, including granular-like dots in the sellar and suprasellar regions, accompanied by an expansion of the sella turcica [Figure 1b and c]. Magnetic resonance imaging (MRI)

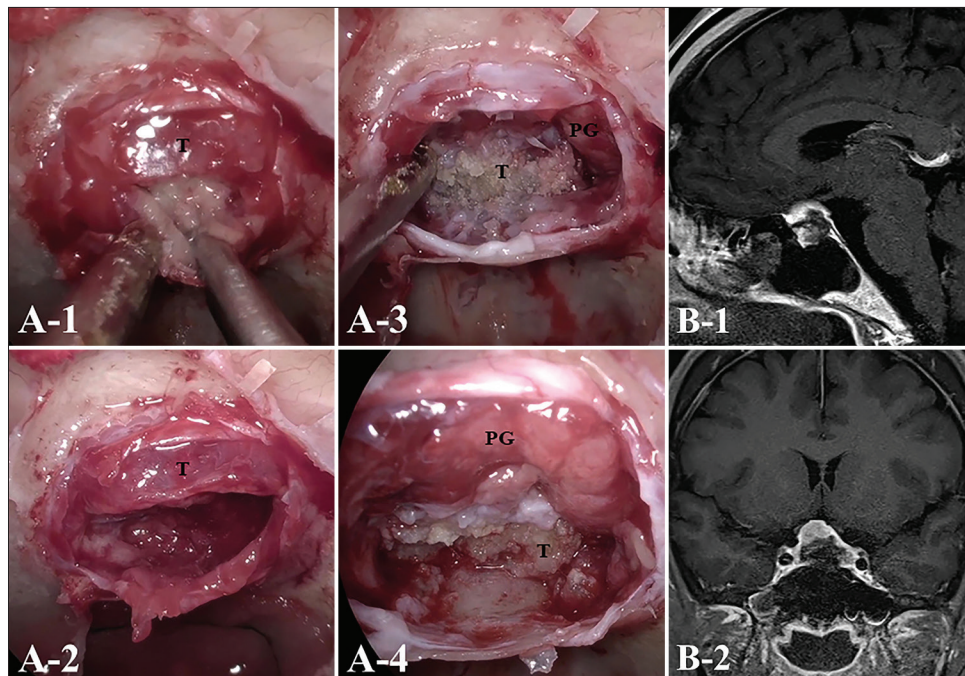
showed well-circumscribed, globular masses. The solid part was isointense, but the inside part of the mass was low intensity on T1-weighted imaging (WI) and T2-WI, and homogeneously enhanced to a moderate degree with gadolinium (Gd). The tumor extended into the suprasellar region, compressing the optic chiasm. The Gd-enhanced anterior pituitary gland was displaced supra-anteriorly, and high intensity on T1-WI suggested that the posterior pituitary appeared [Figure 2a-c]. Measurements of levels of hormones related to the anterior pituitary showed mild hyperprolactinemia (prolactin: 34.6 ng/ml; normal, <32.7 ng/ml). In terms of posterior pituitary function, there was not recognized diabetes insipidus. Preoperative differential diagnoses included pituitary adenoma, germ-cell tumor, sellar meningioma, pituicytoma, and glioma arising from the posterior pituitary. To confirm the histological diagnosis, ETSS was performed. Intraoperative findings demonstrated that this tumor was solid and extremely firm, including myriad yellowish granules without bleeding [Figure 3a and b]. The tumor originated from the posterior pituitary gland and had a clear margin between it and the anterior pituitary gland [Figure 3c]. Subtotal resection was achieved to reduce compression of the optic nerve [Figure 3d]. Pathological examination with hematoxylin and eosin staining demonstrated round or polygonal cells with abundant granular eosinophilic cytoplasm. Most nuclei were round to oval, with no evidence of cellular atypia or mitotic



**Figure 1:** Goldmann perimetry field examination on admission demonstrating a slight visual disturbance (A) Preoperative (B) axial and (C) sagittal computed tomography (CT) shows a high attenuated mass in the sellar region with granular-like high density dots (white arrow) accompanied by expansion of the sella turcica.



**Figure 2:** On preoperative axial T2-weighted (A), T1-weighted (B), and gadolinium (Gd)-enhanced T1-weighted (C) magnetic resonance imaging (MRI), a tumor mass is seen in the sellar region extending into the suprasellar region. The tumor is homogeneously enhanced to a moderate degree with Gd. The enhanced anterior pituitary gland is displaced anteriorly (white arrow), and hyperintense on T1WI which suggested posteriorpituitary is appeared. The tumor is low intensity inside the solid mass on T2-weighted imaging (WI) (white dashed arrow).



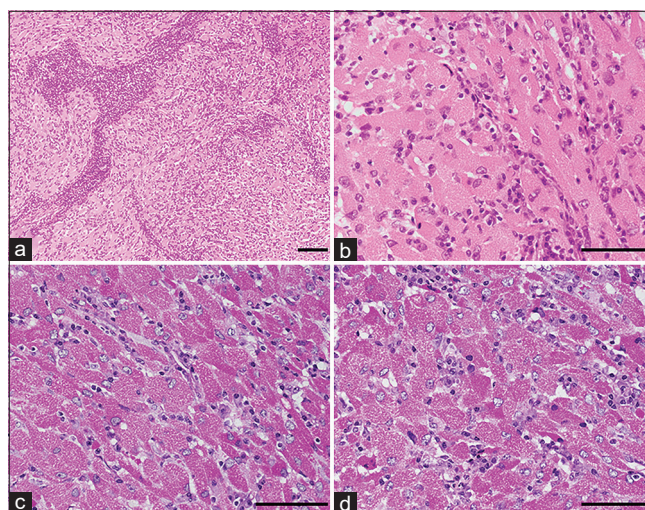
**Figure 3:** A) Intraoperative findings from endoscopic, endonasal, transsphenoidal surgery (PG: pituitary anterior gland; T: tumor). Macroscopic examination of this tumor shows that it is solid and rubbery-firm. The cut surface is yellowish, and uncountable gray to yellow granules are appear to be inside the solid mass. The tumor has infiltrated into the posterior pituitary; therefore, subtotal resection is performed. Postoperative (B-1) sagittal and (B-2) coronal images of Gd-enhanced MRI one year after surgical resection show no signs of recurrence

figures. In addition, perivascular lymphocytic aggregates were recognized [Figure 4a and b]. Periodic acid–Schiff (PAS) staining of cytoplasmic granules was resistant to diastase digestion [Figure 4c and d]. Immunohistochemical studies were performed with antibodies for S-100, glial fibrillary acidic protein (GFAP), Ki-67, and thyroid transcription factor-1 (TTF-1). Tumor cells were immunoreactive for S-100 protein, but negative for GFAP [Figure 5a and b]. The Ki-67 (MIB-1) proliferation-related labeling index was low, at 2.0% [Figure 5c]. In addition, almost all tumor cells appeared strongly positive for TTF-1 [Figure 5d]. Taking all these results into account, the final diagnosis was GCT of the sellar region, belonging to tumors of the posterior pituitary in accordance with the WHO classification of central nervous system (CNS) tumors (2016).<sup>[12]</sup> The patient remained clinically stable with a normal visual field, the residual tumor showed no enlargement at the next 1-year follow-up visit [Figure 3b], and the hormonal dysfunction (hyperprolactinemia) improved to near-normal levels (prolactin: 15.5 ng/ml).

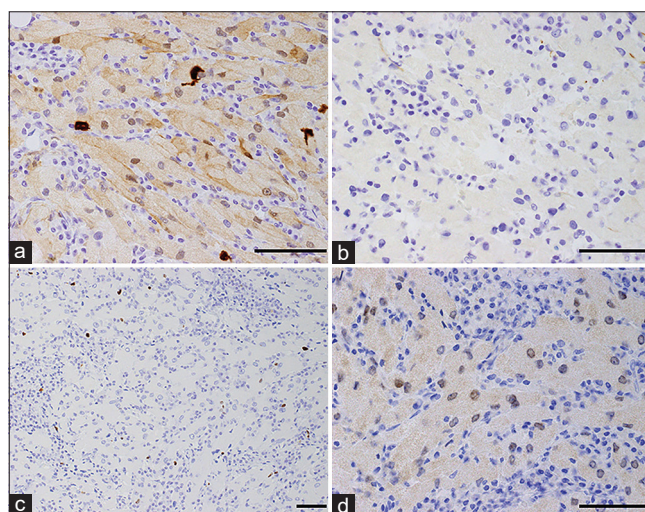
## DISCUSSION

GCT of the sellar region is a relatively rare primary tumor originating from the neurohypophysis, including the posterior pituitary and pituitary stalk/infundibulum.<sup>[12]</sup> Boyce and Beadles were the first to recognize GCT of the neurohypophysis as a distinct entity,<sup>[4]</sup> and the tumor was described in greater detail in the medical literature.<sup>[7,13]</sup> In the current 2016 WHO classification of CNS tumors, the term GCT of the sellar region is restricted to a distinct group of low-grade neoplasms of the sellar region originating in the posterior pituitary or its stalk, presumably arising from pituicytes.<sup>[12]</sup>

Clinically, this tumor often occurs in the sixth decade of life in men and the fifth decade in women and tends to develop slowly over a period of years, although patients can present with acute headache, confusion, diplopia, and visual disturbance.<sup>[12]</sup> Preoperative CT and MRI show well-circumscribed, globular masses located in the sellar region.<sup>[7,10,12]</sup> The solid tumors almost always appear relatively hyperattenuated on CT, and calcification is extremely rare. MRI generally depicts this tumor mass as isointense on T1-WI and iso-hypointense on T2-WI, and homogeneous enhancement has been seen after the administration of contrast agents.<sup>[3,6,7,8,12]</sup> In addition, the enhanced anterior pituitary gland is displaced anteriorly from the tumor mass, potentially reflecting its derivation from the posterior pituitary lobe.<sup>[12]</sup> In addition, other reports noted that the hypointense visualization on MRI/T2-WI may represent the countless eosinophilic granules in the cytoplasm within the solid mass of the GCT.<sup>[7,10]</sup> We hypothesize that this intratumoral hypointense sign on T2-WI is an extremely interesting and important finding and seems to be the key



**Figure 4:** Histopathology of the resected tumor shows round or polygonal cells with abundant granular eosinophilic cytoplasm and perivascular lymphocytic aggregates. Most nuclei are round to oval in appearance without evidence of cellular atypia and mitotic figures (hematoxylin and eosin staining) (a, b). Periodic acid Schiff (PAS) staining of cytoplasmic granules is resistant to diastase digestion (c: PAS staining, d: diastaseresistant-positive PAS reaction). Magnification, a)  $\times 100$ ; b-d)  $\times 400$ . Scale bar, a) 400  $\mu\text{m}$ , b-d) 100  $\mu\text{m}$ .



**Figure 5:** Photomicrographs showing the histopathology of the tumor. Most tumor cells are immunoreactive for S-100 protein (a), but immune-negative for glial fibrillary acidic protein (GFAP) (b). This tumor shows slightly positive staining for Ki-67 (MIB-1) (MIB-1 labeling index: 2.0%) (c). In addition, almost all tumor cells are strongly positive for TTF-1 (d). Magnification, a, b, d)  $\times 400$ ; c)  $\times 100$ . Scale bar, a, b, d) 400  $\mu\text{m}$ , c) 100  $\mu\text{m}$ .

point for making the preoperative diagnosis of GCT of the sellar region. In the present case, the patient was a 42-year-old woman with only mild bitemporal hemianopsia, which seems to be atypical for GCT of the sellar region. However, MRI demonstrated homogeneous moderate enhancement

with Gd, and the anterior pituitary gland was recognized in front of the tumor mass. In addition, the inside part of the solid mass appeared as a hypointense signal on T2-WI. Such clinical signs and imaging findings are very important to diagnose GCT accurately before surgery, and we think that this recognition leads to safe and effective operation for GCT of the sellar region.

In the revised WHO classification of CNS tumors (2016), the definition of GCT of the sellar region is as follows: “A circumscribed tumor that is composed of large epithelioid to spindled cells with distinctively granular, eosinophilic cytoplasm and that arises from the neurohypophysis or infundibulum.” Microscopically, GCT consists mainly of densely packed polygonal cells with abundant granular eosinophilic cytoplasm, which was confirmed as lysosomes on electron microscopy, apparently different from neuroendocrine granules. The nuclei are a small round shape with little pleomorphism, and mitotic figures are rare.<sup>[5,12]</sup> With regard to their immunohistochemical characteristics, GCTs of the sellar region are variably positive staining for S100, GFAP, and TTF-1, but immunonegative for pituitary hormones or neuroendocrine markers.<sup>[12]</sup> It has been proposed that GCT of the sellar region is derived from the Schwann cells and the modified glial cells of the pituitary or the pituicytes, based on the positive immunostaining for GFAP in the tumor cells.<sup>[7,9]</sup> However, some other studies have shown negative staining for GFAP in this tumor, which refutes the theory of a pituicyte origin.<sup>[2,7]</sup> Thus, the immunostaining of GFAP in GCT is still controversial. On the other hand, in the previous reports, pituicytes, which are specialized gliocytes of the posterior pituitary, had five ultrastructural variants: major cells, dark cells, granular cells, ependymal cells, and oncocytic cells. Of the five ultrastructural variants, granular pituicytes were observed in the neurohypophysis at a high incidence and had similar histological features to GCT.<sup>[5,10,11]</sup> In addition, TTF-1 expression in nontumorous pituicytes, pituicytoma, and GCT of the neurohypophysis indicated a common pituicyte lineage.<sup>[1,11]</sup> Therefore, GCT of the sellar region was identified as originating from granular pituicytes.<sup>[11,12]</sup> Thus, TTF-1 is an important molecule for exploring the origin of GCT of the sellar region, but it seems less necessary in terms of performing accurate pathological diagnosis of this tumor. In the present case, the tumor was composed of round or polygonal cells with abundant granular eosinophilic cytoplasm. Most nuclei were round to oval with no evidence of cellular atypia or mitotic figures, and perivascular lymphocytic aggregates were recognized microscopically. This structure was immune positive for S-100 and negative for GFAP, and tumor cells were strongly immune positive for TTF-1. These findings are consistent with GCT of the sellar region, in consideration of morphological studies and immunohistochemical analysis based on the WHO classification in 2016.

Finally, regarding the treatment of GCT of the sellar region, surgical resection has the most important role.<sup>[10,14]</sup> Hence, complete resection should be attempted, but there is a high rate of recurrence in patients after partial resection.<sup>[5,10]</sup> Thus, radiotherapy might be applied to the residual tumor. Recently, ETSS is becoming a common procedure from the viewpoint of its effectiveness and lesser invasiveness for GCT located in the sellar region.<sup>[7,8,10]</sup> On the other hand, these tumors are reported to be more strongly attached to normal anatomical structures, such as the infundibulum or posterior pituitary lobe, than other suprasellar tumors. The strong attachment to normal structures is probably the main reason for the difficulty in achieving complete resection.<sup>[7,8,10,12]</sup> In the present case, gross total resection was not achievable due to the strong attachment to the posterior pituitary lobe and its nature as an unexpectedly hard tumor. Therefore, we decided to perform subtotal resection. However, we did not introduce radiotherapy immediately after the surgery, because the Ki-67 proliferation-related labeling index was low at 2.0% pathologically in this case. If the tumor growth is recognized during the long-term observation, we are going to introduce radiotherapy. Fortunately, follow-up neuroimaging after 12 months showed no signs of recurrence without neurological complications. Further cases and longer patient follow-up are required.

## CONCLUSION

In our view, GCT of the sellar region should be included as an important differential diagnosis for pituitary tumors due to the potential for very strong attachment to normal structures and the difficulty of surgical resection, unlike common pituitary tumors. Therefore, careful identification of the clinical signs and MRI findings and detailed evaluation of immunohistochemical studies are necessary for accurate diagnosis and appropriate treatment selection for GCT of the sellar region.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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