

Clinical and imaging features of granular cell tumor of the neurohypophysis

A retrospective analysis

Fang Han, MD^a, Lu Gao, MD^a, Yin Wang, MD, PhD^b, Yingying Jin, MD, PhD^a, Yi Lv, MD^a, Zhenwei Yao, MD, PhD^a, Jiawen Zhang, MD, PhD^{a,*}

Abstract

The aim of this study was to explore x-ray computed tomography (CT) and magnetic resonance imaging (MRI) characteristics specific to granular cell tumors (GCTs) of the neurohypophysis.

The clinical and imaging data of 6 patients with operation-proven GCTs of the neurohypophysis were analyzed retrospectively.

There were 6 patients with GCTs of the neurohypophysis confirmed pathologically. Five of the tumors were purely suprasellar lesions distinct from the intrasellar pituitary gland. One tumor was both intra- and suprasellar. Solid tumors were hyperattenuated and enhanced homogeneously on CT, while showing isointensity on T1WI and heterogeneous hypointensity on T2WI, with homogeneous (4/5) or inhomogeneous (1/5) enhancement. The cystic tumor showed hypointensity on T1WI and hyperintensity on T2WI, with ring enhancement. “Star-like crack sign” was seen in 2 larger solid cases. Calcification was absent in all cases.

Well-circumscribed intra and/or suprasellar masses, hyperattenuated and homogeneously enhancing on CT, hypointensity on T2WI, rarely seen calcification, should arouse suspicion of GCTs of the neurohypophysis.

Abbreviations: CE-CT = contrast-enhanced CT, CE-MRI = contrast-enhanced MRI, CNS = central nervous system, CSF = cerebrospinal fluid, CT = x-ray computed tomography, GCTs = granular cell tumors, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging.

Keywords: granular cell tumor, neurohypophysis, tomography, x-ray computed, magnetic resonance imaging

1. Introduction

Granular cell tumors (GCTs) of the neurohypophysis are rare tumors seen in the sellar and suprasellar region that are poorly understood because of the confusion regarding their nomenclature and indeterminate imaging features. Boyce and Beadles,^[1] in 1893, were considered the first to recognize GCT of the neurohypophysis as a distinct entity, and the tumor was described in more detail in the medical literature in 1951.^[2] The nomenclature of GCT has been controversial because the origin of the tumor is obscure.^[3] It has been variously referred to as myoblastoma, infundibuloma, choristoma, and pituicytoma. The 2016 WHO Classification of Tumors of the Central Nervous System categorized pituicytoma as an independent diagnostic entity, distinct from GCT of the neurohypophysis.^[4] GCT is more common in 40 to 60-year-old patients. So far, only 2 pediatric cases have been reported.^[5] The

most common clinical symptoms of GCT of the neurohypophysis are visual deterioration and headache. However, no specific radiological features of the tumor have been reported to date. The purpose of this study was to explore the specific x-ray computed tomography (CT) and MRI characteristics of GCT that would enable preoperative diagnosis of GCTs.

2. Materials and methods

2.1. Patients

The radiological findings and clinical materials of 6 patients pathologically confirmed with GCTs of the neurohypophysis were collected between 2008 and 2014. The study was approved with the institutional review board of our hospital. All patients gave informed consent. We retrospectively analyzed the clinical, imaging, and pathology data of 6 patients (4 women and 2 men) aged 40 to 53 years who had pathologically confirmed GCTs of the neurohypophysis according to the WHO criteria of 2016. Information concerning sex, age, presenting symptoms, and clinical history was obtained from hospital records and were reviewed. The CT and MRI data obtained for all patients before surgery were also reviewed. All 6 patients underwent resection of the tumors, which subsequently were confirmed by histopathology as GCTs of the neurohypophysis according to the latest 2016 WHO criteria.

2.2. Imaging analysis

All images were reviewed and analyzed by 4 board-certified neuroradiologists. Radiological images were analyzed for location, configuration, cystic change, calcification, density and signal intensity, and enhancement patterns of the tumors.

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^a Department of Radiology, ^b Department of Pathology, Huashan Hospital, Fudan University, Shanghai, China.

* Correspondence: Jiawen Zhang, Department of Radiology, Huashan Hospital, Fudan University, Shanghai, China (e-mail: jiawenzhang1971@163.com).

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Table 1**The preoperative characteristics of the 6 patients.**

No.	Age, years	Sex	Presenting symptoms	CT	CE-CT	MRI	CE-MRI
1	51	F	Visual loss	Y	Y	Y	Y
2	40	M	Visual loss	N	N	Y	Y
3	45	F	Dizziness	Y	N	Y	Y
4	53	M	Polyuria and polydipsia	Y	Y	Y	Y
5	44	F	Visual loss	Y	Y	Y	Y
6	42	F	Headache	Y	N	N	N

CE-CT = contrast-enhanced CT, CE-MRI = contrast-enhanced MRI, CT = x-ray computed tomography, F = female, M = male, MRI = magnetic resonance imaging, N = no, No. = number, Y = yes.

3. Results

3.1. Clinical findings

The preoperative characteristics of the 6 patients and the imaging methods used in each patient are listed in Table 1. The mean age of the patients was 46 ± 5 years (range 40–53 years). The most common presenting symptom was visual loss (3/6); one patient presented with polyuria and polydipsia, one with dizziness, and one with headache. The duration of the symptoms ranged from 2 months to 5 years.

3.2. Imaging findings

Preoperative CT and MRI revealed well-circumscribed, globular masses located in the sellar region. Five of the GCTs were purely suprasellar lesions, clearly distinct from the pituitary gland (Figs. 1–3). Only 1 of the tumors was both intra- and suprasellar (Fig. 4). Five of the tumors were solid, while one was cystic (Fig. 4). All solid GCTs appeared hyperattenuated to brain parenchyma on noncontrast CT (Figs. 1–3). However, none of the cases revealed obvious calcification. Enhancement patterns from contrast-enhanced CT (CE-CT) images were available in 3 of the 6 cases. After administration of intravenous contrast, the tumors enhanced obviously and homogeneously on CT (Fig. 1). Routine MRI scans and contrast-enhanced T1WI were available for 5 patients (Table 2). All the solid entities were isointense to cortex on T1WI and hypointense to white matter on T2WI. The

signals of the tumors tended to be homogeneous, although a star-like crack, with low signal on T1WI and high signal on T2WI, was apparent within the larger masses, which we termed the “star-like crack sign” (Figs. 1 and 2). Four of the five solid lesions showed homogeneous enhancement on contrast-enhanced T1WI (Figs. 2 and 3), while one showed heterogeneous enhancement (Fig. 1). Interestingly, there was diffusion of gadolinium into the star-like crack (Figs. 1 and 2). The cystic GCT showed hypointensity on T1WI and hyperintensity on T2WI; peripheral enhancement was present (Fig. 4). There was no obvious sign of invasion of adjacent brain or cranial bone and no tendency for vascular encasement. No clear imaging evidence was found for calcification or atypically increased vascularity.

4. Discussion

Symptomatic GCTs of the neurohypophysis are rare tumors of the sellar region. GCT of the neurohypophysis was classified as a benign tumor in the 2016 WHO classification of the central nervous system (CNS) tumors.^[4] Due to the abundant blood supply of the tumor, it become really essential for correct diagnose before operation. Correct diagnosis can accurately assess the risk of bleeding during operation and further make appropriate operation plan. Cystic GCTs are rarer still. As far as we know, only 2 cases of cystic GCT in the sellar region have been reported previously.^[6,7] Because of its rarity, GCT is seldom considered in the preoperative differential diagnosis of a sellar

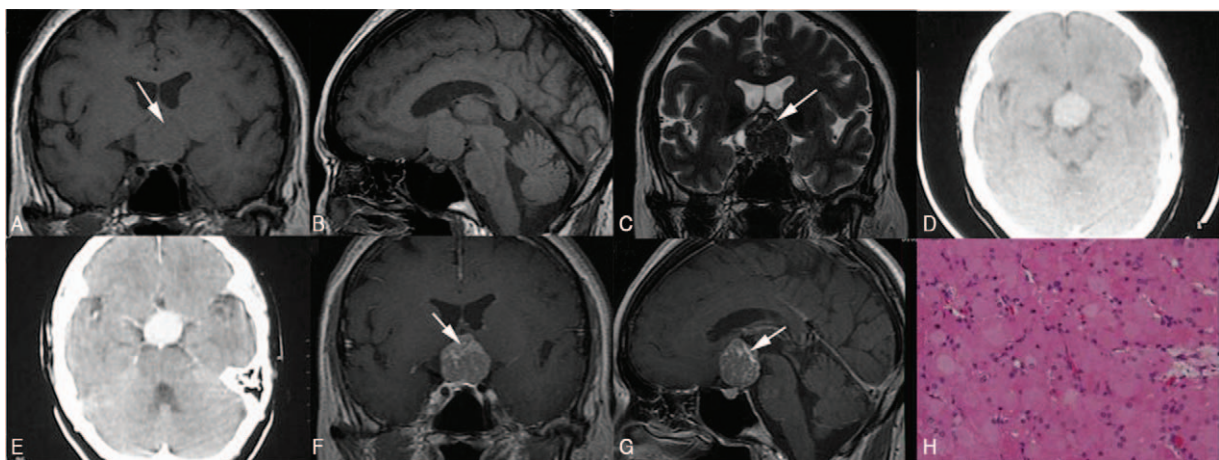


Figure 1. MRI and pathological images of a 51-year-old woman who presented with decreased vision. Coronal and sagittal T1WI (A and B) show a large suprasellar isointense mass. Coronal T2WI (C) demonstrates a heterogeneous hypointense midline lesion. Routine and contrast-enhanced axial CT (D and E) show a suprasellar lesion hyperattenuated to brain, with obvious homogeneous enhancement. Postcontrast coronal and sagittal T1WI (F and G) show a mass with a well-defined margins and granulated enhancement. The pituitary gland appears normal. Note that within the mass there is a star-like crack (arrows in A, C, F, G) that shows hypointensity on T1WI and hyperintensity on T2WI. The star-like crack is enhanced after contrast. Photomicrograph (H) reveals abundant granular cytoplasm within the tumor cells. CT = x-ray computed tomography, MRI = magnetic resonance imaging.

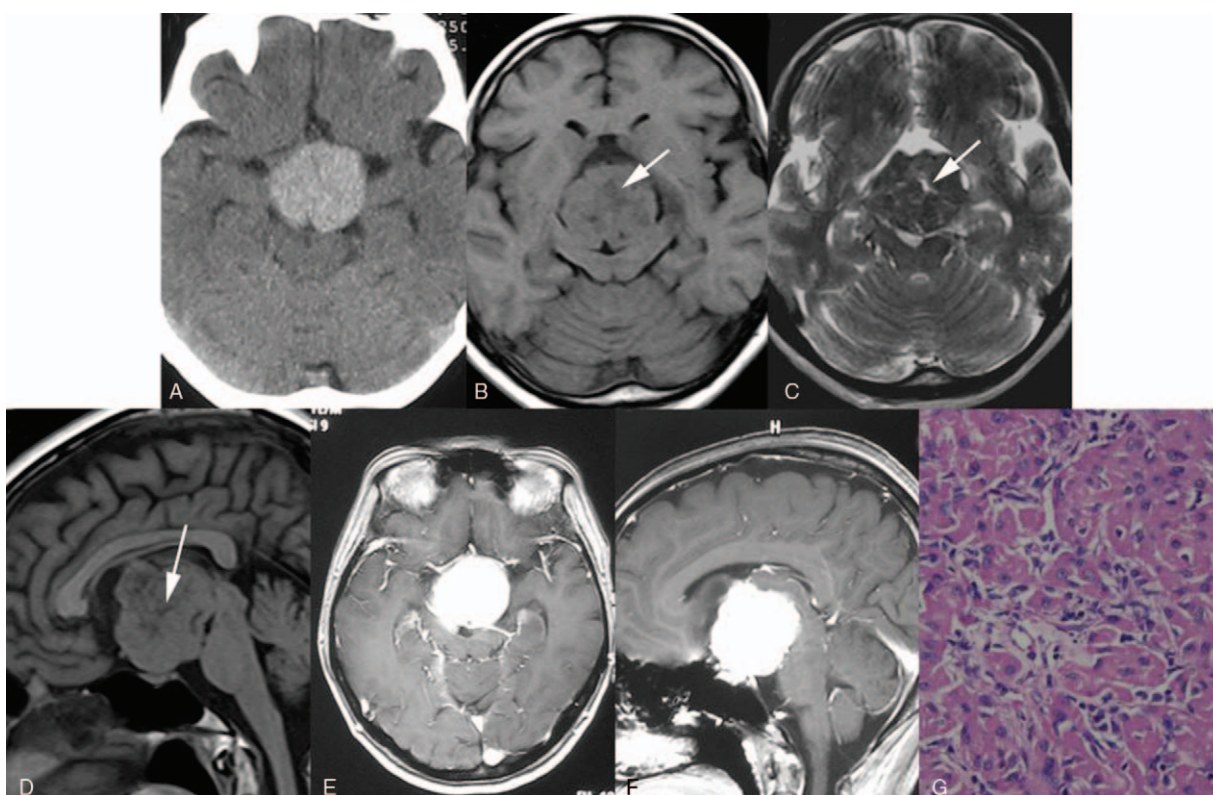


Figure 2. MRI and pathological images of a 44-year-old woman who presented with visual loss. Axial CT demonstrates a well-delineated, homogenous, and hyperdense suprasellar mass (A). The mass mainly shows iso-intensity on axial T1WI (B) and hypointensity on axial T2WI (C); there is an obvious star-like crack (arrows in B–D) within the mass. The star-like crack is enhanced after administration of contrast medium, and the entire mass shows a homogeneous and marked enhancement on postcontrast axial and sagittal T1WI (E and F). The diagnosis of GCT is confirmed by the photomicrograph (G). CT = x-ray computed tomography, MRI = magnetic resonance imaging.

region mass. However, this rarely reported midline lesion in the sellar region may, in fact, may be fairly common. This has been demonstrated on autopsy.^[8] In 1 study,^[9] the investigators found that 9% of 100 pituitary glands at autopsy were confirmed as small GCTs. The data suggest that GCTs cause symptoms at a late stage because of their slow growth. Although the histological character of GCTs is remarkably typical, the histogenesis and nomenclature is controversial. Various terms have been applied to this tumor. The tumor was originally believed to be an aberrant growth of ectopic embryological tissue and was therefore called a choristoma.^[3] Later, the tumor was considered to be derived from embryonic muscle cells because of its histological similarity to GCT of the tongue, and the term granular cell myoblastoma was used. However, there is no evidence to support this theory,^[10] with immunoperoxidase staining for desmin and smooth muscle actin being negative. The dominant view at present is that GCT of the neurohypophysis originates from the Schwann cell and the modified glial cell of the pituitary or the pituicyte; this belief is based on the positive immunostaining for glial fibrillary acidic protein (GFAP) in the tumor cells.^[11–13] On the other hand, several other studies have showed negative staining for GFAP, which refutes the theory of a pituicyte origin.^[14–16] A third hypothesis endorsed by some investigators is that the variable immunoreactivity indicates that these tumors are biologically heterogeneous.^[17–19] Under these circumstances, the descriptive term “granular cell tumor of the neurohypophysis” may be the most reasonable nomenclature for this tumor until its exact origin is determined.

4.1. Clinical presentation

Cohen-Gadol et al^[7] analyzed the data of 50 patients with symptomatic GCTs of the neurohypophysis that have been reported in the earlier literature and illustrated that visual loss, headache, decreased libido, infertility, panhypopituitarism, galactorrhea, and amenorrhea were common presenting symptoms. Due to oppression of the optic chiasma, approximately 90% patients had visual impairment or visual defect.^[20] There was one case of preoperative diabetes insipidus in our series; only other 2 cases that manifested diabetes insipidus have been described to date.^[21,22] GCT itself has no endocrine activity.^[20] Endocrine hyperfunction, may be related to the compression of the hypothalamus, has been reported only in 2 cases, 1 patient presenting with acromegaly and another with precocious puberty.^[19,23] The most common clinical presentation in our series was visual disturbance, which is consistent with earlier reports that suggest that visual disturbance, headache, and dizziness are the commonest presentations in this disease.^[24] Visual disturbances may be explained by compression of the hypothalamus and headache and dizziness may be explained by compression of the cerebrospinal fluid (CSF) pathway by the tumor leading to increased intracranial pressure. Although an overwhelming majority of the tumors have a chronic and progressive clinical course, acute onset of symptoms has been reported in a few cases.^[3,25,26]

Most cases of GCTs reported in the literature have been in adults, and the female-to-male ratio is reported to be 2:1. In addition, the tumor is more common in women in the fourth to

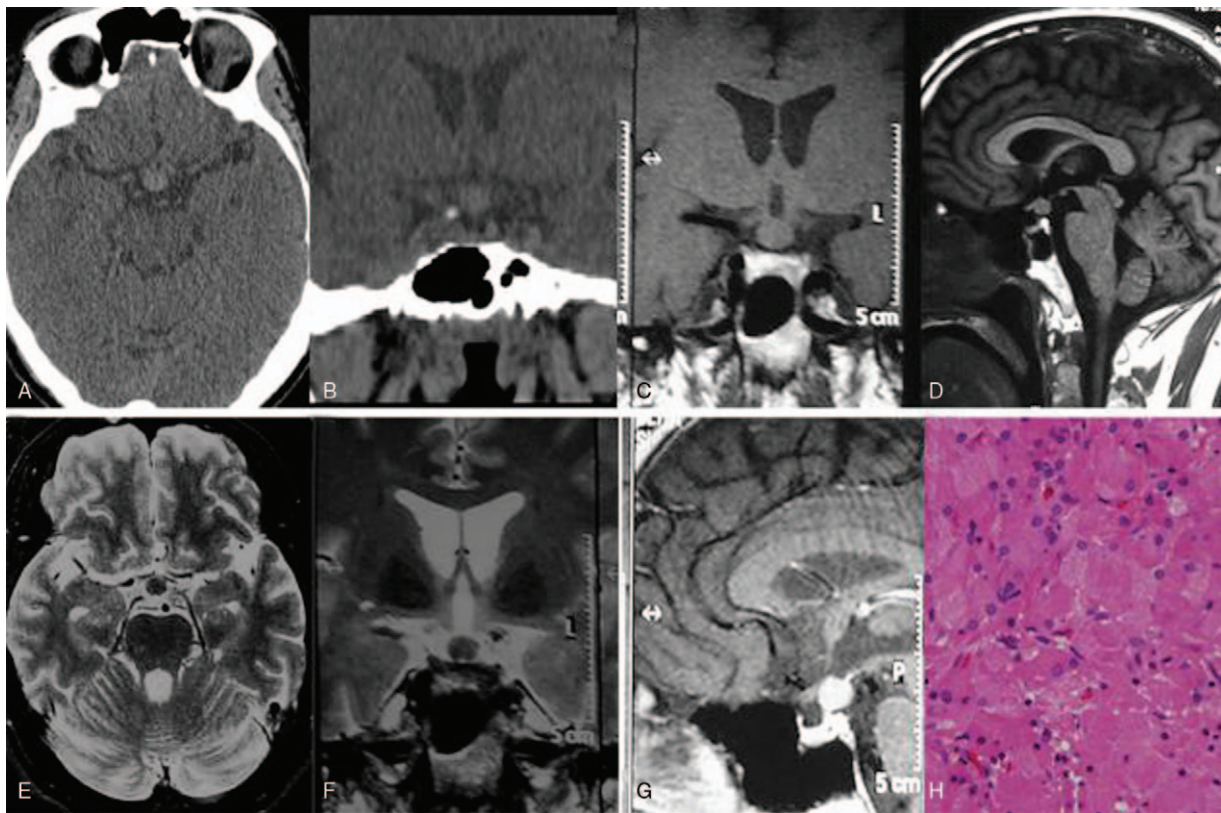


Figure 3. MRI and pathological images of a 53-year-old man with symptoms of polydipsia and polyuria. A well-defined suprasellar mass is seen. Axial (A) and coronal (B) CT scans reveal a hyperdense suprasellar tumor. The mass shows isointensity on coronal (C) and sagittal (D) T1WI, and hypointensity on axial (E) and coronal (F) T2WI. T1-weighted contrast-enhanced scan (G) shows homogeneous enhancement of the suprasellar mass, which appears to have originated from the pituitary stalk. Microscopic section (H) supports the diagnosis of GCT of the neurohypophysis. GCTs=granular cell tumors, MRI=magnetic resonance imaging.

fifth decades of life.^[6,7,19,27] Our findings were consistent with this, as the 6 patients in our study comprised 4 women and 2 men with ages ranging from 40 to 53 years (mean age 46 ± 5 years). GCT of the neurohypophysis is exceedingly rare in the pediatric population, with only 2 patients (both boys; one aged 8 years and the other 11 years) having been reported to date.^[19,28] The tumor should therefore be diagnosed with circumspection in children.

4.2. Imaging characteristics and treatments

Although the CT and MRI characteristics are considered to be nonspecific for diagnosis of GCT, they are still the best options available for preoperative diagnosis of GCT of the neurohypophysis. In our series, preoperative CT and MR images demonstrated well-circumscribed, globular masses located in the intra- and/or suprasellar region. Most of the lesions were entirely suprasellar and clearly separate from the pituitary gland. Only 1 of the 6 cases was both intra- and suprasellar in location. None of our 6 cases appeared as a purely intrasellar lesion, which is consistent with previous reports.^[24] Therefore, detection of a purely intrasellar lesion could offer a relatively high probability of excluding GCT from the differential diagnosis. Most GCTs tend to be solid, and only one of our 6 cases was purely cystic. Only 2 other cases of GCTs with cystic components have been reported to date.^[6,7] The biggest difference is that no intracystic nodule was detected in our cystic case. Therefore, a purely cystic sellar mass also may be indicative of a GCT. The solid tumors in our series almost always appeared relatively hyperattenuated to

brain parenchyma on CT and demonstrated an obvious and homogeneous enhancement after administration of intravenous contrast; this is consistent with previous reports.^[13,24] None of our 6 cases revealed obvious calcification. Calcifications are extremely rare. Schaller et al. reported the first case of GCT with calcification in preoperative imaging studies, and only 6 cases of GCT with calcification have been reported to date.^[6,7,13,20,29,30] All the solid entities were mainly isointense on T1WI and hypointense to white matter on T2WI. The imaging features include hyperattenuation on CT, isointensity on T1WI, and hypointensity on T2WI. After cautiously researched our cases and combine with histological features, we think that different contents of mucoprotein contribute to various imaging features. Meanwhile, it has been reported that when the protein concentration was 10,000 mg/dL or less, it showed hypointense on T1WI and hyperintense on T2WI. When the protein concentration rose to 10,000–17,000 mg/dL, it showed both hyperintense on T1WI and T2WI. When the protein concentration reached 17,000 mg/dL and more, it was hyperintense on T1WI and hypointense on T2WI.^[31] So we suspected that hypointense on T2WI has correlation with higher concentrations of protein, the star-like crack may be the result of the unbalanced distribution of protein. Interestingly, the star-like crack was enhanced after administration of contrast, which has not been reported before. We speculated that this sign on MRI, maybe one of the characteristics of GCT of the neurohypophysis. CT, because of its poor soft tissue resolution, did not demonstrate this sign. The lone cystic GCT in our series showed hypointensity on

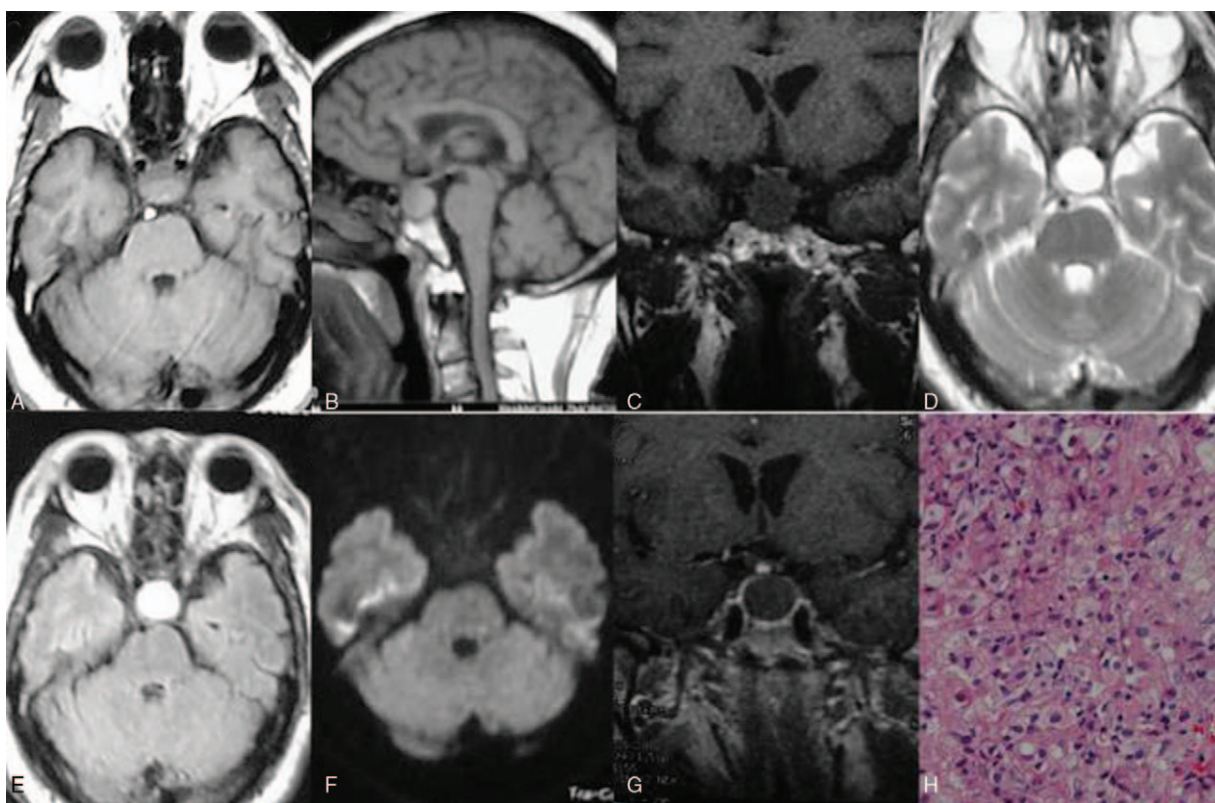


Figure 4. MRI and pathological images of a 40-year-old man with a cystic lesion involving the sella and suprasellar region. The noncontrast axial (A), sagittal (B), and coronal (C) T1WI show a slightly hypointense cystic lesion, isointense interface morphology is noted within the cystic cavity. The axial T2WI (D) and FLAIR sequences (E) reveal high signal intensity. On the DWI (F) image, low signal intensity is noted within the cyst. On the postcontrast coronal (G) T1WI, marked peripheral enhancement is noted. Postoperative pathological image (H) confirms it as a GCT. DWI=diffusion-weighted imaging, GCT=granular cell tumor, MRI=magnetic resonance imaging.

T1WI and hyperintensity on T2WI, with peripheral enhancement. No obvious signs of invasion of adjacent brain or cranial bone or tendency for vascular encasement were seen in any of our cases. The main treatments for GCT are surgery and postoperative radiotherapy. Although a complete resection is limited by hemorrhage and lack of septum with the surrounding tissue, transphenoidal surgery is still the primary treatment.^[20]

Table 2
MR signal characteristics for GCTs.

	Solid tumors (n=4)	Cystic tumor (n=1)
T1WI		
Hypointense	0/4	1/1
Isointense	4/4	0/1
Hyperintense	0/4	0/1
T2WI		
Hypointense	4/4	0/1
Isointense	0/4	0/1
Hyperintense	0/4	1/1
Enhancement		
Heterogeneous	1/4	0/1
Homogeneous	3/4	0/1
Peripheral	0/4	1/1

The figures in the columns represent the number of cases that showed the particular imaging characteristic. n=number.
GCTs=granular cell tumors.

5. Conclusions

Although GCT is rarely reported in clinic, it need pay more attention to differential diagnosis of sellar tumors. GCT should be suspected if the lesion located in intra and/or suprasellar demonstrated well-circumscribed, hyperattenuated on CT, hypointensity on T2WI and homogeneous enhancement. Considering the limited number of patients and follow-up in our series, our results need, however, to be validated on a larger number of cases. And we need more practice and further research for this tumor.

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