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Case report

A patient with primary intracranial granuloma with difficulty in differential diagnosis: A case report and literature review

Wentao Liang [a,c,1], Zhou Qi [b,1], Hu Yang [a,c], Liang Niu [a,c], Qiao Li [a,c], Shiwen Guo [b,2,*], Yawen Pan [a,c,**,2]

[a] Department of Neurosurgery, Lanzhou University Second Hospital, Lanzhou, Gansu, 730030, China
[b] Department of Neurosurgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, 710061, China
[c] Key Laboratory of Neurology of Gansu Province, Lanzhou, Gansu, 730030, China

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ABSTRACT

There are few reports about primary intracranial granulomas without an identifiable infectious history. A 25-year-old male with intracranial granuloma. The patient presented with a history of tinnitus with intermittent headache for 1 week. Consequently, MRI showed pronounced and extensive enhancement lesions in the left frontal lobe involved in the cerebral longitudinal fissure cistern and the inside of the right frontal lobe, accompanied by a moderate degree of oedema; The lesion was a pilomyxoid astrocytoma preoperatively. Following a systemic examination, gross total resection of the lesion was performed, and postoperative pathological examination revealed the presence of inflammatory lesions. The patient exhibited notable symptom amelioration post-surgery, leading to discharge after the treatment. Subsequently, a sequential treatment involving steroid therapy was administered, resulting in successful patient recovery.

1. Introduction

Intracranial granuloma is a rare pathological manifestation, representing tumour-like masses formed in the brain due to chronic inflammation [1]. The tissue structure of intracranial granumolas primarily consists of accumulated modified macrophages, actively proliferating fibroblasts, capillary beds, and chronic inflammatory cells. This disease can be triggered by various infectious and noninfectious pathogens, with common examples including brain tuberculoma, neurosyphilis granuloma, fungal granuloma, parasitic granuloma, and foreign body granuloma [2]. Among them, infectious granuloma is the most common, while noninfectious granuloma is often considered a response to foreign bodies. It has been reported that granulomas often mimic tumours clinically, radiologically, or even grossly, making their differential diagnosis extremely challenging [3]. This study primarily describes a case of primary intracranial granuloma, in which the patient had no history of systemic infection or surgery, and this type of case is reported for the first time.

* Corresponding author. Department of Neurosurgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shanxi, 710061, China.
** Corresponding author. Department of Neurosurgery, Lanzhou University Second Hospital, Lanzhou, Gansu, 730030, China.
E-mail addresses: gsw1962@126.com (S. Guo), pyw@lzu.edu.cn (Y. Pan).
[1] These authors were equally to this work.
[2] These authors were equally to this work.

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1.1. Case presentation

A 25-year-old male was admitted to the hospital and presented with “tdinnitus accompanied by intermittent headaches for one month, with vomiting for one day.” The patient reported experiencing tinnitus, primarily on the left side, without any apparent precipitating factors, along with mild hearing loss for the previous month, and developed secondary epilepsy and peripheral neuropathy. The patient had no history of trauma or surgery and did not report any known comorbidities such as hypertension, diabetes, or autoimmune diseases.

Neurological examination revealed normal muscle tone in all limbs. Muscle strength was graded at 5 in the right limbs and 4 in the left lower limb. Both sides showed reduced tendon reflexes, and the Babinski sign was negative. The patient exhibited hyperalgesia in the left foot, absence of the tuning fork vibration sense in the distal part of the right upper limb, a supple neck without resistance, negative meningeal irritation, an inability to perform the finger nose test accurately in the right upper limb, and instability during the heel-knee-tibia test in both lower limbs. Laboratory examination showed no abnormalities in inflammatory indicators, including routine blood tests, C-reactive protein, procalcitonin, cerebrospinal fluid (CSF) analysis, polymerase chain reaction (PCR) for common pathogens, and serological tests for infections such as tuberculosis, syphilis, and fungal infections. All tests returned negative, ruling out an infectious etiology. Given the possibility of an infectious etiology despite initial negative results, further diagnostic steps were taken to identify any potential sources of infection: Echocardiography: Performed to rule out any cardiac sources of embolic infection. Screening by Otorhinolaryngologist: Conducted to examine the ears, nose, and throat for any potential sources of infection or inflammation. Consultation with Specialist in Oral and Maxillofacial Surgery: Evaluated for any dental or maxillofacial infections that could contribute to the condition.

Next, an enhanced head MRI was performed using multiple sequences to provide a comprehensive assessment of the lesion. The MRI revealed asymmetric structures of the bilateral cerebral hemispheres. In the left frontal lobe, there was a large patchy abnormal signal with unclear boundaries. The lesion appeared hypointense on T1WI (Fig. 1A), hyperintense on T2WI (Fig. 1B), hyperintense on T2-FLAIR (Fig. 1C), and iso-to-hypointense on DWI (Fig. 1D). The enhanced scan showed significant enhancement of the lesion, accompanied by extensive surrounding oedema. The left frontal horn of the lateral ventricle was deformed, while the rest of the ventricles and cisterns were normal in size and shape. There was a mild rightward shift of the midline structures. The sagittal scan showed a normal size, shape, and signal of the pituitary gland (Fig. 2 A-C). The imaging findings suggested an abnormal signal in the left frontal lobe, considering a low-grade glioma, with a higher likelihood of a pilomyxoid astrocytoma. Given the imaging characteristics and clinical presentation, the differential diagnosis included: Glioma: Due to the location and enhancement pattern of the lesion, particularly considering low-grade glioma such as pilomyxoid astrocytoma; Lymphoma: Considered because of the homogeneous enhancement and associated oedema; Autoimmune or inflammatory conditions: Such as neurosarcoidosis or granulomatous diseases.

1.2. Surgical details

To narrow down the differential diagnosis, following a comprehensive systemic examination, deep brain lesion resection was performed on October 20, 2020. After successful endotracheal intubation for general, the patient was placed in a supine position. Next, a left frontal arc incision of approximately 6×8 cm^2 was made, and the surgery was performed under the guidance of a surgical microscope. Microscopically, the appearance of surgical field showed that the left frontal lobe cortex revealed significant brain tissue oedema and gliosis, and the frontal pole was partially resected, followed by exploration of the deep frontal lobe, where tumour tissue was identified in the straight gyrus of the frontal lobe. The tumour exhibited a greyish-yellow colour and had a relatively firm texture. It extended anteriorly and inferiorly to the olfactory groove, with the left olfactory nerve visible. Posteriorly, it approached the suprasellar cistern. Some parts of the tumour were adherent to the skull base dura mater, requiring careful separation to achieve gross total resection (Fig. 2 D-F). The mass was subjected to histopathology, immunohistochemistry, and infectious disease workup postoperatively.

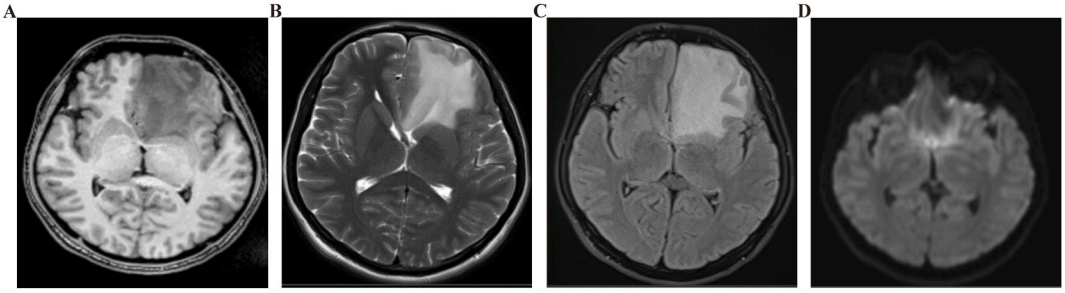

Fig. 1. Pre-operative images of the intracranial granuloma. (A) T1-weighted MRI showed hypointense signal lesion in the left frontal lobe. (B) T2-weighted MRI demonstrated a hyperintense signal mass. (C) T2-FLAIR MRI showed the mass was hyperintense signal. (D) DWI MRI demonstrated an iso-to-hypointense signal mass.

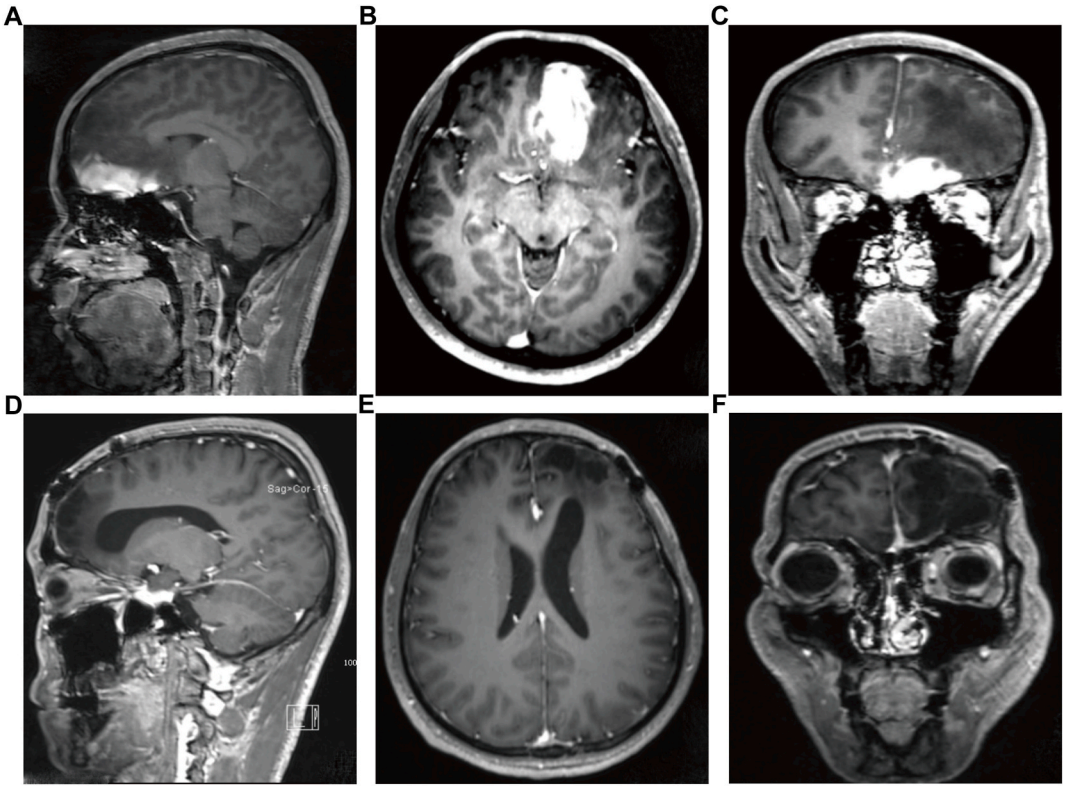

Fig. 2. Pre-operative images of the intracranial granuloma. (A–C) Axial, Sagittal and coronal T1-weighted contrast-enhanced sequences MRI showed the homogeneous enhancement space-occupying lesion in the left frontal lobe. (D–F) Axial, Sagittal and coronal T1-weighted contrast-enhanced MRI images demonstrated achieve the gross total resection of the tumour.

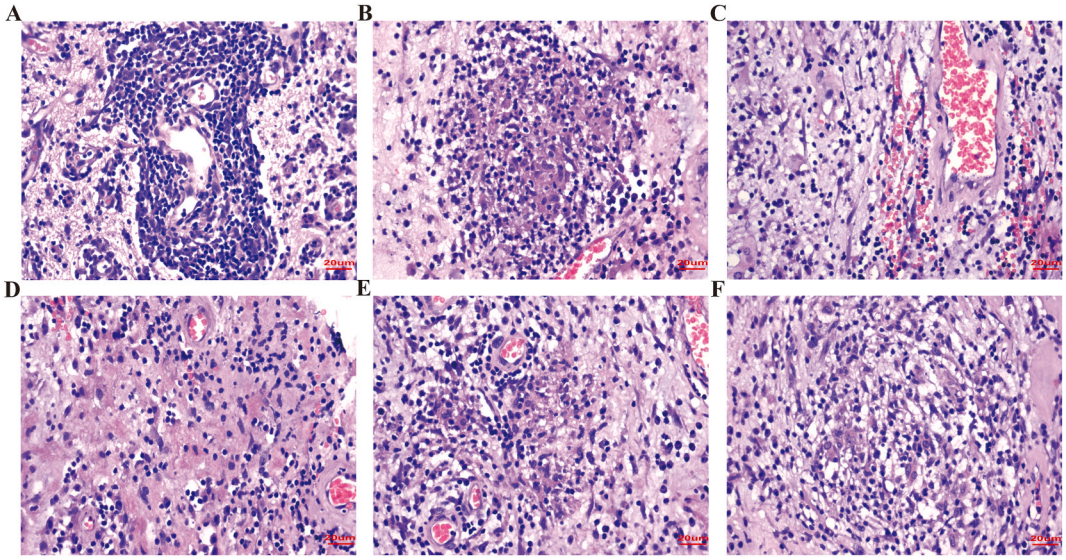

Fig. 3. HE staining observation of tissue structure. Magnification of pictures are 20 × (A) Perivascular lymphocyte mantle formation, scale bar, 20um. (B, D) The brain tissue structure is completely destroyed, Glial cell proliferation and T cell, B cell infiltration, scale bar, 20um. (C) Vascular dilatation and congestion, surrounding inflammatory cell infiltration, scale bar, 20um. (E) segmented nuclear white blood cells, scale bar, 20um. (F) Inflammatory granuloma around vascular congestion, scale bar, 20um.

1.3. Pathological examination

Following postoperative observation of pathological changes combined with immunohistochemical staining, and after differentiating between glioma and lymphoma, our institution currently considers the condition as an inflammatory lesion. Due to the extreme complexity of the differential diagnosis, the pathology slides were sent to the neuropathology department of the Beijing Neurosurgical Institute for consultation, and their report indicated the following: The brain tissue exhibited a state of high-grade oedema, characterized by the perivascular lymphocyte mantle formation (Fig. 3 A) and substantial disruption of the basic components and structure. This was replaced by widespread cellular infiltration, including T and B lymphocytes (Fig. 3B–D), plasma cells, macrophages (Fig. 3 C), and segmented nuclear white blood cells (Fig. 3E). There were notable vascular inflammatory changes (Fig. 3F), with inflammatory cells infiltrating vessel walls, forming densely packed, thick layers. The overall impression was that of an inflammatory lesion.

1.4. Immunohistochemistry

Immunohistochemical staining of tumour cells revealed positive staining for glial cell S-100 (focal+), sporadic olig-2 (+)(Fig. 4A), with T lymphocytes showing CD3 positivity(Fig. 4B–D), a few GFAP (+)(Fig. 4C), Vimentin (+), EMA (+), NeuN (−), synaptophysin (Syn +), P53 (−), INI1 (+), CD56 (−), CD21 (−), CD23 (−), BCL-2 (+), TIA-1 (−), Ki-67 (30 %+), B lymphocytes indicating perivascular (Fig. 4E) and surrounding granulomas CD20 (+)(Fig. 4F), CD79a (+), and tissue cells exhibiting CD68 positivity(Fig. 4G and H). Postoperatively, the patient received supportive treatment, and then the patient received immune globulin pulse therapy. The epilepsy was managed with antiepileptic medications, which successfully controlled the seizures. The peripheral neuropathy was addressed with symptomatic treatment, including pain management and physical therapy, which helped alleviate the symptoms. Based on the assessment conducted by our medical team, it is noted that the patient has exhibited commendable adherence to the treatment regimen along with favourable tolerance levels. Furthermore, there have been no instances of adverse or unanticipated events recorded throughout the course of treatment. Following an improvement in symptoms, the patient was discharged. After discharge, the patient was prescribed prednisone at a dose of 60 mg/day, which was gradually tapered down to 15 mg/day and maintained for two months.

1.5. Postoperative follow-up

During postoperative follow-up, the patient was monitored at 6 months, 1 year, and 3 years after surgery. At each follow-up visit, MRI scans were performed to check for recurrence or residual lesions. The MRI results showed no signs of recurrence, and the patient's symptoms had significantly improved. At the 3-year follow-up, the patient reported marked improvement in headache symptoms, limb weakness, and tingling compared to before the surgery. The patient remained seizure-free and showed no new neurological deficits. Regular follow-up was recommended to continue monitoring the patient's condition.

2. Discussion

This case and review of the literature highlights the clinical, radiological, and histopathological features and treatment of seven patients with primary intracranial granuloma. We believe that Intracranial granuloma is an important differential diagnosis in neuro-oncology patients during imaging examinations. It is rarely possible to correctly differentiate intracranial granuloma from malignant tumours, abscesses, haemorrhages, and other treatment-related diseases based on imaging alone prior to surgery [4–6]. Among the

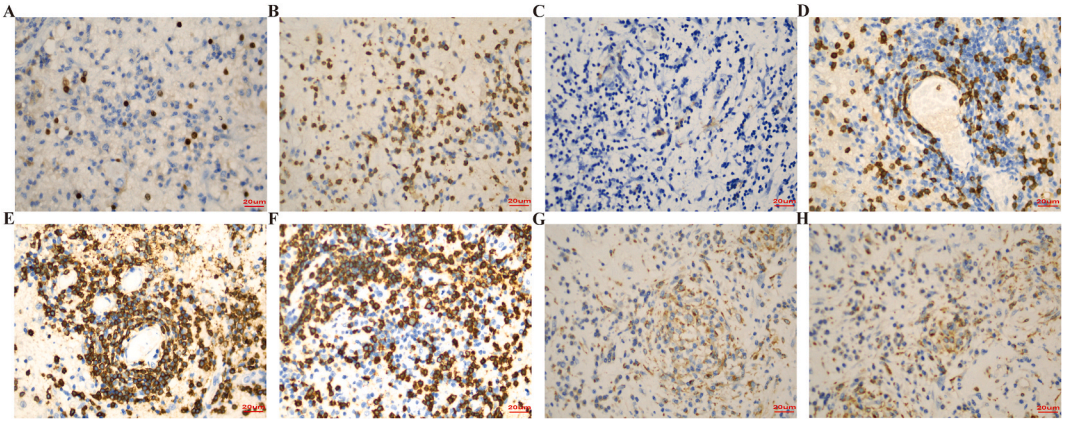

Fig. 4. Immunohistochemical observation of the expression of relevant molecules in samples. Magnification of pictures are 20 × .(A) Olig2 staining of glial cells, scale bar, 20um; (B) CD3 staining of T cells, scale bar, 20um (C) GFAP staining, scale bar, 20um; (D) CD3 staining, scale bar, 20um; (E) CD20 staining of perivascular, scale bar, 20um; (F) CD20 staining of surrounding granulomas, scale bar, 20um; (G) CD68 staining of tissue cells, scale bar, 20um. (H) CD68 staining of the granuloma. scale bar, 20um.

published cases, Primary intracranial granulomas are rare,the diagnosis of intracranial granuloma was mostly established based on postoperative pathological results [7–9].

Intracranial granuloma is an inflammatory lesion affecting the central nervous system and can result from various causes. The main categories of granulomatous disorders are infections, vasculitis, immunological upsets, leucocyte oxidase defects, hypersensitivity, chemicals, and neoplasia. Among these, intracranial foreign body granuloma is the most common, often manifesting several months to years after surgery [4]. Furthermore, intracranial granulomas not related to previous neurosurgical procedures may have a tumour-like origin, such as with plasma cell granulomas [10], or they may have infectious aetiologies, associated or not with extracranial locations, often due to fungal [11] or acid-fast organisms [12]. Primary intracranial granulomas are luckily rare. We selected six representative cases of primary intracranial granuloma have been reported in Table 1 [13–18], including two pituitary tuberculomas, one cholesterol granuloma, one plasma cell granuloma, one granulomatous hypophysitis and one necrotizing intracranial granuloma. The lesion of the patient in this report falls into the category of primary intracranial lesions, with no evidence of systemic infection, marking the first report of its kind in this field. The presentation of intracranial granulomas, regardless of etiology, depends on location in the brain and no specific manifestation.

According to research by Winter [19] et al., affected patients with intracranial granuloma display distinct imaging characteristics resembling Parkinson's disease and may experience associated clinical symptoms. A definitive diagnosis and treatment of intracranial granuloma typically necessitate surgical resection. Therefore, the early recognition of this clinical entity is of paramount importance for the effective management of patients in intracranial granuloma. Ganau [20] et al. realized that intracranial granuloma can mimic tumour recurrence; in this regard, Feldman [21] et al. suggested that MRI findings of low intensity T1-weighted with heterogeneous high intensity on T2-weighted images seem to be the rule for intracranial granulomas. Amer [22] et al. found that intracranial caseating granulomas have homogeneous enhancement via MRI. In our study and based on the literature review, we drew the same conclusion: the head MRI showed homogeneous and significantly enhanced intracranial space-occupying lesions, and the initial diagnosis was glioma. Consequently, the above research demonstrated that there are exceptional and intricate challenges in achieving differential diagnosis of intracranial granuloma, and this condition may be confused with other central nervous system tumours. Thus, it is imperative to engage in large-scale and multicentre research harnessing advanced radiomics technology to refine its diagnostic guidelines.

Histopathological examination is the gold standard for the diagnosis of intracranial granuloma. In recent research, haematoxylin-eosin (HE) staining was performed. A giant multinucleate cell, a typical element of postoperative granuloma, is shown [21]; the plasma cell granuloma contained a perivascular infiltrate of lymphocytes and polyclonal plasma cells, which is characteristic of plasma cell granulomas [23]; and in addition, lesions in intracranial caseating granuloma patients were solid, with small areas of necrosis that were always less than 1 mm in diameter and restricted to the centre of the granulomata. As shown in the above research results, the common pathological feature of intracranial granulomas is macrophage proliferation, but the pathological manifestations vary depending on the type of intracranial granuloma [24]. The pathological manifestations of this case were extremely complex, with complete destruction of the basic structure of the brain tissue, replaced by diffuse infiltration of cells (T and B lymphocytes, plasma cells, phagocytes, and lobulated white blood cells), resulting in vasculitis. This case enriches the diagnostic examples of intracranial granuloma and provides diagnostic ideas for frontline clinical and pathological physicians.

In summary, clinical findings and radiological features are not sensitive or specific for the diagnosis of intracranial granuloma, making its diagnosis particularly difficult. Furthermore, when other tumour lesions are excluded, intracranial granuloma should be suspected. Steroid are effective treatment strategies.

3. Conclusions

This case offers a fresh differential diagnostic strategy for clinicians, given the intricate challenge it poses in distinguishing it from other intracranial neoplastic conditions. In instances where patients with intracranial space-occupying lesions lack overt signs of systemic infection and a surgical history, the possibility of an inflammatory granuloma may be considered when other more threatening causes have been excluded.

Data availability

No data was used for the research described in the article.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and Review and/or approval by an ethics committee was not needed for this study because all patients provided informed consent before surgery, agreeing to the use of their medical records.

Consent for publication

Patient provided written informed consent for the publication of their anonymised case details and images.

Table 1
Cases of intracranial inflammatory granuloma reported in the literature recently.

Report	Age (year/sex)	Publication time	First symptoms	Subgroup	Treatment	Location	Bony Involvement	MRI			Reference
								T1	T2	T1 Contrast	
Kumar et al.	50/F	2021	Headache and diminished vision	Tuberculosis	Isoniazid, rifampin, pyrazinamide, and ethambutol	Pituitary	No	Iso	Hypo-Hyper	+	[13]
Renfrow et al.	55/F	2014	Headaches and left-sided hearing loss	Plasma cell granuloma	Surgery, radiation, and glucocorticoid therapy	Bitemporal frontal	No	Iso	NR	+	[14]
Pal et al.	12/M	2020	Polyuria and polydispsia	Granulomatous hypophysitis	Bleomycin, etoposide, and cisplatin	pituitary	Yes	Hypo	NR	+	[15]
Godbe et al.	77/F	2020	Sinusitis and fatigue	Necrotizing intracranial granuloma	Surgery	Cerebellum	No	NR	Hyper	+	[16]
Adonis N'da et al.	10/F	2013	Intense frontal headaches	Tuberculosis	Surgery and antituberculous chemotherapy	Third ventricle	No	NR	NR	NR	[17]
Nsir et al.	17/F	2015	Primary amenorrhea	Cholesterol granuloma	Surgery	Suprasellar	No	NR	NR	+	[18]

MRI, magnetic resonance imaging; F, female; M, male; Iso, iso intensity; Hypo, hypo intensity; NR, not reported; Hyper, hyper intensity.

CRediT authorship contribution statement

Wentao Liang: Writing – original draft, Project administration, Conceptualization. **Zhou Qi:** Writing – original draft, Resources, Conceptualization. **Hu Yang:** Supervision, Conceptualization. **Liang Niu:** Supervision, Methodology, Conceptualization. **Qiao Li:** Writing – review & editing, Conceptualization. **Shiwen Guo:** Investigation, Conceptualization. **Yawen Pan:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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