
ORIGINAL ARTICLE

Clinical Presentation, Radiological Features, and Treatment Response of Basal Ganglia Germinoma: Case Series

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ABSTRACT

Objective: To evaluate the clinical presentation, radiological features, and treatment response of basal ganglia germinoma upon retrospective review of five patients.

Methods: From 2007 to 2015, five patients had histological diagnosis of basal ganglia germinoma at a tertiary centre in Hong Kong. Their clinical presentation, initial serum beta human chorionic gonadotropin (bHCG) and alpha fetoprotein (AFP) levels, radiological features, and treatment response were reviewed.

Results: All five patients were male (mean [\pm standard deviation] age, 15.6 ± 6.8 years). The most common presentation was contralateral weakness ($n=3$). 80% of the patients ($n=4$) had elevated serum bHCG level (normal range: <5.0 IU/L) while all had normal serum AFP level (normal range: <6.0 ng/mL). Computed tomography (CT) brain studies detected hyperdense component in all basal ganglia germinoma. Magnetic resonance imaging (MRI) brain studies demonstrated complex mixed cystic and solid appearance (mean [\pm standard deviation] diameter, 2.7 ± 0.6 cm) with variable degree of contrast enhancement. Cerebrospinal fluid dissemination was seen in one patient complicated by hydrocephalus. More than half of the patients ($n=3$) showed smaller ipsilateral cerebral peduncle at the time of presentation. Radiotherapy was given to all patients while three received adjuvant chemotherapy. Most ($n=4$) showed complete response without MRI evidence of residual tumour. One patient had excellent recovery without any focal neurological deficit; three experienced mild residual hemiplegia.

Conclusion: Atypical location of germinoma in basal ganglia commonly presents with contralateral weakness and elevated serum bHCG level. Characteristic imaging features include hyperdense component on CT and complex mixed cystic and solid appearance, contrast enhancement and ipsilateral Wallerian degeneration on MRI. Early recognition of the disease is essential for accurate diagnosis and prompt management to improve the neurological outcomes of these patients.

Key Words: Basal ganglia; Germinoma

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中文摘要

基底核生殖細胞瘤臨床表現、影像學表徵及治療反應的病例研究

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目的：回顧性評論五位基底核生殖細胞瘤患者的臨床表現、影像學表徵及治療效果。

方法：由2007年到2015年期間，回顧香港一所專科醫療中心五位組織學確診基底核生殖細胞瘤病人的臨床表現，始初血清內乙型絨毛膜促性腺激素及甲胎蛋白的水平，影像學表徵及治療效果。

結果：五位病人全為男性（平均年齡 \pm 標準差： 15.6 ± 6.8 歲）。最常見的表徵為對側肢體無力（ $n=3$ ）。八成病人（ $n=4$ ）的血清內乙型絨毛膜促性腺激素的水平過高（正常值低於 5.0 IU/L），而甲胎蛋白的水平則為正常（正常值低於 6.0 ng/mL）。電腦斷層掃描（CT）顯示所有基底核生殖細胞瘤均有高密度部分。磁力共振成像（MRI）顯示複雜性囊性及腫塊（平均長度 \pm 標準差： 2.7 ± 0.6 cm），並有不同程度的造影訊號增強。一位病人發現腦脊液擴散導致腦積水。超過一半患者（ $n=3$ ）於病發時的同側大腦腳細小。所有病人均接受放射治療，三位病人接受輔助化療。大部分病人（ $n=4$ ）的治療效果為完全有效並且在MRI上沒有剩餘腫瘤。一位病人康復良好並沒有任何局部神經功能缺損；三位病人則有輕微偏癱。

結論：生殖細胞瘤原發於基底核為非典型的位置，通常表徵包括對側肢體無力，以及血清內乙型絨毛膜促性腺激素水平升高。影像學特性在CT上為高密度部分，在MRI上為複雜性囊性及腫塊，造影訊號增強及同側Wallerian退變。早期發現病情可準確診斷及迅速處理病情，從而改善這些病人的神經學治療結果。

INTRODUCTION

Primary intracranial germ cell tumours are rare, accounting for up to 0.5% to 2.1% of primary brain tumours in children and adolescents. Among the different types of germ cell tumours, germinoma is the most common histological type.^{1,2} Most germinomas arise in the midline from the pineal and suprasellar regions, but about 5% to 10% of intracranial germinomas arise from the off-midline cerebral parenchyma including the basal ganglia or the thalamus.³ Early diagnosis of basal ganglia germinoma (BGG) is usually difficult, owing to its rarity and atypical clinical signs of this pathology, and because the magnetic resonance imaging (MRI) features at early stage may also be non-specific.⁴ This case series aims to describe the clinical presentation, radiological features, and treatment response of BGG upon retrospective review of five patients.

METHODS

Patients diagnosed and histologically confirmed to have BGG from 2007 to 2015 at Tuen Mun Hospital, Hong Kong, were retrospectively reviewed. Five patients were

included: all were male patients, mean age at diagnosis 15.6 years, range 7 to 23 years. Clinical presentation, initial serum tumour marker levels (beta human chorionic gonadotropin [bHCG], normal range <5.0 IU/L and alpha fetoprotein [AFP], normal range <6.0 ng/mL), radiological features (computed tomography [CT] and MRI), and treatment response of all patients were reviewed.

Cases

Case 1

In January 2009, a 19-year-old male patient attended the Accident and Emergency Department of our hospital, complaining of increased clumsiness of the left side of the body for 1 month prior to admission. Neurological examination upon admission demonstrated mild left hemiparesis and hyperreflexia. Plain CT of the brain (January 2009) revealed a mixed hypodense and hyperdense lesion in the right basal ganglia (Figure 1a). Contrast MRI of the brain confirmed a 3-cm complex mixed cystic and solid mass in the right lentiform nucleus and globus pallidus (Figure 1b and c) with partial

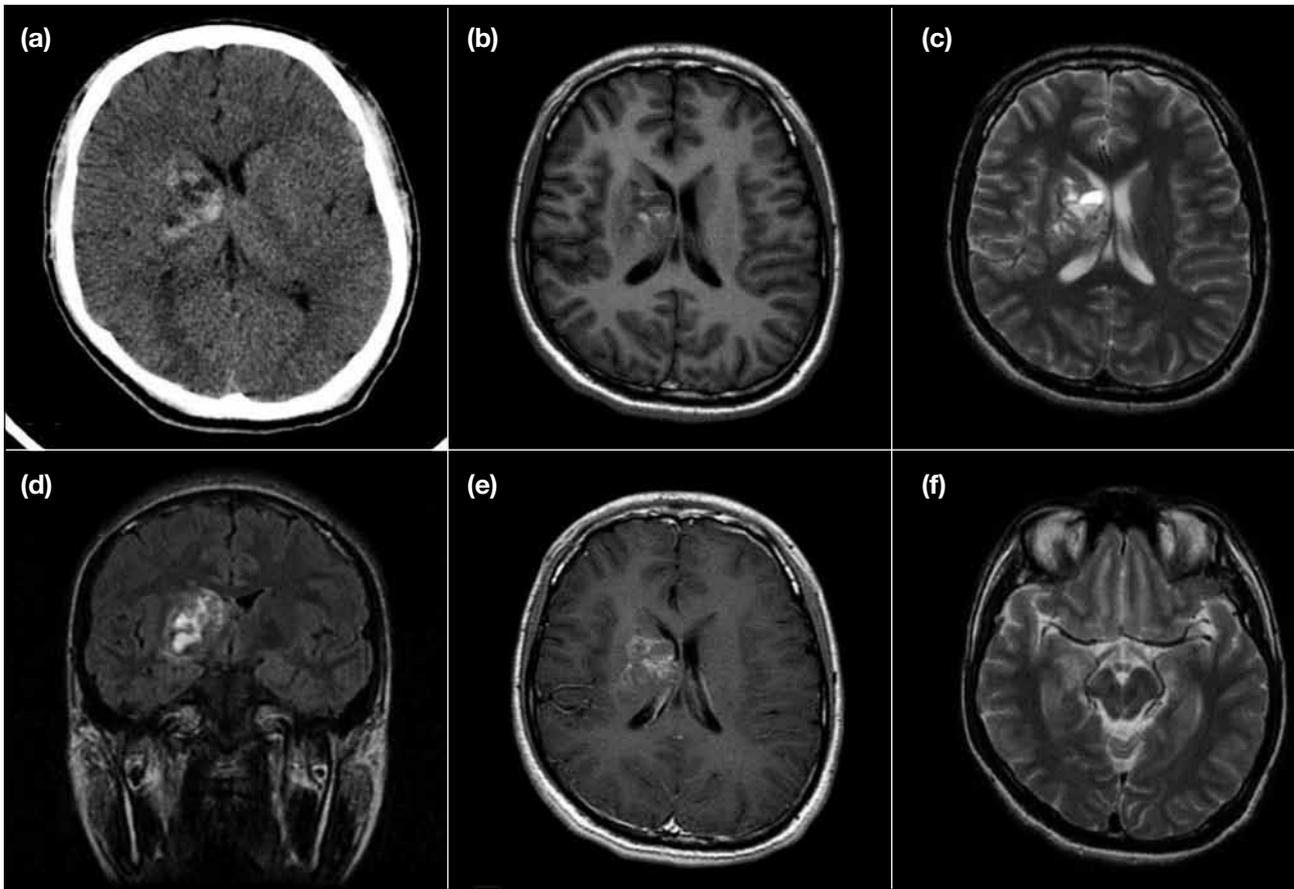


Figure 1. Case 1. 19-year-old male patient. (a) Computed tomography of the brain showed mixed hypodense and hyperdense lesion in right basal ganglia with mild mass effect onto ipsilateral frontal horn. (b) Axial T1-weighted; (c) T2-weighted; and (d) fluid-attenuated inversion recovery magnetic resonance (MR) images confirmed the presence of the lesion with mixed cystic and solid components, together with fluid-fluid levels within the cystic component. (e) Post-contrast T1-weighted MR image revealed patchy enhancement over the periphery of the solid component. (f) Axial T2-weighted MR image at the midbrain level showed a smaller right cerebral peduncle.

extension to right thalamus (Figure 1d). Fluid-fluid levels were observed within the cystic component. There was patchy enhancement over the periphery of the solid component (Figure 1e). The ipsilateral cerebral peduncle was smaller (Figure 1f). The patient was suspected to have BGG and this was later confirmed by biopsy. There was no evidence of cerebrospinal fluid (CSF) seeding in the subsequent spinal MRI. Serum bHCG level was elevated to 191.6 IU/L. He was treated with chemotherapy followed by craniospinal irradiation. The most recent MRI (October 2016) showed residual cystic changes with haemosiderin deposition in the right basal ganglia and no evidence of tumour recurrence. His left hemiparesis improved slightly but there was persistent spasticity in the left upper limb requiring Botox injection.

Case 2

In June 2015, a 19-year-old male patient was admitted

to our hospital because of repeated early morning vomiting for 3 months prior to admission. Neurological examination was unremarkable. Plain CT of the brain (June 2015) showed a hyperdense focus in the right globus pallidus (Figure 2a). The patient's symptoms improved partially after symptomatic treatment. Initial private contrast MRI (April 2016) demonstrated T2-weighted hyperintense signal in the bilateral frontal white matter and the right lentiform nucleus with restricted diffusion and contrast enhancement. The patient was suspected to have dysmyelinating or demyelinating disease. However, subsequent contrast MRI (May 2016) at our centre showed interval enlargement of the lesion in the right lentiform (2.6 cm) with a mixed cystic and solid appearance (Figure 2c and d). Stereotactic biopsy revealed histology of germinoma. The patient then developed diabetes insipidus and cortisol insufficiency. Subsequent MRI (June 2016) revealed subependymal

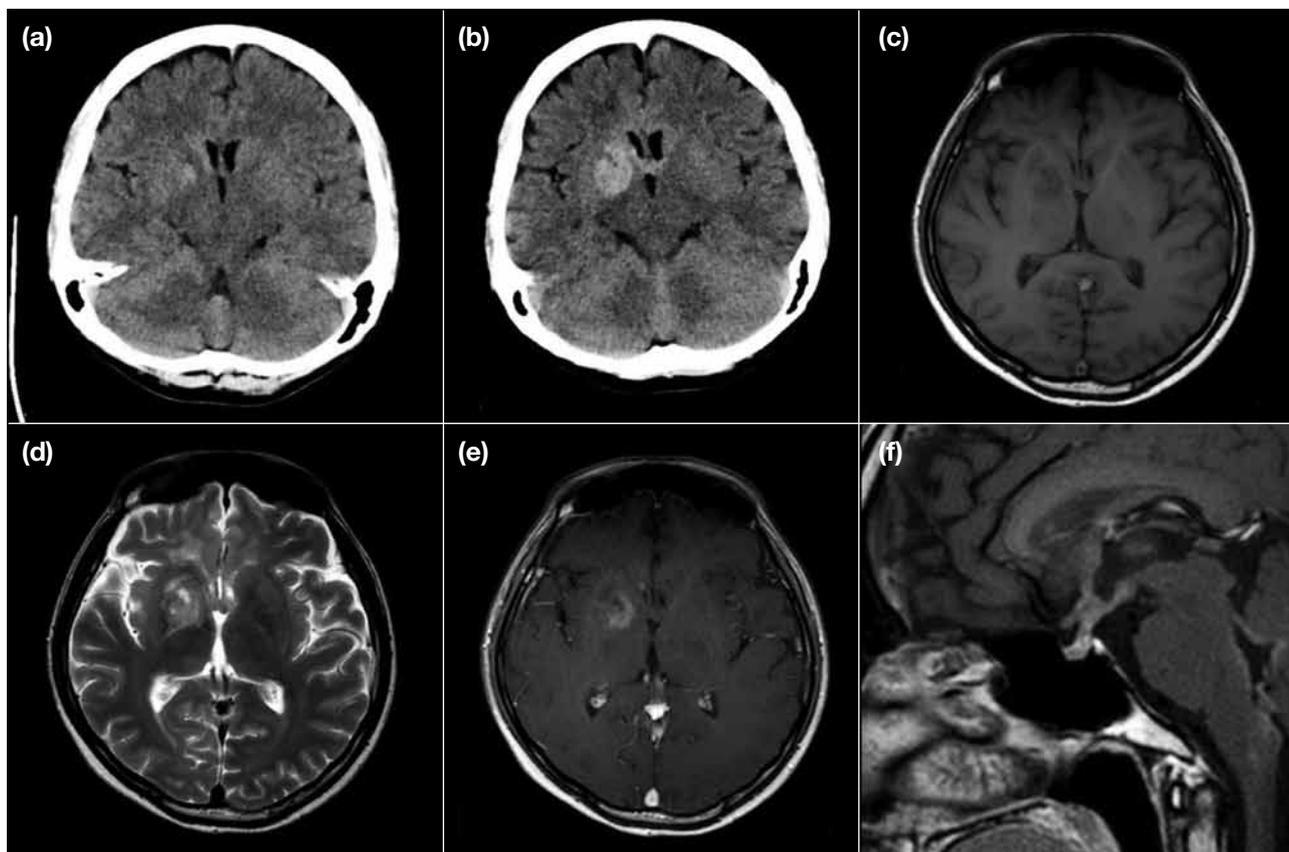


Figure 2. Case 2. 19-year-old male patient. (a) Initial computed tomography (CT) of the brain (June 2015) showed focal hyperdense lesion in the right globus pallidus. (b) Follow-up CT of the brain (May 2016) showed an interval enlargement of the hyperdense lesion occupying the right lentiform nucleus. Repeated magnetic resonance imaging (MRI; May 2016) (c) axial T1-weighted, (d) T2-weighted, and (e) post-contrast T1-weighted images demonstrated the mixed cystic and solid appearance of the right lentiform nucleus lesion. (f) The patient then developed diabetes insipidus and cortisol insufficiency; subsequent MRI (June 2016) sagittal post-contrast T1-weighted image of the pituitary gland demonstrated abnormal thickening of the pituitary stalk with contrast enhancement extending to hypothalamus.

spread to the fourth ventricle and abnormal thickening of pituitary stalk extending to hypothalamus (Figure 2f). Serum tumour markers were all normal. The patient was treated with craniospinal irradiation. The most recent MRI (April 2017) showed complete resolution of tumour with small residual cystic changes in the right globus pallidus and minimal right Wallerian degeneration (Figure 3). The patient experienced persistent diabetes insipidus and cortisol insufficiency and was placed on hormonal replacement, but there was no clinical evidence of contralateral weakness.

Case 3

In February 2008, a 7-year-old male patient complained of progressive left lower limb weakness and clumsiness for 1 month prior to admission, as well as acute-onset left upper limb weakness. Neurological examination revealed left-sided hemiparesis with hyperreflexia. Plain

CT of the brain (February 2008) showed homogenous hyperdense lesion in the right lentiform nucleus with suspicious extension to the right cerebral peduncle. First contrast MRI (February 2008) found a 2-cm solid mass with cystic components in the right globus pallidus (Figure 4a and b), also involving right cerebral peduncle. There was patchy enhancement of the solid part. Follow-up contrast MRI (June 2008) showed an interval enlargement of the lesion (Figure 4c and d) with involvement of right cerebral peduncle (Figure 4e and f) and high choline peak on MR spectroscopy (Figure 4g) but no evidence of CSF seeding. Biopsy confirmed the diagnosis. Serum bHCG was elevated to 6.2 IU/L. The patient completed chemotherapy and radiotherapy in 2009 with good imaging response. The most recent MRI (October 2016) showed static residual cystic changes and haemosiderin deposition. The patient's spastic left hemiparesis remained stable.

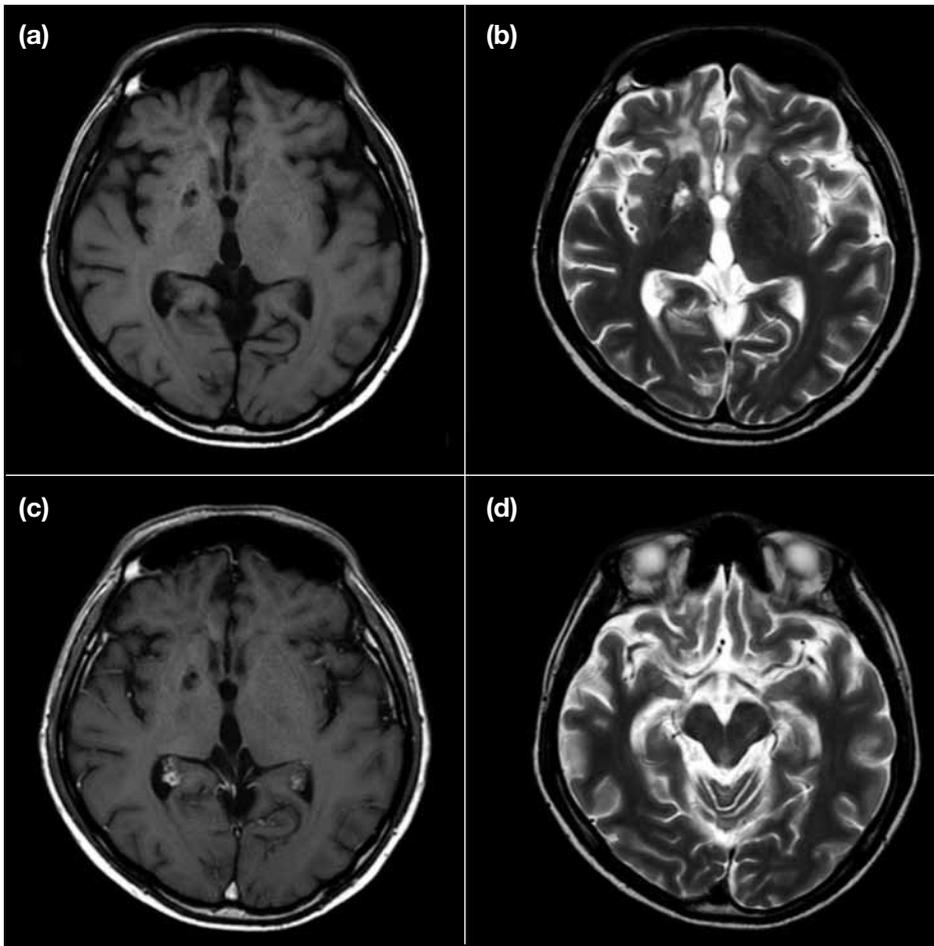


Figure 3. Case 2. 19-year-old male patient. Post-treatment magnetic resonance imaging (MRI) demonstrated cystic changes in the right globus pallidus without evidence of tumour recurrence. (a) Axial T1-weighted; (b) T2-weighted; and (c) post-contrast T1-weighted MR images. (d) Axial T2-weighted MR image at the midbrain level showed minimal right Wallerian degeneration.

Case 4

In September 2014, a 23-year-old male patient was admitted for recurrent syncope. Plain CT of the brain (September 2014) showed a multiloculated cystic lesion in the left basal ganglia with hyperdense solid components and involvement of the left lateral, third, and fourth ventricles and the periaqueductal region, leading to obstructive hydrocephalus. Contrast MRI (September 2014) confirmed the presence of a 3.2-cm mixed cystic and solid lesion in the left basal ganglia, with multiple heterogeneous masses along the walls of frontal horns and the third and fourth ventricles suspicious of CSF metastases, complicated by obstructive hydrocephalus (Figure 5). Serum β HCG level was elevated to 10.3 IU/L. Contrast MRI of the spine (September 2014) excluded drop metastasis. The patient had urgent third ventriculostomy for decompression and tumour biopsy to confirm diagnosis of germinoma. He received local radiotherapy followed by craniospinal irradiation. His latest contrast MRI study (February 2015) showed

a significant reduction in size of the left basal ganglia mass, with residual cystic components and mild contrast enhancement of the septae. There was also regression of the previously detected multiple periventricular heterogeneous masses. In November 2015, the patient was found collapsed at home and was asystolic upon arrival at the Accident and Emergency Department of our hospital. The exact cause of death cannot be determined from reviewing the electronic patient records.

Case 5

In July 2007, a 10-year-old male patient complained of right-hand clumsiness and right-sided weakness for 2 months prior to admission. Plain CT of the brain (July 2007) revealed a heterogeneous hyperdense lesion in the left basal ganglia without perilesional oedema. Subsequent contrast MRI (July 2007) showed a 3.5-cm lobulated T1-weighted isointense T2-weighted hyperintense lesion with cystic components predominantly in the left caudate nucleus with

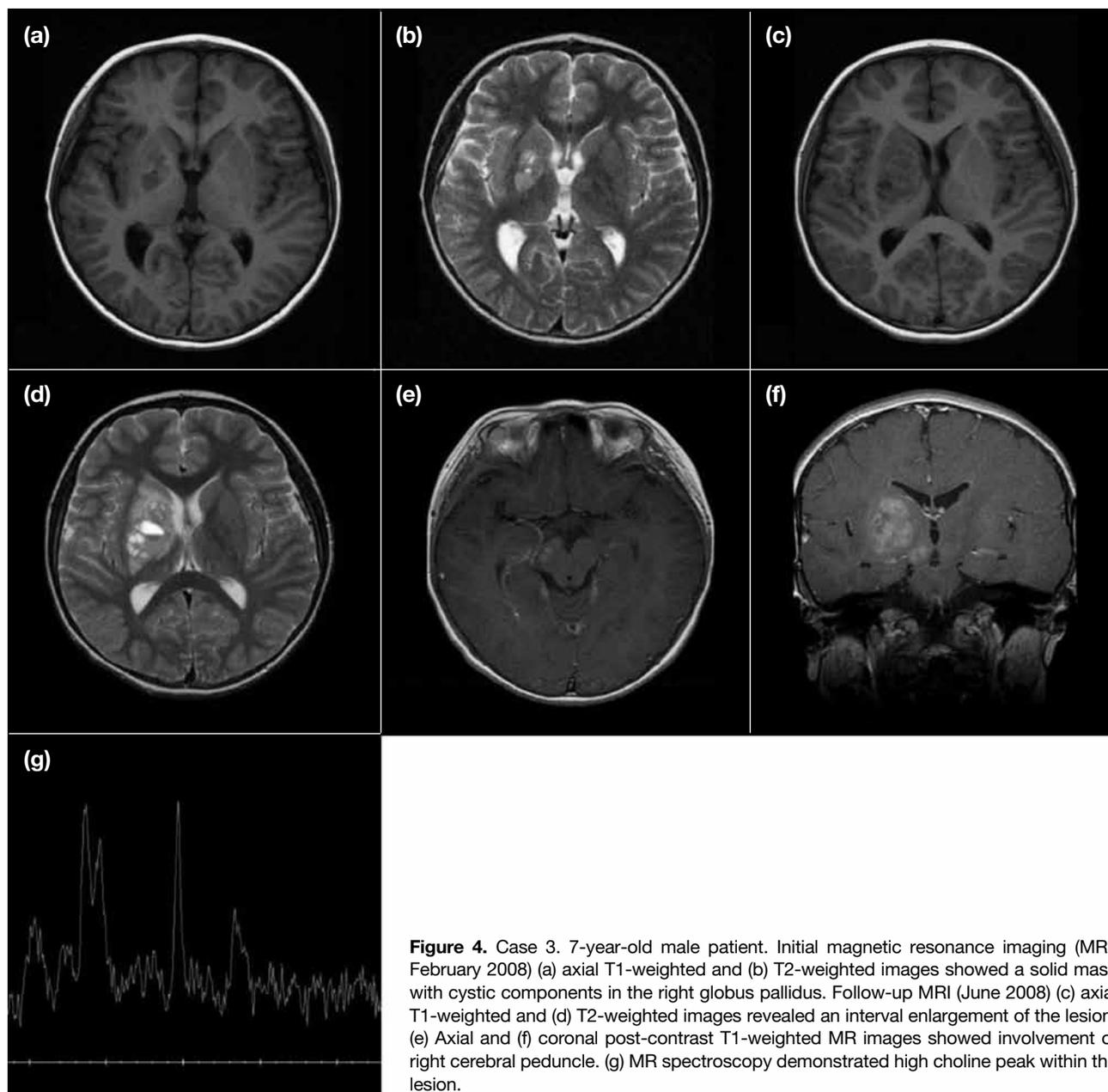


Figure 4. Case 3. 7-year-old male patient. Initial magnetic resonance imaging (MRI; February 2008) (a) axial T1-weighted and (b) T2-weighted images showed a solid mass with cystic components in the right globus pallidus. Follow-up MRI (June 2008) (c) axial T1-weighted and (d) T2-weighted images revealed an interval enlargement of the lesion. (e) Axial and (f) coronal post-contrast T1-weighted MR images showed involvement of right cerebral peduncle. (g) MR spectroscopy demonstrated high choline peak within the lesion.

involvement of the left internal capsule, lentiform nucleus, and anterior corona radiata. Contrast enhancement of the solid component was observed. The left cerebral peduncle was also smaller (Figure 6a). Serum AFP and bHCG were not elevated. Open brain biopsy confirmed the diagnosis of BGG. Postoperative contrast MRI of the brain and whole spine (July 2007) excluded CSF metastasis. After four cycles of reduced-dose chemotherapy, follow-up contrast MRI (October 2007) showed a residual enhancing nodule within one of the cystic components of the left basal ganglia lesion. Excisional biopsy was performed which excluded

residual tumour. The patient completed reduced-dose craniospinal radiotherapy in November 2007. The most recent MRI (May 2017) showed no evidence of recurrence but showed persistent left-sided Wallerian degeneration (Figure 6b). The patient recovered well with mild residual right hemiparesis.

DISCUSSION

Intracranial germ cell tumours are rare primary malignant brain tumours that primarily affect children and adolescents, with a peak incidence in the second decade of life.⁵ These tumours typically affect the

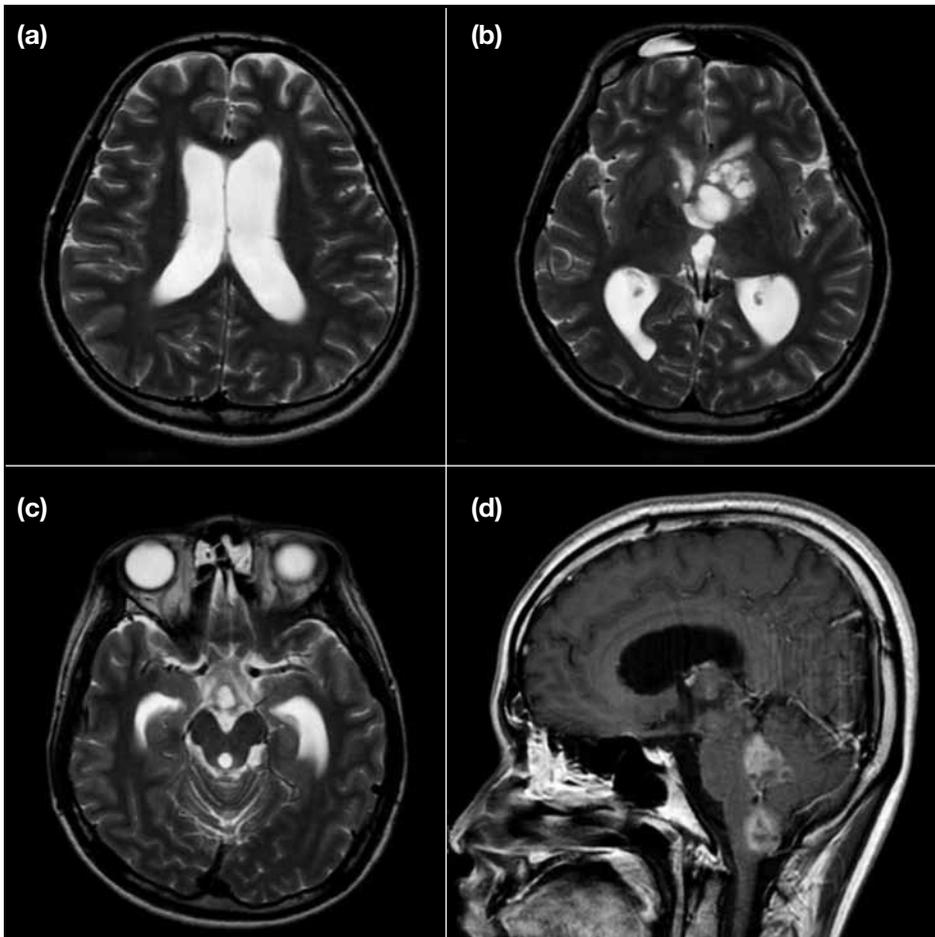


Figure 5. Case 4. 23-year-old male patient. Left basal ganglia germinoma with cerebrospinal fluid metastases in the fourth ventricle and cisterna magna causing obstructive hydrocephalus. (a to c) Axial T2-weighted and (d) sagittal post-contrast T1-weighted magnetic resonance images.

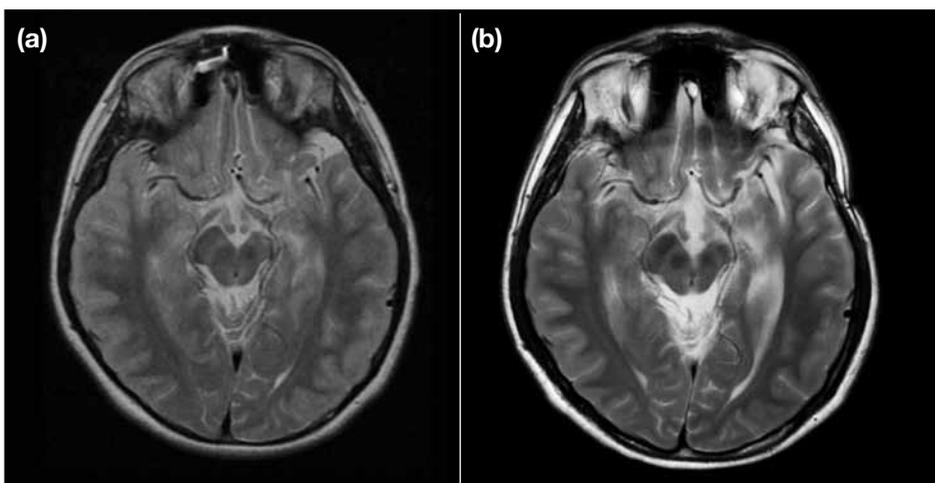


Figure 6. Case 5. 10-year-old male patient presenting with right hemiparesis. (a) First magnetic resonance imaging (July 2007) axial T2-weighted image showed evidence of left Wallerian degeneration. (b) Post-treatment follow-up magnetic resonance imaging (May 2017) axial T2-weighted image showed similar degree of persistent left-sided Wallerian degeneration.

midline structures including suprasellar and pineal regions. However, they can develop away from midline structures in the basal ganglia, the thalamus, and occasionally the telencephalon. Thus, BGG is a distinct type of intracranial germ cell tumour, in terms

of presentation and imaging findings. There is a higher prevalence of BGG in Japan and East Asia, and a striking male predominance.^{6,7} All patients in our small case series were young and male, reflecting the previously reported demographic distribution.

Owing to the location of BGG, the patients usually present with hemiparesis and extrapyramidal signs, such as dystonia, rigidity, bradykinesia, or dyskinesia.¹ In the present study, three of the patients presented with hemiparesis of varying severity and clumsiness (Table 1) with initial MRI studies demonstrating a small ipsilateral cerebral peduncle. Even with proper

treatment, the hemiparesis regressed only partially or not at all, probably due to the infiltrative growth pattern of germinomas.⁴

Diabetes insipidus is often the first and only symptom associated with suprasellar germinoma. In some cases, it develops before MRI visualisation of the tumour.^{8,9} In our case series, diabetes insipidus was found in one case which showed subependymal spread of the disease affecting the pituitary stalk and its functions, indicating a high tendency of the tumour to invade the adjacent brain parenchyma and seed in the subarachnoid spaces.¹⁰

Table 1. Clinical data of patients with basal ganglia germinoma (n=5).*

| Clinical data | |
|---|-------------------|
| Age, mean± SD (range), years | 15.6 ± 6.8 (7-23) |
| Male sex | 5 (100%) |
| Lesion size, mean ± SD (range), cm | 2.7 ± 0.6 (2-3.5) |
| Clinical presentation | |
| Contralateral weakness | 3 (60%) |
| Repeated vomiting | 1 (20%) |
| Recurrent loss of consciousness | 1 (20%) |
| Elevated serum bHCG level (normal range: <5.0 IU/L) | 4 (80%) |
| Elevated serum AFP level (normal range: <6.0 ng/mL) | 0 |

Abbreviations: AFP = alpha fetoprotein; bHCG = beta human chorionic gonadotropin; SD = standard deviation.

* Data are presented as No. (%) of patients unless otherwise indicated.

The literature describes patients with BGG presenting with pathological vomiting without hydrocephalus.⁹ These symptoms are difficult to explain; they may be related to hidden dissemination of the tumour to the medulla oblongata.

Diagnosis of BGG at an early stage can be difficult, owing to the insidious onset of non-specific neurological deficits.¹¹ Imaging is usually the first clue to diagnosis. However, to derive an early diagnosis, it is mandatory to recognise the subtle findings of BGG. Early CT features can be quite variable, but most reports describe

Table 2. Imaging characteristics of basal ganglia germinoma in CT and MRI.

| Case | CT | | | MRI | | |
|------|----------------------|----------|-------|------------------------|-------|------------------------------------|
| | Hyperdense component | T1W | T2W | Appearance | T1W+C | Ipsilateral Wallerian degeneration |
| 1 | + | Hypo/iso | Hyper | Mixed cystic and solid | + | + |
| 2 | + | Hypo | Hyper | Mixed cystic and solid | + | - |
| 3 | + | Hypo | Hyper | Mixed cystic and solid | + | + |
| 4 | + | Hypo | Hyper | Mixed cystic and solid | + | - |
| 5 | + | Iso | Hyper | Mixed cystic and solid | + | + |

Abbreviations: - = study performed with negative results; + = study performed with positive results; CT = computed tomography; Hyper = hyperintense; Hypo = hypointense; Iso = isointense; MRI = magnetic resonance imaging; T1W = T1-weighted; T2W = T2-weighted; T1W+C = T1-weighted with gadolinium contrast.

Table 3. Treatment and clinical outcomes of patients with basal ganglia germinoma.

| Case | Rx | CTx | Tx response based on MRI | Morbidity | Mortality |
|------|-----|-----|--------------------------|--|-----------|
| 1 | Yes | Yes | CR | Left-sided weakness, spasticity requiring botox injection | No |
| 2 | Yes | No | CR | No focal neurological deficit. Diabetes insipidus and cortisol insufficiency | No |
| 3 | Yes | Yes | CR | Left-sided weakness, spasticity requiring botox injection | No |
| 4 | Yes | No | PR | Unsteady gait, mental slowness | Yes |
| 5 | Yes | Yes | CR | Mild right-sided weakness | No |

Abbreviations: CR = complete response; CTx = chemotherapy; MRI = magnetic resonance imaging; PR = partial response; Rx = radiotherapy; Tx = treatment.

the presence of a homogeneous or inhomogeneous hyperdense component in an irregularly defined lesion.^{10,12,13}

Early MRI signs may show small areas of signal changes in the basal ganglia without contrast enhancement, leading to misinterpretation as non-neoplastic lesions (stroke, demyelination).^{10,13,14} In the more advanced stages of the disease, the tumour can present as an irregular solid area with cystic components and variable contrast enhancement.^{3,7,15,16} Despite the size of the tumour, surrounding oedema is usually minimal, indicating its infiltrative nature. Intratumoural haemorrhage is not uncommonly found on MRI, explaining its heterogeneous MRI signals. Ipsilateral Wallerian degeneration is also a feature of germinomas of the basal ganglia (Table 2).¹⁷⁻²⁰ Our observations in the present cases confirm these data. There are reported cases of multifocal germinoma involving the basal ganglia and other parts of the brain,²¹ which was also seen in one of the present cases.

The main radiological differentials for BGG include glioma and lymphoma. It is sometimes difficult to differentiate these entities on imaging findings alone. Assays of serum and CSF tumour markers can be helpful to derive the correct diagnosis.

Germinomas usually show a remarkable response to chemotherapy and radiotherapy, leading a good prognosis and high chance of survival for these patients.^{4,11,22,23} In our case series, all patients had complete or near-complete response of the tumour, with a survival rate of 80%. One patient even had complete neurological recovery (Table 3). However, if the diagnosis is delayed, the disease can become disseminated by local or CSF spread, similar to germinomas elsewhere in the suprasellar or pineal region.

Limitation

Our study is limited by a small sample size owing to the rarity of the disease and retrospective nature of data collection. Future multi-centred study may allow subgroup analysis to provide better information of disease prognosis for treating physicians and patients.

CONCLUSIONS

BGG is a very rare pathology. The atypical location of this type of germinoma usually presents with hemiparesis and extrapyramidal signs, and elevated serum bHCG level. Initial CT and MRI findings can be subtle. Typical imaging findings include hyperdense component within

the lesion on CT, and complex mixed cystic and solid appearance with enhancement on MRI. Evidence of Wallerian degeneration in early imaging often indicates the presence of hemiparesis and perhaps predicts its irreversibility. With recognition of this rare disease entity, early diagnosis can be achieved by clinical and radiological correlation, and imaging-based biopsy. Prompt treatment can thus be given to help improve neurological outcomes of these patients.

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