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Case Report

Germinoma of basal ganglia ☆,☆☆

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ABSTRACT

Basal ganglia germinomas (BGGs) are rare lesions. Because of the atypical features of early-stage clinical symptoms and imaging characteristics, BGGs are easily misdiagnosed with non-tumorous conditions. This article presented cases of 2 young male patients who came to the hospital due to right arm weakness. Brain Magnetic Resonance Imaging (MRI) images in the first case revealed a lobulated mixed component mass on the left basal ganglia. The solid part showed restricted diffusion on diffusion-weighted imaging, heterogeneous strong enhancement, and no signal of calcification or bleeding. The second case in the left putamen showed hypointensity on T2*, mild enhancement, and atrophy of the ipsilateral cerebral peduncle, increased choline, and decreased n-acetyl-aspartate (NAA) on spectroscopy. Follow-up MRI after 6 months showed a mass increase in size and hypointensity part on T2*. BGGs have been confirmed on biopsy in both cases. With isolated chemotherapy application, there is no sign of remission in the first patient. The second patient was treated with chemotherapy and radiotherapy, and MRI images after treatment showed a complete response.

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Introduction

Germinomas are most commonly encountered in the age range of 15-20 years [1], constituting two-thirds of all intracranial germ cell tumors (a relatively rare group, accounting for 2%-3% of new brain tumors in children). Common sites for germinomas include the pineal gland and suprasellar/sellar region, with only 5%-10% occurring in the basal ganglia and thalamus [2]. BGGs have a favorable prognosis, with an 85% 5-year survival rate [3]. Early diagnosis is often challenging due to the subtle clinical symptoms that tend to progressively manifest, encompassing weakness, cognitive decline, and psychiatric disturbances [4,5]. This article will present the clinical symptoms, imaging diagnostic features, and pathological characteristics of 2 cases of basal ganglia germinomas.

Case 1

A 14-year-old male patient presented with gradually increasing headaches over a month, accompanied by hemiparesis of the right upper limb and decreased vision in the right eye. He denied any history of seizures or other relevant medical conditions. Clinical examination highlighted reduced strength in the muscles of the right upper limb (4/5), while the strength in the left upper limb and both lower limbs was normal (5/5). Additionally, there was impaired vision in the right eye, and blood tests did not reveal any abnormalities.

The patient was scheduled for a contrast-enhanced Magnetic Resonance Imaging (MRI) of the brain. The imaging revealed a heterogeneous signal mass in the left basal ganglia and internal capsule, measuring approximately 48 × 54 mm, which compressed the third ventricle, causing dilation of the upper ventricular system and a rightward midline shift. The mass comprises mixed solid and cystic components with restricted diffusion on Diffusion sequences and no calcification or hemorrhage. The post-contrast sequence showed heterogeneously strong enhancement (Fig. 1). These aforementioned findings are suggestive of a Basal Ganglia Germinoma (BGG).

The patient underwent tumor resection surgery. During the procedure, a soft tumor was found in the thalamic and basal ganglia on the left side, extending into the left lateral ventricle. Because of abundant vascular proliferation and deep-seated locations, complete excision was excluded. A partial resection of the tumor was performed, and frozen section results confirmed germinoma.

Pathological examination on Hematoxylin and Eosin-stained sections showed that the tumor cells have large, round

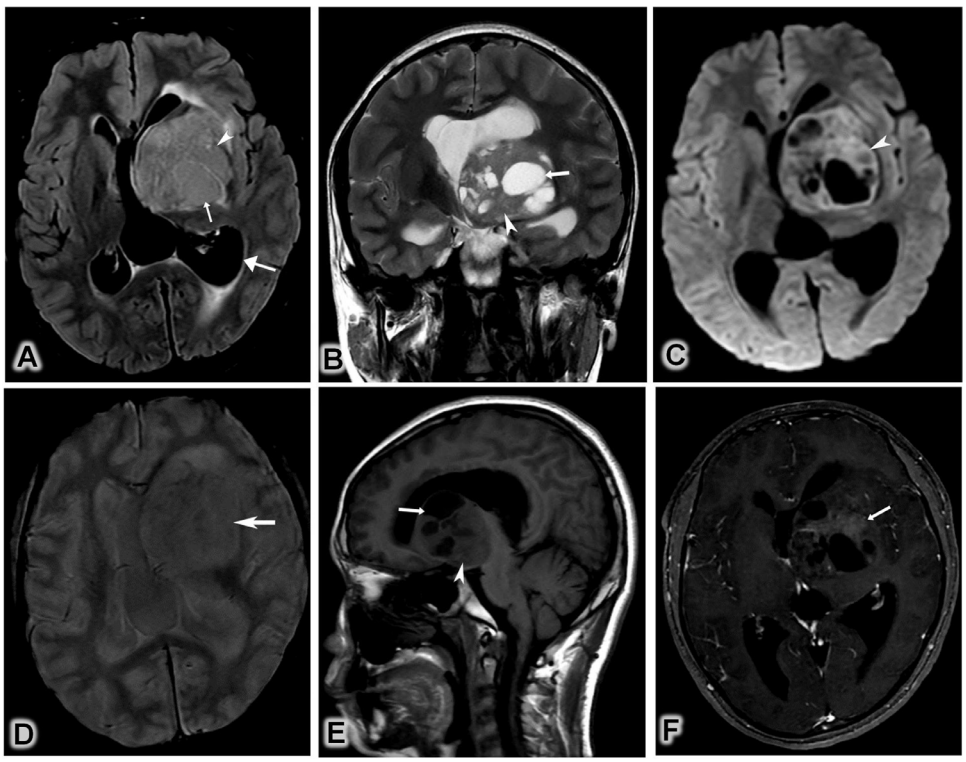

Fig. 1 – Case 1: MRI images (A) axial Fluid-attenuated inversion recovery (FLAIR), (B) coronal T2 Weighted (T2W), (C) Diffusion-weighted imaging(DWI), (D) axial T2*, (E) sagittal T1 Weighted (T1W), (F) post-contrast axial T1W illustrated a mixed signal mass in the left basal ganglia and internal capsule. (A) Axial FLAIR image showed a mixed signal mass comprising a cystic portion (small arrow) and a solid portion (arrowhead), which compressed the third ventricle and caused dilation of the upper ventricular system (large arrow). (B) Coronal T2-weighted image displayed a mixed signal mass, including a cystic portion (small arrow) and a solid portion (arrowhead). (C) DWI revealed restricted diffusion on the solid components (arrowhead). (D) Axial T2* showed no calcification or hemorrhage. (arrow: tumor) (E) Sagittal pre-contrast T1-weighted image demonstrated a mixed signal mass with a cystic portion (small arrow) and a solid portion (arrowhead). (F) Axial T1-weighted post-contrast image showed heterogeneous contrast enhancement in the mass (arrow).

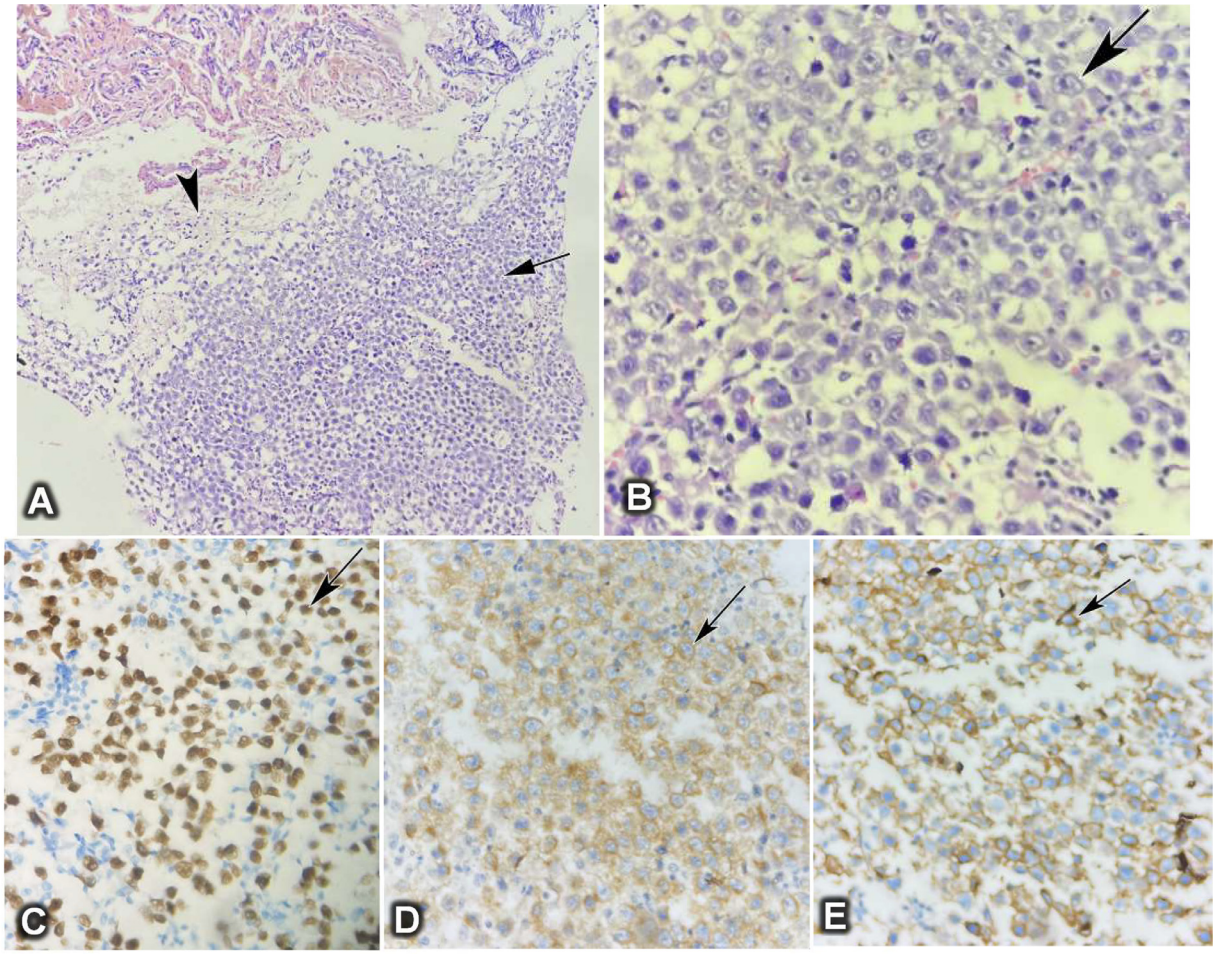

Fig. 2 – Case 1: Histopathological Images. (A-B) Hematoxylin-eosin staining: Tumor cells with large, round nuclei, prominent nucleoli, multiple mitotic figures, and variable eosinophilic cytoplasm (arrows). The cells are dispersed or form clusters, intermixed with a background rich lymphocytes (arrowhead). (C-E) Immunohistochemistry. (C) SALL4 Marker (+): Nuclei of germ cells stain orange (arrow). (D) CD117 Marker (+): Cell membranes stain orange (arrow). (E) PLAP Marker (+): Cell membranes stain orange (arrow). (A: x100 magnification. B-E: x400 magnification).

nuclei with prominent nucleoli, frequent mitoses (or brisk mitotic activity), and varied cytoplasm ranging from pale to eosinophilic. The tumor cells are dispersed or grow clusters, nests, interspersed within rich lymphocyte stroma. Immunohistochemical staining demonstrated positive reactivity for SALL4, CD117, and PLAP markers in the germ cells (Fig. 2). The histopathological findings were consistent with a diagnosis of germinoma.

A follow-up noncontrast CT scan of the brain after 2 weeks revealed a residual tumor at the left basal ganglia measuring 38 × 35 mm, which still resulted in a rightward midline shift. Besides that, there is a surgical cavity in the left frontal lobe, with the left hemisphere's subdural fluid collection (Fig. 3).

The treatment plan consisted of chemotherapy with a regimen of 4 cycles of Ethylenedicysteine/ Vin-endoxan, followed by radiation therapy.

Case 2

An 11-year-old boy was admitted to the hospital due to a progressive hemiparesis of the right upper limb for a month without associated fever. His medical history was unremarkable. Clinical examination revealed reduced strength in the muscles of the right upper limb (4/5), while the strength in the left upper limb and both lower limbs was normal (5/5). Blood tests did not reveal any abnormalities.

The patient was scheduled for a contrast-enhanced MRI of the brain, which demonstrated a mass in the left lentiform nucleus measuring 28 × 19 mm, comprised of cystic components, solid components with restricted diffusion, areas of calcification, and heterogeneous contrast enhancement after injection. Furthermore, this neoplasm showed no mass effect and atrophy of the ipsilateral cerebral peduncle (Fig. 4). The differential diagnosis could not rule out vasculitis or encephalitis. The cerebrospinal fluid puncture showed no abnormality. Follow-up contrast-enhanced MRI and noncontrast CT scans of the brain were performed after six months. On MRI brain images, the mass size has increased to 41 × 26 mm, extending from the thalamus to the head of a caudate nucleus. The calcification, contrast enhancement, and atrophy of the ipsilateral cerebral peduncle are more significant. The spectroscopy illustrated elevated choline levels and de-

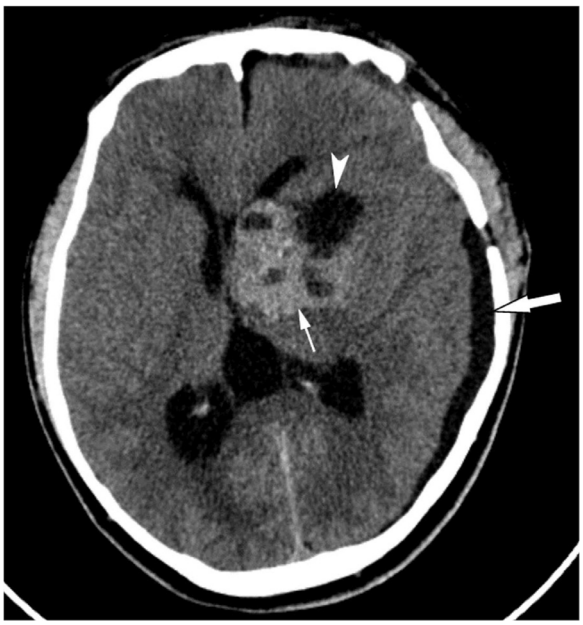

Fig. 3 – Case 1: Postoperative computed tomography (CT) image after 2 weeks demonstrated a heterogeneous mass in the basal ganglia and thalamic region, extending into the left lateral ventricle (small arrow), a cavity in the brain tissue (arrowhead), and subdural fluid collection (large arrow).

creased N-acetylaspartate (NAA) (Fig. 5). The mass appears hyperdense on the CT brain images, with some hypodense areas suggestive of fluid components (Fig. 6). The patient was diagnosed with basal ganglia germinoma. Pathological results confirmed the diagnosis of basal ganglia germinoma (Fig. 7). Blood tests for hCG (human chorionic gonadotrophin) and AFP (α-fetoprotein) are normal.

The patient underwent radiation therapy and chemotherapy. After six months of treatment, MRI imaging revealed a cystic structure with evidence of hemorrhage and no post-contrast enhancement (Fig. 8).

Discussion

Germ cell tumors (GCTs) are relatively uncommon tumors that are typically found in young people (mainly under 20 years old), with a predominance in men (>90%) and Asians (>72%) [6]. They usually appear in midline intracranial structures, like pineal and suprasellar regions [2]. GCTs can also be seen in off-midline structures such as the basal nuclei and thalamus (6%-10%) [2]. Clinical symptoms based on tumor location. Patients with GCTs arising from basal ganglia or thalami frequently present with only vague symptoms, late-onset, slowly progressive, and especially a limb weakness, which gradually progresses to hemiplegia [7]. Histolog-

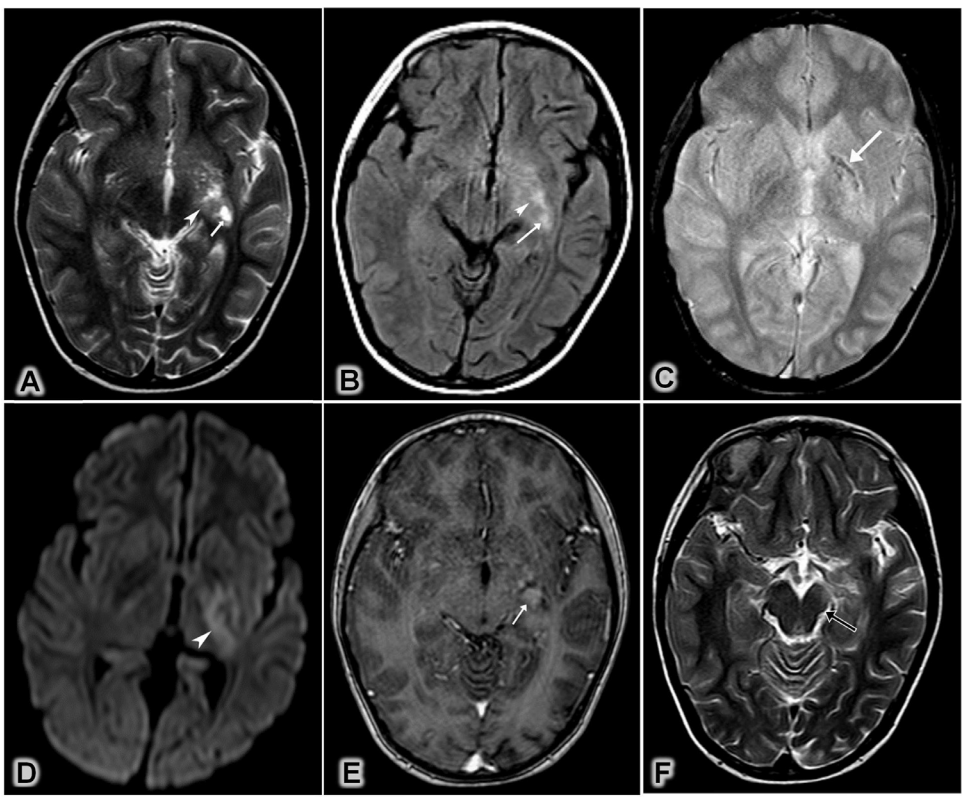

Fig. 4 – Case 2: MRI Images, including (A) axial T2W, (B) axial FLAIR, (C) axial T2*, (D) axial DWI, (E) postcontrast axial T1W, demonstrated. (A-B) Axial T2W and FLAIR showed A heterogeneous mass in the left lentiform nucleus comprising a solid portion (arrowhead) and a cystic portion (arrow). (C) Axial T2* showed a calcifying component (arrow). (D) DWI showed a restricted diffusion (arrowhead). (E) Axial T1W post-contrast showed heterogeneous enhancement (arrow). (F) Axial T2W image showed atrophy of the ipsilateral cerebral peduncle (black arrow).

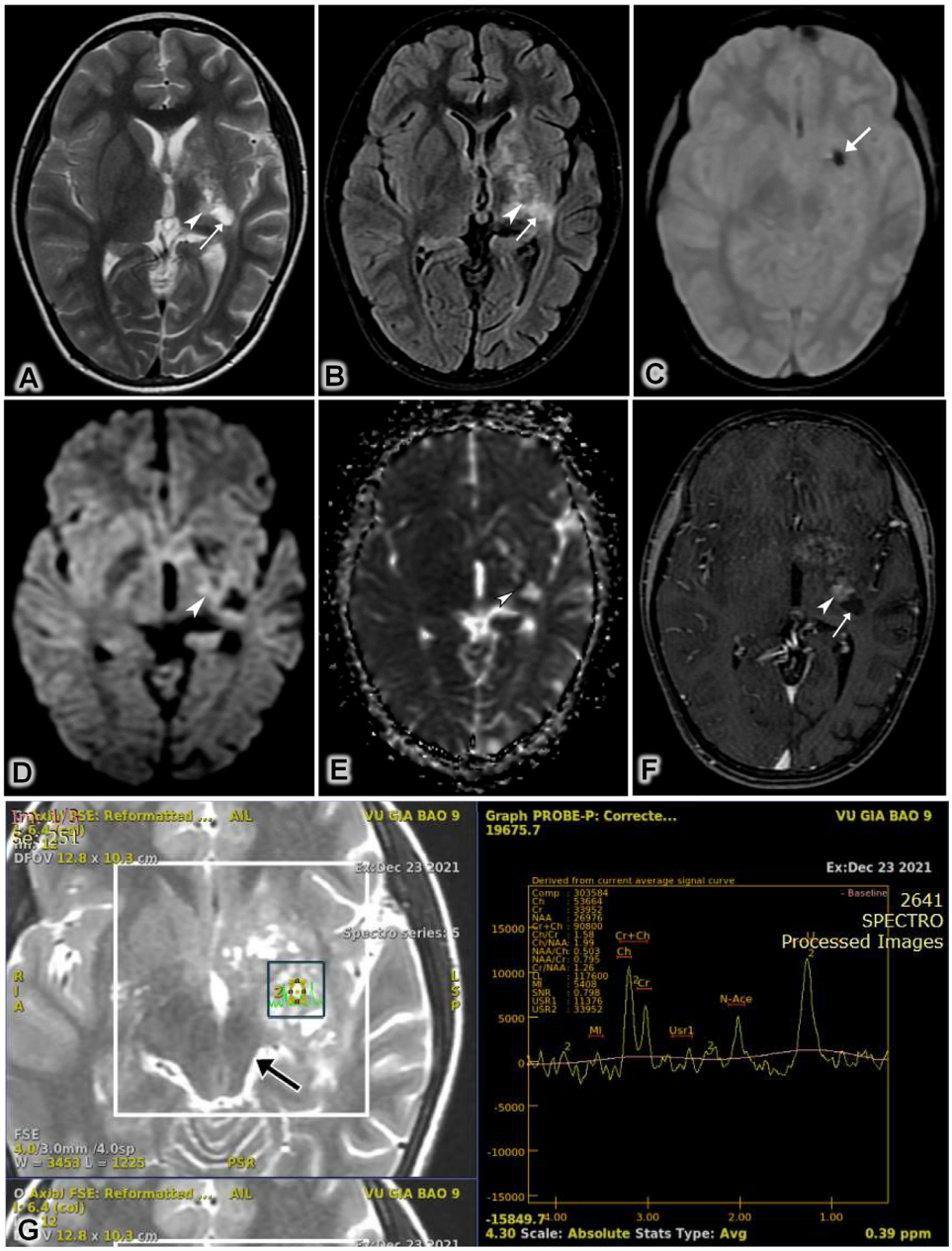

Fig. 5 – Case 2: MRI Images, including (A) axial T2W, (B) axial FLAIR, (C) axial SWI, (D) axial DWI, (E) axial ADC, (F) axial T1W post-contrast, (G) spectroscopy, demonstrating. (A-C): A mixed-density mass involving the lentiform nucleus, head of the caudate nucleus, and left temporal uncus, comprising a solid portion (arrowhead) and a cystic portion (small arrow), with calcification (large arrow). (D-E): Restricted diffusion of the solid portion on DWI/ADC (arrowhead). (F) Axial T1W post-contrast: Enhancement of the mass (small arrow). (G): Atrophy of the ipsilateral cerebral peduncle (black arrow).

ically, GCTs are divided into germinomas, which account for 70%, and non-germinomatous germ cell tumors (NGGCT) [8]. GCTs may be associated with increased AFP and HCG values in serum and/or cerebrospinal fluid (CSF) [9].

Diagnosis of BGGs in the early stage may be challenging because the clinical symptoms and neuroimaging findings are not specific. Due to the origin of GGT, these entities are unsurprisingly radio-chemosensitive and potentially curable. Early diagnosis is essential for good outcome (complete response and minimum nervous system damage). Diagnostic imaging tools play an important role preorperatively. The radiologic appearance of BGGs changes during tumor progression. In the early stage, even though a normal brain CT scan is often expected, insidious neurological findings are sometimes presented [7]. On brain MRI, BGGs usually appear as an ill-defined, heterogeneous solid lesion without mass effect [10,11,12]. They are generally isointense to hyperintense compared with the grey matter on T2-weighted, T1-weighted, and FLAIR images, with no restricted diffusion and no or minimal enhancement [13,14,15]. Several studies have proven that SWI

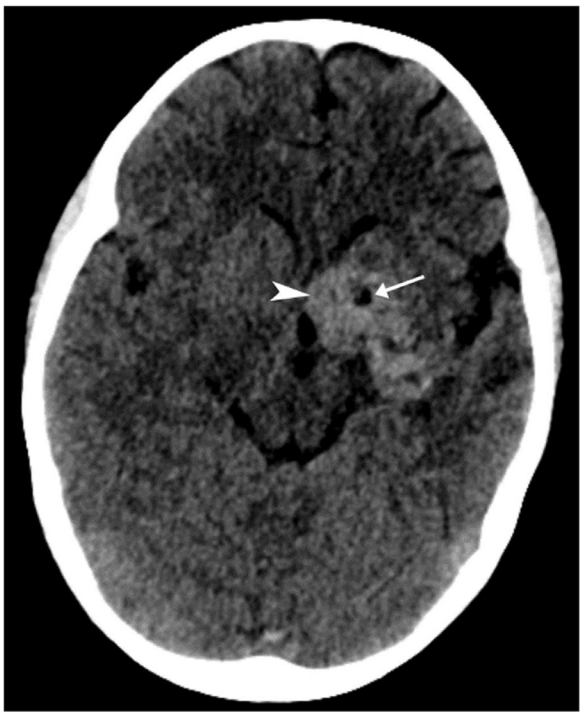

Fig. 6 – Case 2: CT Images showed a mass involving the lentiform nucleus, head of the caudate nucleus, and left temporal lobe uncus, comprising an increased density solid portion (arrowhead) and a cystic portion (white arrow).

can help in the early diagnosis of BGG [11,12,16]. Small tumors are hypointense on SWI due to intratumoral hemorrhage and tumor-induced metal deposition [12]. Ipsilateral cerebral and brainstem hemiatrophy, which is frequently present in the early stage, also plays a critical role in diagnosing BGG [15,17]. In the past, this sign was a characteristic of BGG; however, recent studies have shown it can be seen in any neurological disease with lesions in the internal capsule or thalamic ganglion cell [18].

During tumor progression, the intratumoral tiny cysts may develop, making the tumor more heterogeneous, although tumor size is insignificantly changed. The intratumoral cysts gradually increase in size, and intracystic bleeding leads to finding fluid-fluid level and peripheral hypointense rim on T2W [11]. In this stage, BGGs consist of a solid, cystic portion, hemorrhage, and calcification with heterogeneous enhancement after contrast infusion, but they show relatively less mass effect and peritumoral edema [19]. On CT scan, the solid component is hyperdense [19]. In our cases, the lesions appear as a lobulated mass with internal solid and multicystic components with a significant heterogeneous enhancing component after gadolinium injection. However, the mass effect and peritumoral edema are minimal. In the second case, the patient was examined relatively early. MRI showed an ill-defined lesion with tiny cysts with intratumor hypointense on T2* and ipsilateral hemiatrophy. Post-gadolinium contrast-enhanced images revealed a minor homogenous enhancement of the solid part. On MRI after 6 months, intratumoral cysts increase in size, the hypointensity observed on T2* is higher, and the enhancement pattern is more heterogeneous. Thus, the second case had all the signs of BGG from the early stage. In the first case, although detected late when the lesion had created a large mass, hypointense on T2* and atrophy of the ipsilateral cerebral peduncle has not occurred.

Early diagnosis of BGGs is challenging. BGGs usually appear as an ill-defined, homogeneous lesion without mass effect. CT may be normal. Conventional MRI shows an isointense to slightly hyperintense lesion without restricted diffusion and post-contrast enhancement. In addition, nontumorous lesions and other slowly growing tumors from basal ganglia may also have ipsilateral hemispheric and brainstem atrophy signs. The finding of germinomas can be inconspicuous in the early stage, so they are often diagnosed in the advanced stage or misdiagnosed with non-tumorous lesions such as subacute lacunar infarction and encephalitis. [13]. Xin Lou et al. reported that the early stage of BGGs was defined as tumors with the largest diameter of less than 10mm, without cystic degeneration, necrosis, and bleeding on conventional MRI [12,16]. According to these studies, BGGs in the initial

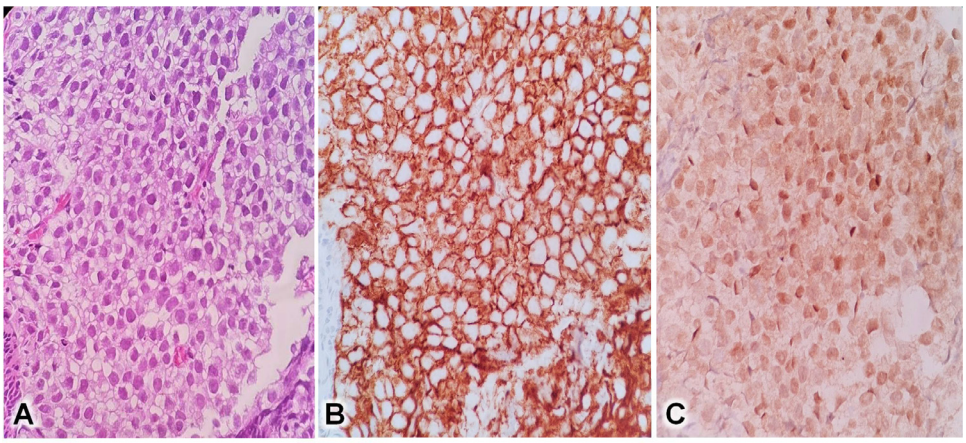

Fig. 7 – Case 2: Pathological images. (A) Hematoxylin-eosin staining reveals large-sized tumor cells with abundant, clear, round nuclei, relatively uniform cytoplasm, and distinct nucleoli (black arrowhead). (B-C) Immunohistochemistry: (B) OCT3/4 Marker (+): Strong and diffuse positivity. (C) CD117 Marker (+): Strong and diffuse positivity. (A-E: x400 magnification).

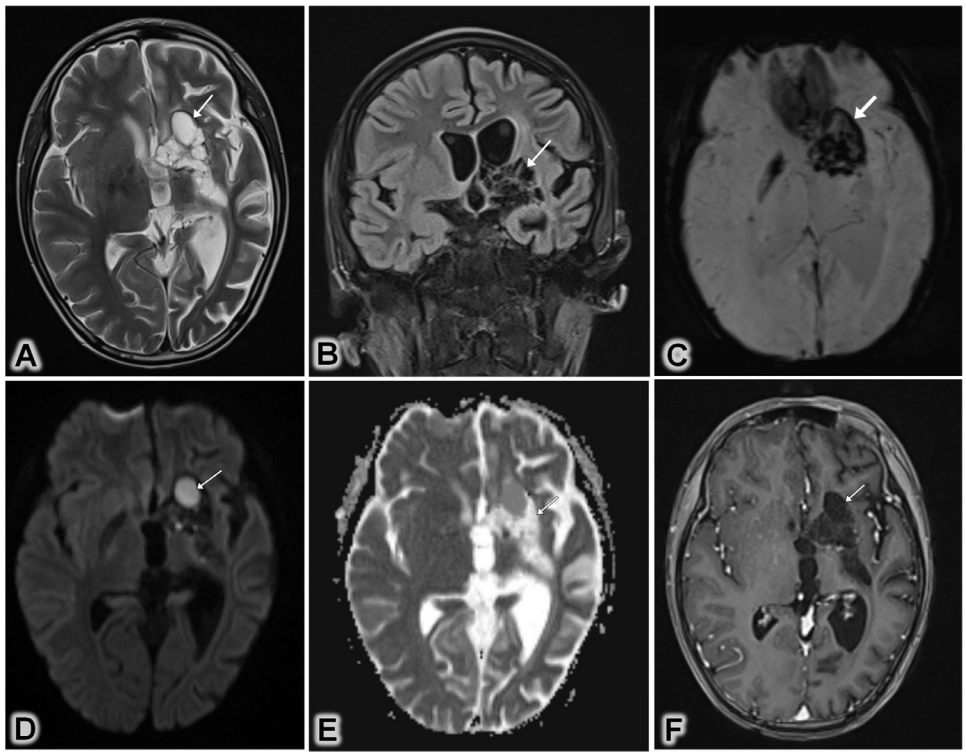

Fig. 8 – Case 2: Post-treatment MRI image, including (A) axial T2W, (B) coronal FLAIR, (C) axial SWI, (D) axial DWI, (E) axial ADC, (F) axial T1W post-contrast, demonstrated a cystic lesion in the lentiform nucleus, head of the caudate nucleus, and the left temporal lobe uncus, with evidence of bleeding, and no postcontrast enhancement (white arrowhead).

stage have hypointensity on SWI/T2*, and the tumor size on this sequence may be larger than the size observed on other pulse sequences [16]. In contrast, this sign is relatively not remarkable in non-tumorous conditions such as infarction. Therefore, SWI could be helpful in differential diagnosis and early detection of BGGs. Several studies have shown that 11C-methionine positron emission tomography (MET-PET) can be used to differentiate early-stage BGGs from nontumorous lesions because the demand for amino acids of the tumor cells is higher. This substance is less affected by inflammation than 18F-FDG-PET [20,21]. In an advanced stage, BGGs should be considered in the differential diagnosis with all tumors arising in the basal ganglia or thalami, mainly gliomas and lymphoma. The late stage of BGG and gliomas can present as complex solid and cystic masses with bleeding, calcification, and heterogeneous enhancement. On unenhanced CT scans, generally, germinomas are hyperdense, whereas gliomas are isodense to hypodense. With a similar large size, peritumoral edema, and mass effect are usually slighter and uncommon in BGGs than in gliomas [7,19]. Magnetic resonance spectroscopy (MRS) is also a technique to help differential diagnosis because gliomas demonstrated increased choline (Cho) and decreased N-acetyl aspartate (NAA). In contrast, germinomas appeared with typical metabolic patterns in the peritumoral region [22]. In our second case, there was an increase in the choline, lipid, lactate peak and a decrease in the NAA peak on the MRS. Lymphoma is also often hyperdense on non-enhanced CT scans, with minimal surrounding edema like germinomas. However, lymphoma rarely has cystic degeneration, bleeding, or necrosis, usually well visualized on DWI with low ADC values and intense homogeneous enhancement [23]. Hypermetabolism on 18F-FDG-PET was observed in high-grade gliomas and lymphoma, while germinomas often have typical values for 18F-FDG uptake [13]. The differential diagnosis of BGGs with other tumors and non-tumorous lesions based on imaging findings alone is challenging. Tumor markers (serum and CSF levels of AFP and HCG) should be performed for an early and formal diagnosis. The change of concentration of these substances in serum and CSF make up only less than 50%. Furthermore, the degree of change in AFP and HCG concentrations in serum and CSF varies between patients, so it is necessary to have a diagnostic threshold for these tests [9]. International Society of Pediatric Oncology (SIOP) studies demonstrated diagnostic serum or CSF AFP levels of $\geq$ 25 ng/mL and/or HCG levels $\geq$ 50 IU/L [24,25]. Biopsy should be performed to confirm diagnosis in case of uncertainty or atypical radiological findings and regular tumor marker testing.

Germinomas respond well to chemotherapy and radiotherapy (RT) and are potentially curable by RT alone if correctly diagnosed at their early stage. The prognosis of germinomas depends on various factors, including the tumor's size and location, the metastasis level, and the radiation dose [3]. Many studies reported that germinomas have 5-year event-free survival (EFS) greater than 85% [3,26]. According to SIOP research in 2017, EFS is 72%, and the overall survival rate (OS) is 82% in patients with germ cell tumors without metastasis. This rate in patients with metastases is 68% and 75%, respectively [27]. Therefore, early recognition of BGGs can improve survival rates and decrease neurological deficits.

Conclusion

Clinical symptoms are often insidious, and imaging in the early stage is not typical, so BGGs are easily misdiagnosed with non-tumorous conditions as well as other tumors, leading to delays in treatment. Combined with clinical symptoms, the laboratory examination, imaging characteristics, especially early signs such as hypointense on SWI and ipsilateral hemimesencephalic atrophy, and biopsy can help diagnose BGGs in patients with progressive neurological deficits, avoid delayed treatments of a prognostically favorable tumor.

Author's contributions

Ho XT and Nguyen MD: Case file retrieval and case summary preparation. Ho XT and Nguyen MD: preparation of manuscript and editing. All authors read and approved the final manuscript.

Availability of data and materials

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Our institution does not require ethical approval for reporting individual cases or case series. Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Patient consent

Informed consent for patient information to be published in this article was obtained.

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