GERMINOMA WITH INVOLVEMENT OF OFF-MIDLINE INTRACRANIAL STRUCTURES: A CASE REPORT

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ABSTRACT

Introduction*: The exercised skeletal muscle may induce oxidative stress (OS) leading to contractile dysfunction, fatigue and weakness during a strPrimary germ cell tumor presents with diverse clinical symptoms and imaging features. Less than 10% are localized in off-middle structures, and only midline involvement of parenchyma has been extensively researched. A case of a 21-year-old male patient with progressive mental disorder and intermittent fever was reviewed. Brain MRI showed demyelinating lesion at the paraventricular side of the lateral ventricle at an early stage. Alfa-fetoprotein (AFP) levels were negative in both serum and cerebrospinal fluid (CSF). Misdiagnoses were made frequently. When MRI displayed a cystic and solid lesion at the left frontal lobe, a clear diagnosis could not be given with clinical, laboratory and imaging examinations. Thus, we performed craniotomy and removed the intracranial lesions. The pathological results showed that the tissue morphology and immunohistochemistry were indicative of germ cell tumor, and CD117 and PLAP immunohistochemical staining was positive.*

Conclusion*: Germinoma must be considered in patients with demyelinating lesion at the midline and with a long history of mental disorders. In addition, ectopic germinoma must be suspected in these patients. Although a rare condition, colocalization of midline and off-midline germinoma must be considered in the presence of these typical signs of both localizations.*

Keywords*: Germinoma, Off-Midline Intracranial.*

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Introduction

Germ cell tumors represent approximately 3% of the malignant tumors in children[(1)]. They account for 0.1 to 2.4% of all childhood intracranial tumors in North America and Europe, while they constitute almost 2.1 to 9.5% of tumors in Japan and the Far East[(2,3)]. Primary central nervous system germ cell tumors are rare, and most occur in patients between 10-20 years old[(4)]. The diagnosis of the disease is very challenging due to the its diverse clinical manifestations[(5)]. Central nervous germ cell tumors have been divided into secreting and non-secreting classifications. Secreting tumors present with an elevated CSF AFP ≥ 10 ng/mL or above the local laboratory's normal range, and/or a CSF ß-HCG level ≥50 IU/l or greater than the accepted laboratory normal range. This has been proven to be associated with the patient's prognosis and treatment response[(1)]. These markers of brain germinomas are often serologically negative[(6)]. Intracranial germ cell tumor is most often located in the pineal or suprasellar regions, and can also involve both sites at the time of diagnosis[(1,5)].

In addition, it can also involve the midline area, sch as basal ganglia, thalamus and internal capsule, which is also known as ectopic germ cell tumor, accounting for 5-10% of the central nervous system germ cell tumors[(5,6)]. In this study, we report an unusual case of a young male with

brain parenchymal germ cell tumor involvement of midline structures. Such a case presenting clinical symptoms and imaging findings is rare.

Case

A 21-year-old male patient was admitted to the hospital with weight loss for 4 years, intermittent fever for 2 years and epileptic convulsions for 5 days. In 2014, the patient was 18 years old at first onset, presenting with weight loss and poor spirit without obvious cause, and had visited many hospitals that could also not determine a clear cause for his condition.

In 2015, the patient presented with mental retardation, and cerebral MRI in the outpatient department showed slightly longer T1 and slightly longer T2 signals in bilateral paraventricular regions and corpus callosum. Laboratory examination of CSF was negative. No clear treatment was available in this patient, whose symptoms were not no obviously improved.

In July 2016, the patient had unprovoked paroxysmal headache and fever, and the temperature reached 39 degrees in the morning and evening. Conventional antipyretic drugs could be obtained from the local hospital, such as Reduning and cephalosporins. However, the symptoms were not significantly improved. The patient received further treatment in our hospital. Physical examination showed right eye mild lid ptosis, mouth slanting towards the left, tongue slanting towards the right, and 5 levels of limb muscle strength. Brain magnetic resonance imaging (MRI) showed slightly longer T1 and slightly longer T2 signals in bilateral paraventricular regions, bilateral basal ganglia and corpus callosum. The volume of the corpus callosum was smaller than before (Figure 1). AFP levels were negative in both serum and CSF. The hormone laboratory examination showed decreased estradiol (E2 <5 pg/ml, normal values). A treatment of viral encephalitis was given but did not produce an obvious effect. After subsequent visits to many hospitals, the etiological agent could not be identified.

In September 2017, unprovoked paroxysmal lockjaw, head tilting towards the right, right eyes gaze and right limbs hyperspasmia, and conscious eating occurred, which were treated using antiepileptic drugs. The patient had poor appetite and poor sleep. AFP and β-HCG levels were negative in both serum and CSF.

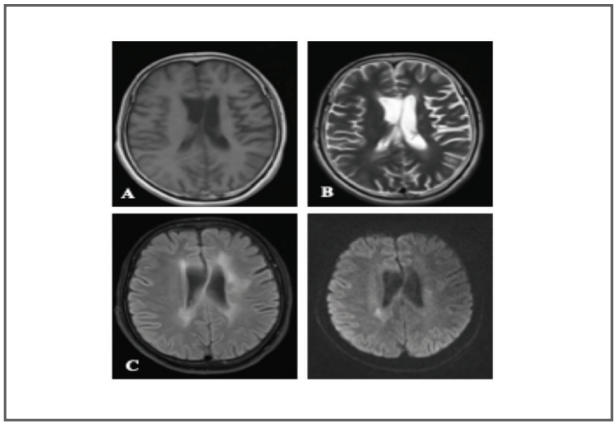

Fig 1: Preoperative MRI.
Axial T1WI(A), T2FLAIR(B), T2WI(C), and DWI(1000). The lesion demonstrated slightly longer T1 and slightly longer T2 signals in bilateral paraventricular regions, bilateral basal ganglia and corpus callosum

Brain magnetic resonance imaging (MRI) showed a round cystic and solid lesion of low signal on T1WI, high signal on T2WI, and T2FLAIR sequence within liquid level. The lesion also presented a high signal on Diffusion-weighted imaging sequence, and ring and nodular enhancement in left frontal lobe and corpus callosum (Figure 2). With clinical, laboratory and imaging examinations, a clear diagnosis could not be made, and thus we performed craniotomy and removal of intracranial lesions. The biopsy showed a solid portion with rich blood supply and a cystic part with hemorrhage during the operation.

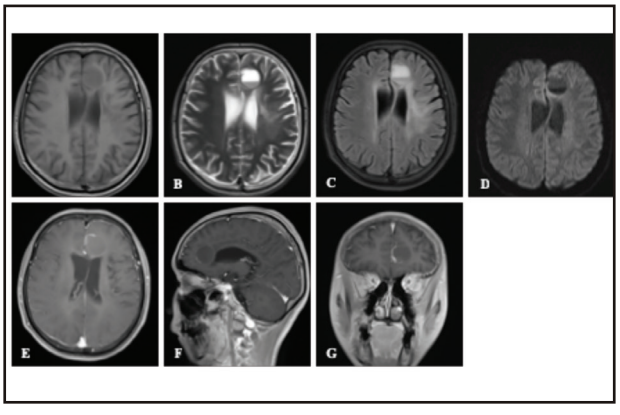

Fig 2: Preoperative MRI: axial T1WI(A), T2FLAIR(B), T2WI(C), and DWI(1000). The lesion showed a round cystic and solid lesion of low signal on T1WI, high signal on T2WI, and T2FLAIR sequence within liquid level. The lesion also presented a high signal on Diffusion-weighted imaging sequence. Enhanced image (E-G): ring and nodular enhancement can be presented in left frontal lobe and corpus callosum.

The pathological results showed that the tissue morphology and immunohistochemistry were indicative of germ cell tumor, and the CD117 and PLAP immunohistochemical staining was positive. A PET-CT examination excluded metastatic lesions. Brain MRI was accepted for review 7 days postoperatively, showing a patch with low signal on T1WI, high signal on T2WI in left frontal lobe surrounded with high signal on T1WI, low signal on T2WI and mild diffusion limited to the edge of the lesion on DWI (b=1000) (Figure 3). One month later, the patient was admitted to the hospital due to paroxysmal twitching and received two cycles of whole brain spinal cord radiotherapy. The cerebral MRI displayed that the lesion in the original operation area was smaller than before, and nodular enhancement was accepted after 1 month (Figure 3).

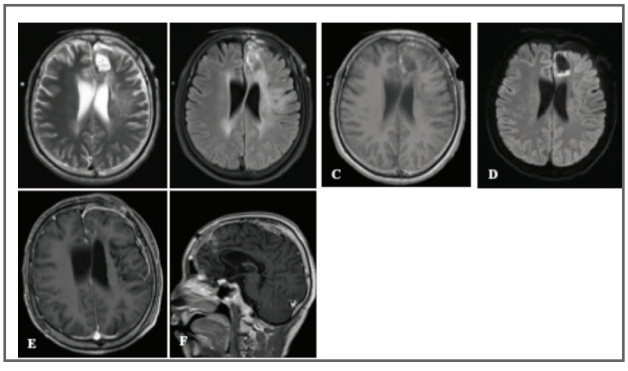

Fig 3: : Brain MRI was accepted for review 7 days postoperatively(A-D), showing a patch with low signal on T1WI, high signal on T2WI in left frontal lobe surrounded with high signal on T1WI, low signal on T2WI and mild diffusion limited to the edge of the lesion on DWI (b=1000). The MRI displayed that the lesion in the original operation area was smaller than before, and nodular enhancement was accepted after 1 month(E,F).

Discussion

Primary intracranial germ cell tumors are usually found in the pineal and sellar regions and rarely in off-midline structures[5]. Lesions that are located in the frontal lobe parenchyma are rare. Diversity of clinical presentation depends upon the size and the localization of the tumor. The earliest clinical symptoms usually include slow progressive hemiplegia, neuropsychiatric symptoms, and cognitive abnormalities[4,7-13]. Duration of clinical symptoms ranged from 1 month to 4.5 years, with a mean period of 1.5 years[10]. The initial symptom of the patient was mental disorder of 3 years, which could have been associated with invasion of the corpus callosum.

Neuroimaging studies are helpful for diagnosis and differential diagnosis. The disease's imaging features include calcification, cystic change, and enhanced enhancement[14-17]. Non-secretive germ cell tumors often present with bleeding and a variety of signals[18]. Intratumoral hemorrhage may be caused by high vulnerability of vascular brittleness[19]. This case showed cystic fluid with blood and a solid part with rich blood supply during the operation. Brain MRI showed a single cyst that was a cystic and solid lesion. At the fluid level, less edema around the lesion and the solid part was found with slight enhancement. From the imaging findings, a differential diagnosis of single benign cystic lesions and cystic gliomas in the left frontal lobe was made. Simple cystic lesions have no solid part with enhancement. Cystic glioma shows invasive growth with an unclear margin and rarely present with stratification.

Early diagnosis is very important because a delay in treatment can result in more severe neurologic deficits, as observed in our case. In this case, we misdiagnosed the pathology as a non-neoplastic disease frequently based on MRI examination, although a space occupying lesion was not shown. This demonstrated that the biological behavior of germ cell tumor is different from that of other intracranial tumors.

The manifestations of white matter demyelinating lesions on both sides of the ventricle, anterior corpus callosum and anterior corpus callosum, as well as ischemia, inflammation and brain white matter dystrophy, were found at the first two MRI sessions, thus resulting in misdiagnosis. Imaging manifestations of germ cell tumors as ischemia and inflammation may be related to the effect of tumor tissue on the local microvessels of the lesion. Differentiation from ischemic and inflammatory lesions should be combined clinically. This patient experienced a slow progression and a hidden disease and was of an age uncommon for cerebrovascular disease onset with no risk factors for cerebrovascular disease.

These factors suggest that the patient had a non-vascular disease. In addition, the patient had no meningeal irritation but had increased intracranial pressure with intermittent fever for 2 years. In addition, CSF examination did not support the diagnosis of intracranial inflammatory lesions.

In addition, the patient had intermittent fever for 2 years without occurrence of meningeal irritation and intracranial hypertension. The symptoms and CSF examination did not support the diagnosis of intracranial inflammation. The imaging features of this disease are not characteristic; therefore, special tumor markers are needed to make a clear diagnosis.

A tumor biopsy is required for the diagnosis, except in cases where tumor markers are elevated (20). The special feature of this patient is that the cerebrospinal fluid and blood examination suggest that both alpha fetoprotein and human chorionic gonadotropin were negative, which may be related to the tumor's special location and pathological type. Germ cell tumors usually disseminate via the cerebral spinal fluid.

PET-CT examination did not demonstrate lesions at other parts of the patient's body, suggesting that there were no disseminated lesions. Germ cell tumor is considered to be a primary lesion of the brain, which results in negative examination of CSF and serum. Currently, immunohistochemical staining of CD117 and PLAP is a well-known diagnostic method[21,22]. Therefore, minimally invasive stereotactic biopsy is feasible when the diagnosis is not clear. Germ cell tumors are sensitive to two cycles of radiotherapy and platinum chemotherapy, but the recurrence rate is 10% or even higher after initial treatment[13,23-25]. Therefore, the standard treatment for germ cell tumor is whole brain and whole spinal cord irradiation, which results in a survival rate of up to 90%. To reduce the recurrence, a larger scale and large dose of radiation therapy can be used in the patient. In this case, the symptoms can be obviously improved after whole brain and whole spinal cord irradiation.

In conclusion, this case could not be diagnosed early due to atypical imaging manifestations as well as undefined blood and cerebrospinal fluid examination. Therefore, when young patients suffer from mental disorders for a long time and when imaging examinations show an early stage demyelinating lesion at the midline with no abnormal laboratory results, minimally invasive stereotactic biopsy can be used to make a definite diagnosis to avoid misdiagnosis.

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