Primary Yolk Sac Tumor of Bilateral Basal Ganglia

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A primary intracranial yolk sac tumor (YST) is a type of germ cell tumor (GCT) and usually involves the pineal or suprasellar regions, as do other GCTs. Primary YST in the basal ganglia is not common, and bilateral basal ganglia involvement is even rarer. Early diagnosis is often difficult because of minimal or subtle findings without space-occupying lesions shown on neuroimaging during the early course of the disease. We report a case of primary intracranial YST encountered in the basal ganglia bilaterally and describe the clinical presentation, diagnostic problem, imaging characteristics, histopathologic features, and prognosis of the tumor. To the best of our knowledge, this is only the third reported case of primary YST confined to the basal ganglia in the literature. [*J Chin Med Assoc* 2010;73(8):444–448]

Key Words: basal ganglia, germ cell tumor, yolk sac tumor

Introduction

Yolk sac tumor (YST), also known as endodermal sinus tumor, is a member of the germ cell tumor (GCT) group. YSTs are estimated as less than 8% of all primary intracranial GCTs and usually develop in the midline at the pineal or suprasellar regions, as do other GCTs. However, rarely, they may arise from "ectopic sites", most notably the basal ganglia and thalamus, where they present ill-defined infiltrations with little to no mass effect shown on neuroimaging during the early course of the disease. YSTs involving the bilateral basal ganglia are exceedingly rare. We report a patient with bilateral basal ganglia YST in whom conventional magnetic resonance imaging (MRI) findings were not specific, highlighting the difficulty of early diagnosis.

Case Report

A previously healthy and developmentally normal 7-year-old girl presented with a 2-month history of progressive left hemiparesis and was evaluated at another hospital. Physical examination showed left-sided weakness, spasticity, and hyperreflexia. She had no sensory or cranial nerve deficits. She used to be left-handed and became right-handed gradually. She had neither diabetes insipidus nor precocious puberty. Computed tomography (CT) of the brain demonstrated faint calcification in bilateral basal ganglia. MRI of the brain demonstrated ill-defined abnormal signal intensity without enhancement in the left caudate head, right internal capsule, and right basal ganglia (more prominent in the right globus pallidus and putaman) with a smaller right cerebral peduncle (Figure 1). Neurodegenerative or metabolic or autoimmune disease was suspected because of the bilateral nature of the findings. However, there was no family history, and the laboratory data did not support such a diagnosis. Empiric trial of intravenous methylprednisolone did not lead to any improvement. The patient had a hemiparetic gait and needed assistance with ambulation. She received rehabilitation and was discharged for follow-up.

Brain MRI was performed again 6 months later and demonstrated enlarged left caudate nucleus and progressive atrophy of right cerebral peduncle. On T2-weighted images, the hyperintense lesions of the right internal capsule and basal ganglia had become more heterogeneous compared with the previous examination (Figure 2).

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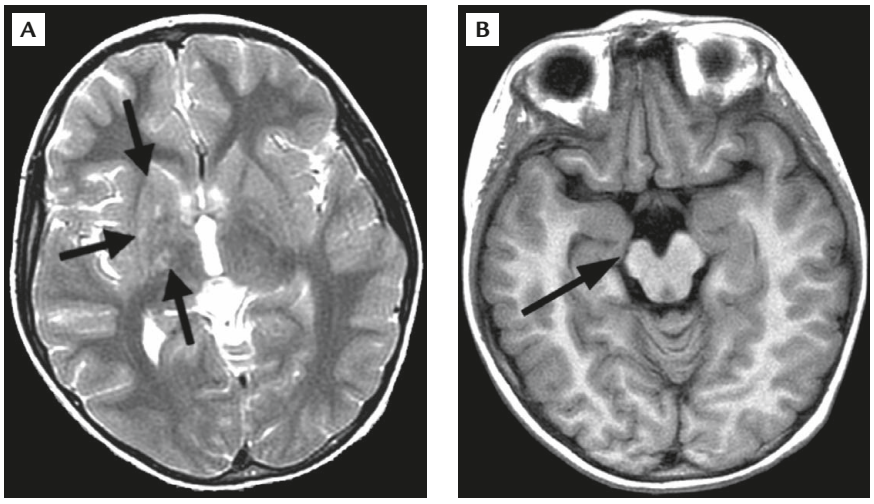

Figure 1. Axial magnetic resonance imaging shows: (A) ill-defined abnormal signal intensity in the left caudate head, right internal capsule, and right basal ganglia (more prominent in the right globus pallidus and putaman) (arrows) on T2-weighted imaging; and (B) a smaller right cerebral peduncle (arrow) on T1-weighted imaging.

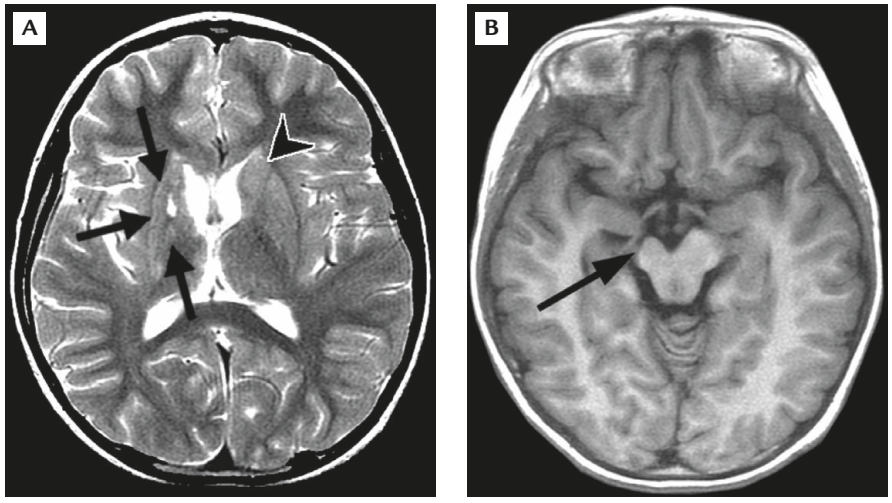

Figure 2. Axial magnetic resonance imaging shows: (A) enlarged left caudate nucleus (arrowhead) and more heterogeneous hyperintense lesions of the right internal capsule and basal ganglia (arrows) on T2-weighted imaging; and (B) progressive atrophy of the right cerebral peduncle (arrow) on T1-weighted imaging.

Three months later, the patient had developed additional symptoms including gradual onset right hand tremor and weakness, cognitive decline, speech and language regression, and difficulty in swallowing. Brain MRI demonstrated a huge tumor mass with internal hemorrhage and perifocal edema, 5 cm in diameter, in the left basal ganglia with midline shift (Figure 3). Serum biochemistry revealed a raised α-fetoprotein (AFP) level of up to 1,649 ng/mL, whereas the β-human chorionic gonadotropin (β-hCG) value was normal.

The patient was subsequently brought to our hospital to seek another medical opinion. Craniotomy with tumor resection was performed at our hospital. Histopathological examination revealed YST without other GCT component. The tumor cells were immunoreactive for AFP, glypican-3 and focally for placental alkaline phosphatase, while they were nonreactive for β-hCG and podoplanin (D2-40) (Figure 4). Her neurological function remained unimproved after the operation. We initiated chemotherapy comprising three courses of vinblastin, bleomycin, cisplatin and etoposide, and planned radiation therapy to start at the completion of this induction therapy.

Discussion

Intracranial GCTs constitute not more than 3% of all primary brain tumors in Western countries. However,

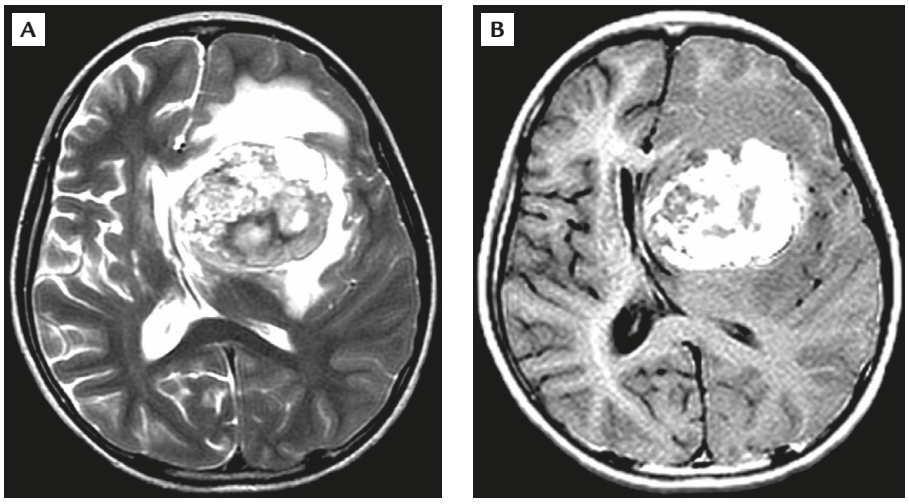

Figure 3. Axial magnetic resonance imaging shows a huge tumor mass with internal hemorrhage and perifocal edema, 5 cm in diameter, in the left basal ganglia with midline shift on: (A) T2-weighted imaging; and (B) T1-weighted imaging.

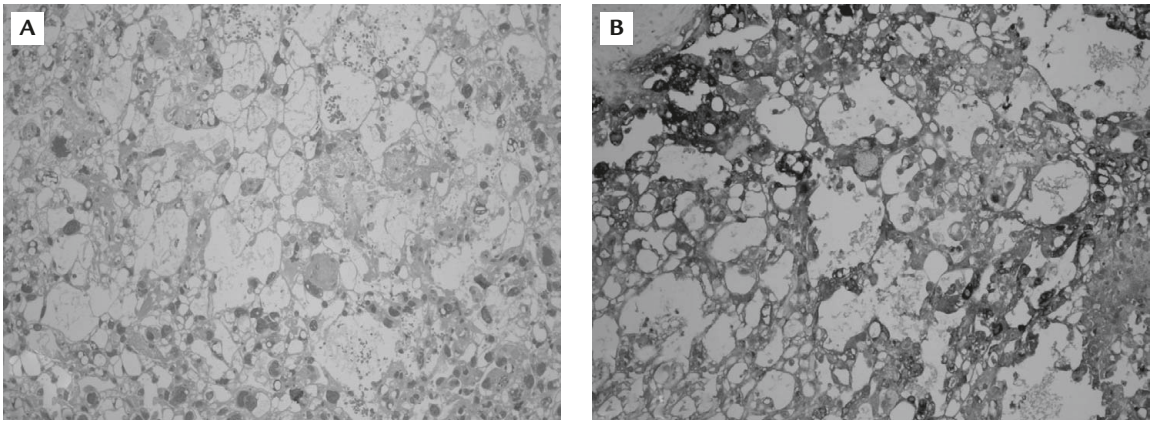

Figure 4. Microscopically, the tumor had a reticular growth pattern with: (A) numerous hyaline globules; and (B) α-fetoprotein immunolabeling.

they are more common in Far Eastern countries and account for 11.2–14.0% of all primary brain tumors in Taiwan, Japan and Korea.[1–3] The incidence of YST is estimated as less than 8% of all primary intracranial GCTs. Intracranial GCTs most commonly occur either in the pineal or suprasellar region or both. The basal ganglia is a relatively uncommon location for intracranial GCTs (3.3–18.1%).[1,4,5] Most of the reported basal ganglia GCTs are germinomas or mixed GCTs. Primary YSTs situated in the basal ganglion are extremely rare. To the best of our knowledge, this is only the third reported case of primary YST confined to the basal ganglia (Table 1).[6,7]

YST was originally described as a GCT of the ovary and testis. The histogenesis of extragonadal YST is thought to be either from primordial germ cells that have migrated aberrantly during embryonic development or from undifferentiated pleuripotent embryonic cells that have been entrapped into the lateral mesoderm due to misfolding and misplacement, and then undergo malignant transformation.[8,9] Additionally, YST is often associated with components of other GCTs due to the same reason that YST is a neoplasm derived from the pleuripotent stem cells that are susceptible to differentiate into other GCTs. Although uncommon, YST can present outside the midline and exhibit a multifocal growth pattern in the brain. Histopathologically, YSTs are composed of primitive-appearing epithelial cells linked to extraembryonic mesoblast and characterized by the presence of embryonic structures resembling the normal fetal yolk sac, Schiller-Duval bodies, periodic acid Schiff-positive intracellular and extracellular hyaline globules, and AFP immunoreactivity.

The presenting symptoms of intracranial GCTs will vary depending on the site of origin. Hemiparesis is the most common symptom in patients with basal ganglia GCTs, and hemiparesis might occur before neuroimaging can detect a lesion in the basal ganglia. The other

Table 1. Summary of 3 cases of primary yolk sac tumor confined to the basal ganglia

Authors	Age (yr)	Sex	Location	Initial symptoms	Serum AFP	Treatment	Outcome
Masuzawa et al[6] (1986)	10	M	Right thalamus + BG	Hemiparesis	N/A	Surgery + radiation	Died of disease
Oshita et al[7] (1993)	8	F	Left BG	Hemiparesis	Elevated	Surgery + radiation + chemotherapy	Alive, handicapped
This case (2010)	7	F	Bilateral BG	Hemiparesis	Elevated	Surgery + radiation + chemotherapy	Alive, handicapped

AFP = α-fetoprotein; BG = basal ganglia; N/A = not available.

clinical presentations include mental deterioration, change of character, sensory disturbance, precocious puberty, slurring speech, dysarthria, and dysphagia. Signs of increased intracranial pressure present during the late stage of the disease if obstructive hydrocephalus occurs. The clinical course usually progresses slowly, with the average period between initial symptom onset (usually hemiparesis) and diagnosis being 1 year and 8 months (range, 1 month to 4 years and 6 months).[10]

The CT findings of basal ganglia GCTs are characterized by an irregularly defined, slightly high-density area without significant mass effect, often with faint calcification and non-homogeneous contrast enhancement. Basal ganglia GCTs often show only mild intensity changes or just a tiny lesion on MRI in the early stage. The tumors enlarge during the period of slow progression of hemiparesis. In the later stage, the tumors occupy the basal ganglia and show a large, irregular, heterogeneous enhancing mass with or without a cystic component. The tumors extend to the regions of the thalamus and deep hemispheres in later stages of the disease. Although MRI is the imaging modality of choice, the findings are rarely specific enough to distinguish the different GCT subtypes or to distinguish GCTs from other tumors. In addition, CT and MRI findings of ipsilateral hemiatrophy of the cerebral hemisphere and brain stem are highly characteristic of GCTs of the basal ganglia and thalamus, as the result of Wallerian degeneration caused by tumor infiltration into the internal capsule with interruption of thalamocortical connections.[11]

Our case had bilateral basal ganglia lesions. Bilateral basal ganglia GCTs are rare; only a few cases have previously been reported, most of them germinomas.[12,13] Diagnosis of bilateral GCTs of the basal ganglia at an early stage is even more difficult than that of unilateral GCTs of the basal ganglia. The bilateral nature of the lesions suggest metabolic or neurodegenerative disease rather than neoplasm, although the involved lesions are not usually completely symmetrical. Clinically, bilateral progressive paresis may occur concomitantly or sequentially. On neuroimaging, the presence of ill-defined, bilateral imaging abnormalities in the absence of a well-defined mass may suggest this kind of case.

A slowly progressive clinical course and nonspecific subtle findings or ill-defined infiltrations without space-occupying lesions shown on CT or MRI in the early stages may lead to a delay in diagnosis. Tumor markers such as AFP and β-hCG are useful tools for noninvasive diagnosis. Also, ^{11}C-methionine positron emission tomography is a technique that is not only for diagnosis but also for precise localization of biopsy if there is no overt mass formation.[14,15]

The outcomes differ among histological subtypes. In general, intracranial YST is known to entail a poor prognosis. The highest survival rates are seen in patients with germinoma or mature teratoma (10-year survival rate > 90% in both groups); the lowest survival rates are seen in patients with choriocarcinoma, followed by embryonal carcinoma, YST, and mixed GCTs composed mainly of choriocarcinoma, embryonal carcinoma, or YST. Patients with pure intracranial YST have a 3-year survival of only 33%, even after multidisciplinary treatment of operation, radiotherapy, and chemotherapy.[16] However, Kirkove et al[17] and Lu and Chen[18] reported long-surviving cases of pineal YST, treated by a combination of surgery, adjuvant chemotherapy, and craniospinal irradiation. They emphasized that chemotherapy as an adjuvant to surgery and/or irradiation significantly extended survival.

In conclusion, the present case consisted of a pure YST in bilateral basal ganglia, which is exceedingly rare. But GCTs are the most common tumors in the basal ganglia of children in Far Eastern countries. Early diagnosis of basal ganglia GCTs requires special attention to subtle neuroimaging findings with ipsilateral cerebral peduncle atrophy, especially in young patients with characteristic symptoms such as slowly progressive hemiparesis, and serial neuroimaging studies should be performed. A progressively enlarging lesion in the basal ganglia of children implies a tumor, especially a GCT. Examination of tumor markers and/or ^{11}C-methionine

positron emission tomography may be helpful for early diagnosis.

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