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Case Report

Can mixed pure hepatocellular carcinoma and germinoma arise together in the brain?

Lu-Jen Chen [a,b,c], I-Chun Lai [a,e], Tai-Tong Wong [d,e], Shih-Chieh Lin [e,f], Donald Ming-Tak Ho [e,f], Kai-Ping Chang [g], Wan-Yuo Guo [e,h], Sang-Hue Yen [a,i], Ming-Teh Chen [e,j], Yi-Wei Chen [a,e,*]

[a] *Division of Radiation Oncology, Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[b] *Department of Medical Research and Education, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[c] *Department of Nuclear Medicine, China Medical University Hospital, Taichung, Taiwan, ROC*
[d] *Division of Pediatric Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[e] *Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, ROC*
[f] *Department of Pathology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[g] *Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[h] *Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[i] *Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taipei, Taiwan, ROC*
[j] *Department of Neurosurgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

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Abstract

Intracranial germ-cell tumors (GCTs) represent 10–15% of all pediatric brain tumors in East Asia. There is a wide histopathological spectrum of intracranial GCTs. Germinomas and nongerminomatous GCTs are the two major classifications. It is difficult to distinguish different subtypes of intracranial GCTs based solely on imaging studies, however, some tumor markers, such as α-fetoprotein or β-human chorionic gonadotropin, are helpful for diagnosis. In this study we present the case of a 13-year-old girl with an intracranial mixed GCT containing a hepatocellular carcinoma and germinoma without a primary liver tumor. Based on this unique pathological diagnosis, a series of treatments were applied, including surgery for gross tumor removal, adjuvant radiotherapy, and chemotherapy. Long-term follow up indicates fair disease control.
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Keywords: germ-cell tumor; germinoma; hepatocellular carcinoma; pediatric brain tumor; radiotherapy

1. Introduction

Intracranial germ-cell tumors (GCTs) represent approximately 2–4% of pediatric central nervous system neoplasms in North America and Europe, and there has been a fivefold increase of incidences in East Asian countries such as Taiwan and Japan.[1,2] GCTs have been categorized into two groups, namely, germinomas (60–70% of intracranial GCTs) and nongerminomatous GCTs (NGGCTs), based on histologic characteristics and the degrees of differentiation.[1] Clinical presentation of intracranial GCTs is often based on the location and size of the tumor. There are three sites in which intracranial GCTs commonly arise: the pineal, suprasellar, and basal ganglia regions.[1] In addition, intracranial GCTs can be classified as having good, moderate, or poor prognosis, according to Matsutani et al.[3] Pure germinomas have the best

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* Corresponding author. Dr. Yi-Wei Chen, Cancer Center, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: chenyw@vghtpe.gov.tw (Y.-W. Chen).

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prognosis because they are highly sensitive to radiotherapy (R/T). NGGCTs, however, are reported to have a poorer prognosis than germinoma, even after standard treatment involving combined chemotherapy (C/T) and R/T. Herein, we describe a very rare case of a mixed GCT, composed of hepatocellular carcinoma (HCC) and germinoma, which has never been reported before.

2. Case Report

2.1. History and examination

A 13-year-old girl presented with congenital hypothyroidism but was euthyroid due to regular thyroxine therapy. Her symptoms began 1 month prior to her admission in May 2006 and included nausea, vomiting, and headaches. A diagnosis of gastroenteritis had been made at another hospital, although her symptoms persisted despite the respective treatment. During that same period, she experienced a total weight loss of 4.5 kg, and a 7000-mL increase in daily urine production was also noted in the following days. On the day before her admission, the patient lost consciousness several times; each episode lasted for 1 hour. She was brought to our emergency department in June 2006. Following admission, magnetic resonance imaging (MRI) of her brain revealed an extensive mixed-solid and cystic tumor extending from the left basal ganglia to the bilateral anterior horns of the lateral ventricles, measuring approximately 65 mm in maximum diameter (Fig. 1). There was no evidence of seeding in other sites in the brain or spinal column. The patient's serum levels of α-fetoprotein (AFP) were markedly elevated to 20,095 ng/mL, whereas her β-human chorionic gonadotropin levels were within a normal range (<10 mIU/mL). Her antihepatitis B antibody was reactive, and hepatitis B virus surface antigen as well as antihepatitis C virus tests were all negative. Her liver biochemical measurements, including liver transaminases, aspartate transaminase and alanine transaminase, and alkaline phosphatase levels were all within normal limits.

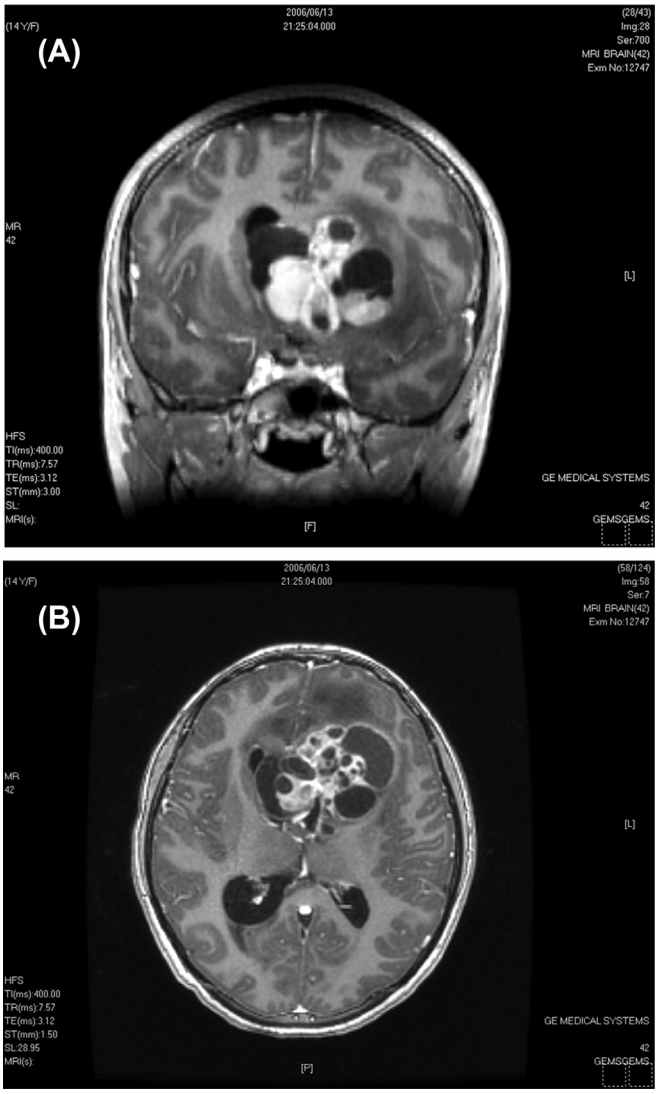

Fig. 1. T1-weighted brain magnetic resonance imaging with contrast in (A) coronal and (B) axial planes: a mixed cystic and solid tumor over the basal ganglia with extension to bilateral lateral ventricles.

2.2. Operation and pathology

Because of obstructive hydrocephalus and increased intracranial pressure, the patient underwent emergency surgery on June 14, 2006. After craniotomy, the tumor was removed piece by piece by a transcortical approach and near total tumor removal was achieved. The pathology seemed to be a mixed GCT, which included germinoma as well as HCC without other components such as squamous epithelium, respiratory epithelium, other teratomatous tissue, embryonal carcinoma, choriocarcinoma, or yolk sac tumors (YSTs). The gross pathology view of the tumor could not be obtained due to the fragmented specimen provided. Microscopically, the germinoma tumor cells had large, centrally located nuclei, prominent large eosinophilic nucleoli, as well as clear cytoplasm (Fig. 2A). Lymphocytic infiltration was noted within the tumor. Placental alkaline phosphatase (PLAP; Fig. 2B) immunoreactivity was seen in the germinoma tumor cells. The other tumor component showed tumor cells arranged in sinusoidal or trabecular patterns. The tumor cells were polygonal, having a distinct cell border with a moderate amount of eosinophilic granular cytoplasm. The nuclei were round to ovoid, with discernible nucleoli (Fig. 2C). The tumor cells were immunoreactive for cytokeratin, hepatocyte-specific antigen (Fig. 2D), and AFP (Fig. 2E), but negative for PLAP. However, an abdominal computed tomography scan and sonography did not reveal any evidence of a primary liver tumor lesion. Most importantly, despite our pathologists' suggestion that it was most likely derived from a teratoma, there was no other teratoma component noted in the pathological examination.

2.3. Post-operative course and follow-up

Adjuvant R/T and C/T were arranged. Adjuvant R/T was planned with curative intent, and a tumor dose of 54 Gy was

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