CASE STUDY

A GIANT GERMINOMA MIMICS HIGH-GRADE GLIOMA: A RARE FORM OF THALAMIC REGION TUMOR

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ABSTRACT

A fourteen-year-old boy initially presented with weakness in the right extremity, worsening in the last three months with stiffness and convulsions in his right extremity. Magnetic resonance imaging of the brain revealed an intra-axial tumor measuring 8.3x7.3x6.8 cm, leading to obstructive hydrocephalus. The patient's condition suddenly worsened with decreased consciousness, and then emergency surgery was performed for tumor resection and external ventricular drainage before switching to a ventriculoperitoneal shunt on the fifth day after surgery. Histopathological examination revealed a germinoma, which is rare in the thalamic region. The patient responded well to radiation therapy after surgery. Ectopic GCT may be difficult to differentiate on radiological examination alone. The current case was initially diagnosed as a high-grade glioma based on radiological findings. A definite diagnosis can be made only after a histopathological examination, which requires a tissue sample. Therefore, many tumors are surgically excised for biopsy purposes A good preoperative examination is very important to determine the approach to patient management. Furthermore, radiotherapy is mandatory for germinoma because of its radiosensitivity.

KEY WORDS: Germ Cell Tumor, tumor resection, radiotherapy, neoplasm, child health

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INTRODUCTION

Intracranial germ cell tumors (GCT) are an uncommon and diverse category of neoplasms that mostly affect children and teenagers [1]. Germ cell tumors (GCTs) account for around 1% of children's primary brain tumors in North America [2]. During the period 2005–2012, the incidence rate of GCTs in Korea was 0.179 per 100,000 children [3]. GCTs account for roughly 3% of malignancies in children aged 0–18, and their frequency rises with the start of puberty. GCTs account for 15% of malignancies identified throughout adolescence [4].

This tumor type is classified by the World Health Organization (WHO) into six histologic subtypes: germinoma, teratoma, embryonal carcinoma, choriocarcinoma, yolk sac tumor, and mixed tumor. Germinomas account for roughly two-thirds of all intracranial GCTs [5]. Germinomas are most commonly seen in the midline, particularly in the pineal and suprasellar areas, surrounding the third ventricle. The basal ganglia and thalamus account for just 5–10% of intracranial germinomas. An ectopic germinoma is another name for an off-midline germinoma [5, 6].

Here, we report a patient with an ectopic giant germinoma in the thalamic region who mimics a high-grade glioma. The patient had a satisfactory response after radiotherapy.

CASE REPORT

A 14-year-old boy came to Dr. Soetomo General Academic Hospital Surabaya with the main complaint of right extremity weakness for one year before admission. Symptoms worsened in the last three months, with stiffness and spasms in his right extremity. There was no history of seizures, decreased level of consciousness, visual disturbances, or headaches. The patient vomited twice in the 3 hours before admission. This study has received informed consent from the patient.

Head magnetic resonance imaging (MRI) radiological examination (Figure 1) showed an 8.3x7.3x6.8 cm intraracial lesion in the left thalamic region with heterogeneous contrast enhancement and perifocal edema. The mass also compresses the left lateral ventricle, third ventricle, and midbrain with a 1.4 cm midline shift to the contralateral side. There are also some necrotic areas within the lesion. These features suggest a high-grade intraracial glioma tumor. Obstructive hydrocephalus is also seen due to the mass effect of the tumor. Surgical resection is planned electively after the completion of preoperative preparations. However, the patient's condition suddenly worsened with a loss of consciousness. Emergency surgery was then performed for tumor resection. Total tumor resection was not achieved due to the location of the tumor. On day

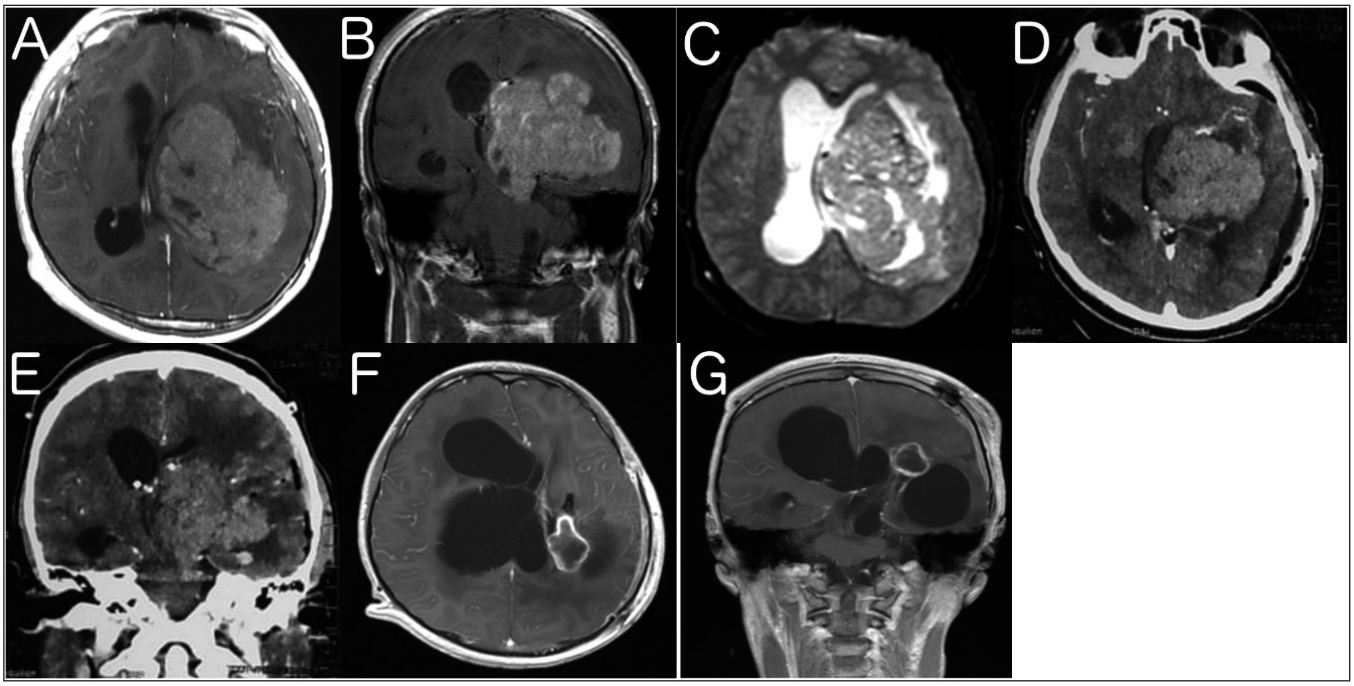

Fig. 1. Radiological examinations; Preoperative MRI in T1-WI sequence of axial, coronal view (A, B) showing a mass in the left thalamic region with a size of 8.3x7.3x6.8 cm with heterogeneous contrast enhancement and necrotic areas; DWI sequence (C) showed restricted diffusion area suggestive of high-grade glioma; Post-operative head CT scan with contrast (D, E) showed partially resected thalamic mass with a size of 5.7x5.5x7.6 cm; Post-radiotherapy MRI (F, G) showed a satisfactory response with significant mass reduction with a size of 3.5x2.2x1.8 cm.

five after surgery, external ventricular drainage (EVD) was also placed for obstructive hydrocephalus before switching to a ventriculoperitoneal shunt.

Histopathological examination revealed the malignant tumor was arranged in lobules separated by delicate fibrous septa containing lymphocytic infiltrate. The tumor cells were large, with rounded vesicular nuclei, prominent nucleoli, and clear cytoplasm (Figure 2). These morphological features are consistent with germinoma. This histopathological examination refuted the previous interpretation of the MRI, which suggested a high-grade intracranial glioma tumor.

After radiotherapy, the patient was brought to our center one month later with an open surgical wound in the right frontal area, around the Kocher area, where the ventriculostomy was performed in the previous operation. There were no other related events during the historical taking. Physical examination revealed an open wound above the shunt with a diameter of 1 cm with no signs of inflammation or infection. Assessment of neurological function showed the same results as the status of pre-radiotherapy therapy. The patient still experienced weakness and stiffness in the right extremity and cognitive impairment. Further diagnosis is carried out to assess the patient's condition.

Cerebrospinal fluid (CSF) was aspirated from the shunt chamber for analysis, showing signs of Central Nervous System (CNS) infection from its cloudy appearance and a significant increase in cell count (1720/μL). The radiological examination also shows an increase in the ventricular wall after contrast administration as a sign of ventriculitis. An MRI examination was shown (Figure 1) to evaluate tumor response after radiotherapy. Tumor size shrank significantly after radiotherapy, from 5.7x5.5x7.6 cm after partial resection to 3.5x2.2x1.8 cm after radiotherapy, indicating a satisfactory response. The patient then underwent shunt removal and EVD placement. CSF culture showed Klebsiella pneumonia and was sensitive to amikacin. Systemic and intrathecal amikacin were given, followed by systemic meropenem. The EVD was removed after the patient showed no signs of shunt dependence. The patient showed improvement in his general condition without further neurologic deficits.

GCTs nearly always develop along the midline axis. It is mostly seen in the pineal and suprasellar regions. Because the GCTs are positioned outside the midline axis in the form of a germinoma in the thalamus, this instance is regarded as unusual. GCTs can develop in other intracranial locations outside the thalamus, such as the cerebral hemispheres, basal ganglia, and cerebellum. Germinomas of the basal ganglia and thalamus constitute about 5–10% of all intracranial germinomas [6, 7]. Recognition of this disease is important to decide on patient management, including the extent of surgical resection.

The clinical symptoms of GCTs are mostly determined by the tumor's location and size. As seen in this patient, cognitive and speech impairment are suggestive signs of thalamic involvement leading to fiber

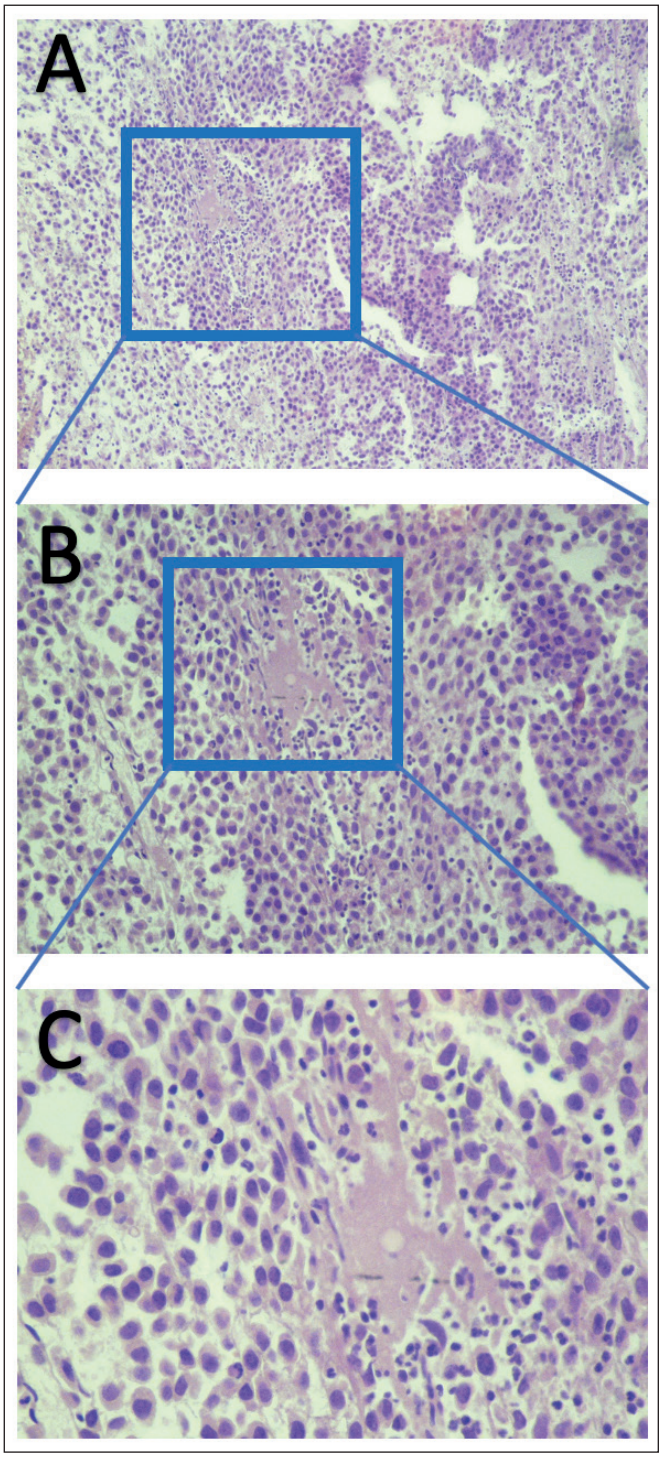

Fig. 2. Histopathology examination with a magnification of 40x (A), 200x (B), and 400x (C) from thalamic germinoma displayed large tumor cells with round vesicular nuclei, prominent nucleoli, and clear cytoplasm.

disturbances. Thalamic germinoma can also produce involuntary movements associated with disorders of the extrapyramidal system, but these are not present in the current case. According to the literature, due to the non-invasive nature of the tumor, symptoms normally develop slowly in most instances (2–24 months). Because the tumor was located in the thalamus, no endocrine problems were detected in these individuals, but GCT in the pineal area can induce endocrine issues such as premature puberty and diabetes insipidus, as well as reduced eye movement [8].

Ectopic GCTs may be challenging to differentiate on radiological examination alone [6]. The current case was initially diagnosed as a high-grade glioma based on radiological findings. Then it shows multiple necrotic areas. From an MRI of the patient's brain, the tumor showed multiple necrotic areas, heterogeneous contrast enhancement, limited diffusion areas on diffusion-weighted imaging (DWI), and increased regional cerebral blood volume (rCBV), suggesting radiological features of high-grade gliomas. Other preoperative tests to determine the type of GCT are serum and/or CSF biomarkers. Germinomas are known to have normal levels of beta-human chorionic gonadotropin (β-HCG) unless trophoblast cells are present and high levels of alkaline phosphatase in serum or CSF [9, 10].

A definite diagnosis can be made only after a histopathological examination, which requires a tissue sample. Therefore, many tumors are excised surgically for biopsy purposes [11]. In this patient, surgical resection was performed because of the preoperative assessment of the high-grade glioma and its large size. Experience from the present case has expanded the differential diagnosis for tumors of the thalamic region in pediatric patients. Minimally invasive procedures are usually preferred where possible, and stereotactic biopsy is an alternative to minimally invasive biopsy in GCT. A correct sampling of the entire tumor is very important, and this cannot be overemphasized; it is important to perform a periscope or intraoperative histological examination to determine the tumor during resection [12].

Based on the histopathological classification, GCT can be divided into all germinoma, non-germinoma, or a combination thereof [13]. Approximately two-thirds of intracranial GCTs are germinoma. In ectopic GCT, especially in the thalamus, the histopathological type is mostly germinoma [14]. Positive placental alkaline phosphatase (PLAP) staining or positive Octamer-binding transcription factor 4 (OCT4) staining can be used to identify germinomas, with the latter being preferable, whereas endodermal sinus tumors test positive for Alpha Fetoprotein (AFP) [15].

Chemotherapy and radiation are effective treatments for GCTs, particularly germinomas. Chemotherapy was included in the treatment of intracranial germinoma in conjunction with radiation when its action against GCT was discovered in other regions and its ability to pass the blood-brain barrier was demonstrated. GCT is reported to be resistant to actinomycin-D, vinblastine, bleomycin, doxorubicin, cisplatin, carboplatin, etoposide, ifosfamide, and cyclophosphamide. These medicines are combined to form chemotherapy regimens, with the most popular combinations being PEB (cisplatin, etoposide, and bleomycin), PVB (cisplatin, vinblastine, and bleomycin), and JEB (carboplatin with etoposide and bleomycin) [16, 17].

CNS germinoma is also one of the most radiosensitive cancers, having good radiation results. It can be administered in conjunction with chemotherapy or as a stand-alone treatment. Recurrence of germinoma after radiation treatments is uncommon in stand-alone radiotherapy. The 5-, 10-, and 15-year overall survival rates of germinoma patients after radiotherapy were found to be 90–97 percent, 85–97 percent, and 80–87 percent, respectively. Meanwhile, chemotherapy alone for germinoma does not have the same effects as radiation alone. Two-thirds (45) of germinoma patients treated with chemotherapy-only PEB regimens relapsed following treatment [18]. They had only 5-year overall survival and progression-free survival of 75% and 36%, respectively, even after carboplatin replacement for cisplatin and the addition of cyclophosphamide to the regimen [19]. Although the combination of radiotherapy and chemotherapy may improve overall survival, stand-alone radiotherapy treatment in these patients is done because of its high radiosensitivity and avoids chemotherapy side effects such as hematological effects, hormone deficiency, or neurocognitive disturbances [16, 20, 21]. In this study, the patient received 27 radiotherapy procedures, with a total dose of 36 Gy of craniospinal radiotherapy and 15 Gy as a tumor boost. The patient responded well to therapy with a smooth course.

CONCLUSIONS

A thalamic germinoma is a rare form of GCT presentation, usually located in the midline, especially in the pineal and suprasellar regions. It is important to recognize all tumors of the thalamic region, including the rare GCTs. A good preoperative examination is very important to determine the approach to patient management. Furthermore, radiotherapy is mandatory for germinoma because of its radiosensitivity.

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Conflict of interest:

The Authors declare no conflict of interest.

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