Case Report

Thalamic germinoma: A case report

Nithisha Thatikonda[1], Anand Pathak[2]

From [1]Medical Officer, Department of Medical Oncology, National Cancer Institute, Jamtha, Maharashtra, India, [2]Director of Medical Oncology, National Cancer Institute, Jamtha, Maharashtra, India

ABSTRACT

Germinomas involving non-midline structures such as thalamus and basal ganglia are relatively uncommon contributing up to 5–10% of all intracranial germ cell tumors. Here, we describe a case of thalamic germinoma in a 16-year-old boy who presented with recurrent episodes of headache and blurry vision for 2 months. Magnetic resonance imaging revealed heterogenous mass in the left thalamus with contrast enhancement causing mass effect and obstructive hydrocephalus. Total excision of the tumor was done by suboccipital craniotomy. Histopathology showed poorly differentiated round cells with vacuolated cytoplasm, round nuclei with prominent nucleoli which were separated by thin fibrovascular stroma infiltrated by lymphocytes. Immunohistochemistry showed diffuse immunoreactivity for placental alkaline phosphatase and octamer-binding transcription factor 3/4, and negative for glial fibrillary acidic protein, cluster of differentiation (CD)-45, and CD-30, confirming it to be a pure germinoma. With a combined approach of surgery, chemotherapy, and radiotherapy, these patients have better long-term survival rates.

Key words: Intracranial germinoma, Octamer-binding transcription factor 3/4, Placental alkaline phosphatase, Thalamus

Germinomas involving non-midline structures such as thalamus and basal ganglia are relatively uncommon contributing up to 5–10% of all intracranial germ cell tumors following more frequent locations such as the pineal gland and suprasellar region [1-3]. Intracranial germinomas occur mainly in the first two decades of life with absolute male predominance (2:1) [1,2]. Germinomas display certain characteristic radiological features which facilitate their differentiation from other tumors, but often remain inconclusive [2,3]. Recognition of this tumor with a tissue biopsy, immunohistochemistry (IHC), and cerebrospinal fluid (CSF) tumor markers is important because the germinomas have better long-term progression-free survival rates with surgical, chemotherapy, and radiotherapy management [4-6].

CASE REPORT

A 16-year-old boy without significant medical history presented with recurrent episodes of headache accompanied by nausea and blurry vision for 2 months and could be relieved using analgesics. No accompanying seizures, fever, vomiting, and hemiparesis were reported. Patient's vitals were stable and neurological examination was unremarkable. Fundoscopy showed Stage 1 bilateral papilledema. Endocrinological investigations such as prolactin, TSH, T3, T4, and cortisol were within the normal range. Magnetic resonance imaging (MRI) has revealed heterogeneous mass involving the left thalamus which was hypointense on T1 and hyperintense on T2 with post-contrast enhancement along with mass effect causing obstructive hydrocephalus (Fig. 1). Gradient echo sequence showed a tiny spot within the tumor indicative of calcification or hemorrhagic focus. A provisional diagnosis of glioma was made along with differentials of germinoma and malignant lymphoma and the patient was taken for surgery. The gross total excision of the tumor was done by suboccipital craniotomy through the supra cerebellar infratentorial approach. The tumor was yellowish, soft, suckable, and moderately vascular.

Histopathology showed poorly differentiated cells arranged in a nested pattern separated by thin fibrovascular stroma infiltrated by lymphocytes. Individual cells were round, intermediate in size with round nuclei and prominent nucleoli (Fig. 2). CSF cytology did not reveal any malignant cells. The tumor markers α-fetoprotein and β-HCG were not elevated both in serum (alpha-fetoprotein [AFP] = 0.66 ng/ml, βhcg <2 mIU/ml) and CSF (AFP <0.2IU/ml, βhcg <1.2 mIU/ml). IHC showed immunoreactivity for placental alkaline phosphatase (PLAP) and octamer-binding transcription factor 3/4 (OCT-3/4) and negative for glial fibrillary acidic protein and cluster of differentiation (CD)-45, and CD-30. He had no headaches in the post-operative period and recovery was uneventful. Patient was discharged on the 7th post-operative day. The patient's informed consent was obtained for writing this report.

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Correspondence to: Dr. Anand Pathak, National Cancer Institute, Jamtha, Maharashtra, India. E-mail: info@ncinagpur.in

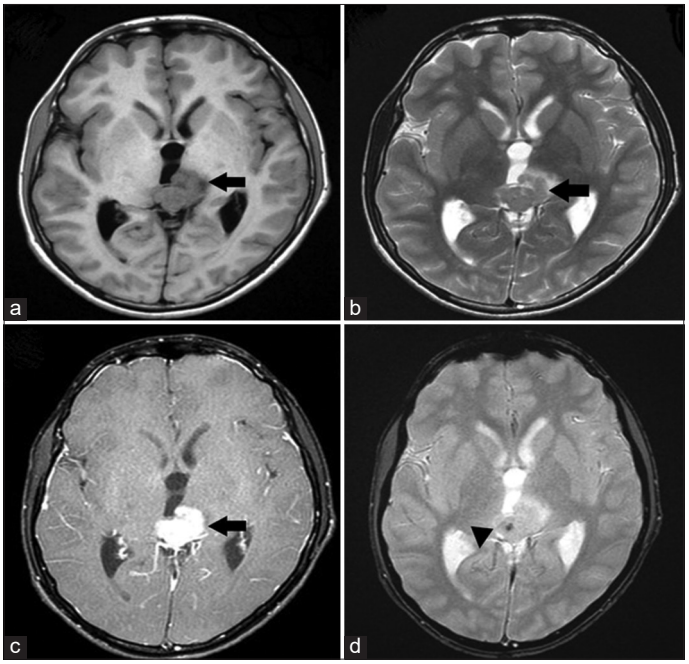

Figure 1: A 16-year-old boy presenting thalamic germinoma. Axial magnetic resonance imaging showed well defined mass in the left thalamus compressing the third ventricle and aqueduct of sylvius. Lesion is hypointense on T1 (a) and hyperintense on T2 (b) with post-contrast enhancement on T1 (c). Gradient echo sequence revealed a hemorrhagic focus/calcification (d)

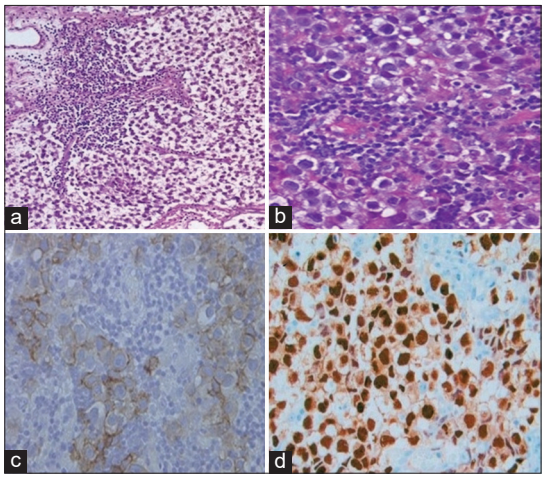

Figure 2: 16-year old boy who presented with thalamic germinoma. (a) Showed poorly differentiated cells arranged in lobules separated by thin fibrous septae infiltrated by lymphocytes, (b) showed round to polygonal cells with vacuolated cytoplasm and round nuclei and were positive for PLAP (c) and OCT3/4 (d)

DISCUSSION

The thalamic germinoma are known to be prevalent in male in the first 20 years of life and age and sex of the present case is in accordance with the reported cases [1-3]. The clinical manifestations include; (1) neurological signs such as progressive weakness of limbs; (2) headaches, nausea, and vomiting caused by mass effect; and (3) endocrine dysfunction [2,4,5], which progress slowly over 2–24 months [1,2]. The tumors involving only basal ganglia and thalamus do not cause endocrine dysfunction such as puberty precocity and diabetes insipidus. These findings are consistent with our case presentation [1,2]. Absent neurological signs in this patient could be possibly due to the short duration of symptoms and early diagnosis. Several theories have been proposed to explain the intracranial origin of GCTs such as Teilum's germ cell theory, embryonic cell theory, and recent theory of neural stem cell origin with overexpression of OCT4 gene. However, none of these hypotheses is widely accepted [2,5].

Although the conventional radio imaging by MRI is not sufficient for diagnosis, few characteristic features of germinomas were reported. On MRI, the germinoma typically presents as a poorly circumscribed heterogeneous mass with multiple intratumoral cysts, calcifications, intratumoral hemorrhage, peritumoral edema, and mass effect causing obstructive hydrocephalus [1-3]. MRI findings of the present case were consistent with the above features except for the intratumoral cysts. Ipsilateral hemiatrophy, frequently reported in various reports, was considered to be caused by Wallerian degeneration of the internal capsule due to tumor invasion. It was thought to be a characteristic of germinomas initially, but is now recognized that any kind of thalamic tumor can have associated hemiatrophy [3,4]. However, this feature is not observed in the present case. The above findings favor but are insufficient for definitive diagnosis and biopsy is always recommended.

Stereotactic biopsies for intracranial germinomas usually are limited, secondary to deeper location, and associated morbidity. Furthermore, the amount of tissue obtained was sometimes insufficient and favors misdiagnosis [1,3]. Recent advances in surgical techniques have allowed total removal of germinomas with safety in contrast to high mortality that was reported before the 1960's. Hence, tumor resection is advised to obtain definitive tissue biopsies [1,5]. Apart from establishing the correct diagnosis, surgery has its role in cytoreduction especially in tumors producing a mass effect [1]. In addition, up to half of the germinomas contain other histological cell types and surgical resection aids in the removal of these cells which are insensitive to radiotherapy [2,3,6].

As previously said, germinomas frequently contain non-germinomatous components that favor poor prognosis [4]. Hence, confirmation of the cell type with IHC is essential [1,2,7]. PLAP is an immunohistochemical marker expressed in the cell membrane and cytoplasm of primordial germ cells and is commonly employed as a routine diagnostic marker for germinoma [7-10]. Recently, a new marker OCT3/4 has been reported to have higher sensitivity than PLAP [7,8,11]. In a study conducted by Gao *et al*., PLAP and OCT3/4 markers were found to be expressed in 80.6% and 100% of the germinomas [7]. However, OCT3/4 is not specific for germinomas and might be expressed in other subtypes such as embryonal carcinomas. CD30 is often used as a marker to distinguish germinoma from embryonal carcinoma [7,11].

At present, the standard treatment strategies of intracranial germinomas are continuously evolving to achieve better long-term effects. Germinomas are considered to be highly radiosensitive tumors and have long-term progression-free survival rates (>85%

over 5 years with radiation alone) [2,4,5]. Recently, the late effects of radiation such as visual field impairments, endocrinopathies, cognitive decline, and learning disabilities were emphasized and the efficacy and safety of combining chemotherapy with radiation therapy at the lower volumes and doses were explored [12]. At present, chemotherapy in conjunction with total ventricular field irradiation plus primary site boost is recommended for localized germinomas as an effective strategy for long-term survival [5,6]. At the time of writing this report patient was receiving his third cycle of bleomycin, etoposide, and cisplatin chemotherapy.

CONCLUSIONS

Germinomas occurring in the non-midline structures such as thalamus are relatively uncommon. The clinical and radiological features of germinomas are highly nonspecific. However, the timely diagnosis with a tissue biopsy, IHC staining, and serum markers is almost always necessary because if properly managed, they have better long-term survival rates.

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