Case Report

Capsuloganglionic Germinoma: A Rare Site for Uncommon Childhood Tumor

Kuntal Kanti Das, Jeena Joseph, Amit Kumar Singh, Pradeep Sharma, Jayesh Sardhara, Kamlesh Singh Bhaisora, Anant Mehrotra, Arun Kumar Srivastava, Sushila Jaiswal[1], Rabi Narayan Sahu, Awadhesh Kumar Jaiswal, Sanjay Behari

Departments of Neurosurgery and [1]Pathology, SGPGIMS, Lucknow, Uttar Pradesh, India

Abstract

Germ cell tumors (GCTs) are rare intracranial tumors with a strong predilection for children. Commonly, these tumors arise either in the suprasellar or the pineal region. The basal ganglia-thalamus complex represents a rare site of nonmidline intracranial GCTs. Such basal ganglionic GCTs have been reported to produce certain interesting clinico-radiological features, the knowledge of which may provide important diagnostic clues preoperatively. We present the case of a 9.5-year-old boy who presented with right hemiparesis and precocious puberty. Imaging revealed a heterogeneously enhancing mass involving the left capsuloganglionic region, sparing the thalamus. There was little perilesional edema and midline shift. Because of the deep location of the mass and a lack of mass effect, a neuronavigation-guided tumor biopsy was performed which unraveled a pure germinoma. The child was referred for adjuvant radiotherapy following an uneventful postoperative course. At the time of writing the report, the child was on radiotherapy and doing well.

Keywords: *Adjuvant therapy, Caudate nucleus, cerebral atrophy, germ cell tumor, precocious puberty, stereotactic biopsy*

Introduction

Germ cell tumors (GCTs) represent a rare subset of intracranial tumors in childhood. These tumors are most commonly located in the midline involving the suprasellar area in girls and the pineal region in boys.[1] Off-midline intracranial GCTs, often known as ectopic GCTs, are very rare and may be located in the basal ganglia, the thalamus, the spinal cord, the corpus callosum, or the fourth ventricle.[2] Germinoma located in the basal ganglia-thalamus complex is an extremely rare occurrence. The incidence of basal ganglionic GCTs (BGGCTs) is estimated to be 10%–18.8%.[1,3] Most of the reported cases so far have emanated from Japan, a fact that points toward a possible geographical locus.[1] These tumors are usually unilateral in location although people have reported bilateral tumors as well.[3-6] While their management and prognosis are apparently similar to those located in the midline, these BGGCTs are known to display unique clinico-radiological characteristics.[3,6-14] In this report, we present the case of a 9.5-year-old boy who presented with a progressive right hemiparesis and precocious puberty. On contrast-enhanced magnetic resonance imaging (MRI) of the brain, the boy showed an inhomogeneously enhancing mass involving the left caudate nucleus and the adjoining lentiform nucleus/internal capsule. A neuronavigation-guided biopsy of the tumor was performed which revealed features consistent with pure germinoma on histopathological examination. The child was referred for adjuvant radiotherapy subsequently. We discuss the unique clinical and radiological aspects of this entity and review the literature to gain further insight into these tumors.

Case Report

A 9.5-year-old boy presented with a progressive right hemiparesis of 4-month duration. It was accompanied by slurring of speech for 3 months. There were no accompanying visual complaints, seizures, headache, or vomiting. On examination, the boy had evidence of precocious puberty in the form of fully grown pubic and axillary hair, and he had started growing a mustache. Neurologically, he had dysarthria, a right-sided upper motor neuron type of facial weakness associated with spastic right hemiparesis (Medical Research Council grade 3/5). There were no other positive findings.

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Address for correspondence:
Dr. Kuntal Kanti Das, Department of Neurosurgery, SGPGI, Lucknow - 226 014, Uttar Pradesh, India.
E-mail: drkuntalkantidas@gmail.com

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On MRI, there was a T1 hypointense and T2 heterogeneously hyperintense left basal ganglionic mass of about 2.5 cm diameter [Figure 1a-c]. It was involving the caudate nucleus and lentiform nucleus along with the intervening anterior limb and genu of the internal capsule. The thalamus was completely preserved. The mass had cystic areas with fluid level within the center as seen on T2 fluid attenuation inversion recovery image more clearly [Figure 1d]. On contrast, the mass showed patchy enhancement with poorly enhancing satellite areas adjoining the main mass [Figure 1e and f]. In addition, there was prominent ipsilateral sylvian fissure and thinning of cortical gyrus compared to the contralateral side suggesting hemicerebral atrophy [Figure 1a and b]. On T2-weighted image, a hyperintense halo was also seen around the main tumor mass [Figure 1c].

Keeping a diagnosis of glioma in mind at this moment, the patient was taken up for neuronavigation-guided biopsy. We decided against an open surgical excision because of the deep and eloquent location as well as the lack of any significant mass effect produced by the mass. The biopsy specimen looked grossly cellular and hemorrhagic. The representativeness of the biopsied area was subsequently confirmed by postoperative computed tomography, which showed a small air pocket that was left deliberately.

The patient recovered uneventfully postoperatively. High power microscopy showed the tumor cells arranged in sheets. The cells were large, epithelioid, and showed placental alkaline phosphatase (PLAP) and Cluster of differentiation (DC) 117 (c-kit) positivity with negative alpha-fetoprotein (AFP) staining on immunohistochemistry. There were areas of mature lymphocyte infiltration in the tumor [Figure 2a-d]. All these features pointed toward a diagnosis of pure germinoma.

The patient was referred to radiation oncology department for further treatment. The patient was doing well after a course of radiotherapy and is currently under follow-up. Patient's informed consent was obtained for writing this report.

Discussion

Germinomas affecting the basal ganglia-thalamus complex represent a rare site of intracranial GCT, a condition in itself being rare. A review of the literature reveals an incidence of 10%–18.8% when all intracranial GCTs are taken together.[1,3] Most often, these tumors are unilateral although rarely these can also be bilateral.[3-6] Most reports on these off-midline GCTs have emanated from Japan, until recently when other parts of the world have also started to report similar cases.[1] A striking point noted by all previous authors remains an almost exclusive male preponderance, the reason for which remains unknown.[1,3-15] Furthermore, the cases reported so far have been affected in the first two decades of their lives.

Because of the location, these GCTs clinically present with progressive hemiparesis and slurring of the speech as we saw in our patient. Abnormal movements have also been

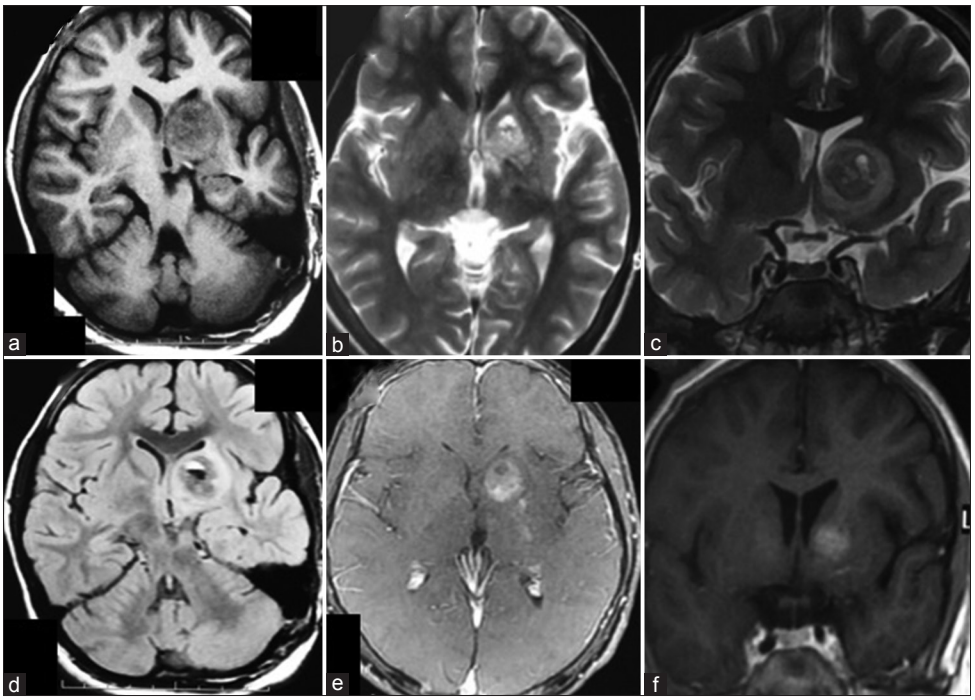

Figure 1: T1-weighted image shows a hypointense (a) mass located in the left caudate-lentiform nucleus (corpus striatum). The mass is heterogeneously hyperintense on T2-weighted image (b). A T2 hyperintense halo can be seen around the tumor (c). The intratumoral cyst with fluid level is appreciated on T2 fluid attenuation inversion recovery image (d). On contrast, the mass showed patchy enhancement with poorly enhancing satellite areas adjoining the main mass (e and f). In addition, there was prominent ipsilateral sylvian fissure and thinning of cortical gyrus compared to the contralateral side suggesting hemicerebral atrophy (a, c and d)

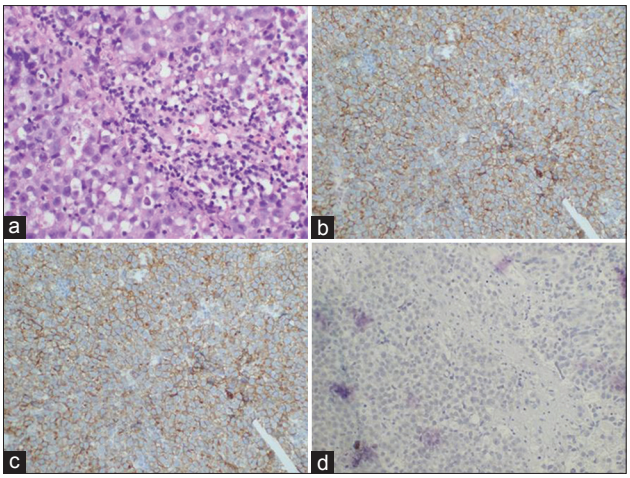

Figure 2: Section shows tumor (H and E, ×400) disposed in sheets of large neoplastic cells with clear to lightly eosinophilic cytoplasm that are intermixed with small mature lymphocytes (a). On immunohistochemistry, tumor cells (×200) are positive for placental alkaline phosphatase (b), c-kit (CD117) (c) and negative for alpha-fetoprotein (d)

reported with these tumors, owing to their proximity to the centers ensuring smooth conductance of movement on the contralateral side of the body.[7,8] Although rare, features of raised intracranial pressure may be present as noted by Wong *et al*.[3] Raised intracranial pressure is secondary to the intratumoral hemorrhages. Certain unusual clinical presentations of these off-midline GCTs are worth mentioning. These include mental retardation, diabetes insipidus, and precocious puberty. These symptoms may occur even without a coexistent suprasellar component which can lead to hormonal disturbances. Our patient had precocious puberty with the presence of pubic and axillary hair with a shallow mustache at the age of 9.5 years. Others have also reported basal ganglionic germinoma presenting with precocious puberty.[4,6] Hypersecretion of beta-HCG (human chorionic gonadotropin) by the tumor has been postulated for these unusual clinical presentations.

Radiologically, these off-midline GCTs do not vary much from their midline counterparts in term of signal characteristics or contrast enhancement. However, certain unique radiological features have been reported.[1,3,4,6-14] These include the presence of intratumoral cyst, calcification, and atrophy of the ipsilateral cerebral hemisphere often with atrophy of the ipsilateral cerebral peduncle. Intratumoral cysts result from recurrent microhemorrhages occurring within these tumors. These cysts impart heterogeneity within the tumor and also prevent their complete disappearance with radiochemotherapy even when they are pure germinomas. Calcifications have been reported inside these tumors, in contradistinction to the midline GCTs. In our patient, intratumoral cyst with fluid level was found although there was no radiological evidence of calcification inside the tumor. These tumors are known to cause demyelination of the adjacent white matter, often resulting in the production of a bright halo surrounding the actual tumor, a feature best seen on T2 image.[12] We noted such peritumoral T2 hyperintense halo in our patient as well [Figure 1c]. Similar tumor-induced neuronal demyelination also occurs at the level of coronal radiata, internal capsule, and cerebral peduncle thus leading to ipsilateral cerebral hemispheric atrophy.[9-12] We also noted ipsilateral hemiatrophy of the cerebral hemisphere. These findings are present in 33% of the patients and may serve as a pointer to the diagnosis preoperatively.[10] Interestingly, such volume loss may occur even after successful therapy as if the tumor leaves its mark even after it is gone!

Some authors have noted atrophy of the basal ganglia itself and consider it as an early sign of germinomas in this location.[9,12] The ganglio-thalamic volume loss is due to the loss of ganglion cells secondary to the tumor destruction.

Histopathologically, GCTs anywhere in the body, including the intracranial ones can be either pure germinomas or nongerminomatous tumors or a combination of both. The nongerminomatous GCTs can have a varied histopathology. Approximately two thirds of the intracranial germ cell tumors is constituted by germinomas. Non-germinomatous tumors comprise the remaining 3rd.[15] Although the BGGCTs can also display a similar pathological diversity, almost all authors have found an almost exclusive prevalence of pure germinomas in this location. Germinomas often have CD 117 (c-kit) and PLAP positive cells with lymphocyte infiltration. These are AFP negative. Beta-HCG positivity may indicate coexistent choriocarcinoma or more commonly presence of normal syncitiotrophoblastic giant cells within germinoma.[15] Often, there may be a combination of germinomas and nongerminomas. Such histopathological diversity inside the tumor, if unrecognized, is often the cause of treatment failure.

Germ cell tumors respond in an excellent fashion to radiation and chemotherapy. This is especially true for pure germinomas. However, the diagnosis is known only after a histopathological examination, which necessitates some form of surgical intervention. Hence, many of these tumors end up receiving cytoreductive surgery in some form or the other. Apart from establishing the diagnosis, surgery has its role in cytoreduction especially in large tumors producing mass effect. Minimally invasive biopsy is always preferable if it can be performed. While the same can be done using an endoscope in intraventricular GCTs, a stereotactic biopsy offers a minimally invasive alternative in these off-midline GCTs. Although it was quite effective in our case, there are certain caveats to it. For example, stereotactic biopsy may fail to sample the tumor in entirety leading to missing out of components that do not respond to chemoradiotherapy. Furthermore, intratumoral cysts may interfere with procuring enough representative tissue for histopathological sampling. Proper sampling of the entire tumor is very important and this cannot be overemphasized.

Adjuvant radiation with or without chemotherapy is a very important component in the treatment of intracranial germinomas. The 5-year survival is >80% with adjuvant focused or whole brain radiation.[3] While there is hardly any doubt regarding the effectiveness of radiation therapy (RT), concerns have been raised regarding its deleterious effects, especially in the developing young brain. As spinal seedling is rare with ectopic germinomas, prophylactic spinal irradiation does not provide any additional benefit.[2]

Chemotherapy has also been tried in intracranial germinomas.[3,7,13,16] Similar to the extracranial germinomas, bleomycin, etoposide, cisplatin, vinblastine regimen is popular among those who use it. Chemotherapy has been used mostly with RT either to lessen the dose of RT or to delay it or sometimes as a sole adjuvant therapy. The results of chemotherapy have been promising, but disease tends to recur after stopping chemotherapy.[3,7]

The prognosis of GCTs primarily depends on the histopathology. Pure germinomas are associated with excellent prognosis with >80% 5-year survival.[16] The presence of malignant components such as endodermal sinus tumor, immature teratoma, or choriocarcinoma often portends a poor prognosis. The presence of teratomatous component imparts radioresistance to these tumors.

Conclusion

Although rare, germinomas may affect the basal ganglia-internal capsule complex in children. The presence of hemiparesis with precocious puberty must clinically point to such a possibility, more so if radiology shows an inhomogeneously enhancing mass in the capsuloganglionic region. Radiological findings such as peritumoral halo and ipsilateral cerebral atrophy are characteristic of tumors in this location. When there is no mass effect, stereotactic biopsy offers a safe and effective means of establishing the histopathological diagnosis and instituting adjuvant therapy.

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Conflicts of interest

There are no conflicts of interest.

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