Mature Teratoma with Somatic-Type Malignancy: An Entity of Unacquaintance—A Case Report

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Abstract

Primary intracranial teratomas are nongerminomatous germ cell tumors. They are infrequent lesions along the craniospinal axis, with their malignant transformation extremely uncommon. A 50-year-old-male patient presented with one episode of generalized tonic–clonic seizure (GTCS), without any neurological deficit. Radiological imaging revealed a large lesion in the pineal region. He underwent gross total excision of the lesion. Histopathological examination was representative of teratoma with adenocarcinomatous malignant transformation. He underwent adjuvant radiation therapy and had an excellent clinical outcome. The present case highlights the rarity of malignant transformation of the primary intracranial mature teratoma.

Keywords

► germ cell tumors
► teratoma
► malignant transformation
► adenocarcinoma
► cranial

Introduction

Central nervous system (CNS) teratomas, a group of nongerminomatous germ cell tumors (GCTs), are rare neoplasms containing tissues derived from all three germ cell layers. These account for 0.3 to 0.6% of all intracranial tumors,¹ with a slightly higher incidence in the pediatric age group and male predominance.²,³ They can be found at any location along the craniospinal axis, usually in the midline,⁴ and have a varied presentation depending on their location. They can further be categorized into three subtypes, including mature teratoma, immature teratoma, and teratoma with malignant transformation (TMT).⁵ Their prognosis is good, with 5-year survival rates ranging from 87 to 100% for mature teratomas and 33 to 71% for malignant teratomas.⁶ A teratoma with somatic-type malignancy is an exceptionally rarely encountered lesion with only six cases reported so far (►Table 1).

Case Report

A 50-year-old male patient presented with one episode of generalized tonic–clonic convulsion (GTCC) and drowsiness. He had a history of holocranial headaches for 4 months. There were no other neurological symptoms. His neurological examination revealed no abnormality. Computed tomography (CT) scan of the brain revealed a large lesion in the pineal region. The lesion extended underneath the falx toward the right side. Magnetic resonance imaging (MRI)


<table>
<thead>
<tr>
<th>Sl. no.</th>
<th>Study</th>
<th>Age &amp; sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Radiological features</th>
<th>Approach</th>
<th>HPE</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Freilich et al.¹¹</td>
<td>Case 1 26/M</td>
<td>Persistent Headache, nausea, vomiting</td>
<td>Pineal region</td>
<td>Solid nodular tumor on CT with hydrocephalus</td>
<td>Not mentioned; subtotal resection + postoperative radiation</td>
<td>Yolk sac tumor with mucin secreting adenocarcinomatous transformation of teratoma</td>
<td>Recurrence after 6 mo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case 2 8/M</td>
<td>Persistent headache, nausea, vomiting</td>
<td>Pineal region</td>
<td>Cystic lesion initially; solid cystic lesion after 4 y</td>
<td>VP shunt followed by radiation; subtotal resection + postoperative radiation</td>
<td>Yolk sac tumor initially; enteric-type adenocarcinomatous transformation of teratoma</td>
<td>Recurrence after 6 mo</td>
</tr>
<tr>
<td>2</td>
<td>Matsutani et al.¹⁷</td>
<td>Cases 3–6 31 ± 14.8/M</td>
<td>Symptoms of raised intracranial pressure</td>
<td>Pineal region (1) Neurohypophysis (1) Other regions (2)</td>
<td>Solid-cystic lesion</td>
<td>Infratentorial approach (1) Pterional approach (3) Subtotal resection</td>
<td>Epidermal carcinoma (3) Sarcoma (1)</td>
<td>Intermediate prognosis</td>
</tr>
<tr>
<td>3</td>
<td>Current study</td>
<td>50/M</td>
<td>Headache, GTCS</td>
<td>Pineal region</td>
<td>Solid cystic lesion</td>
<td>Left parieto-occipital approach; gross total excision + postoperative radiation</td>
<td>Adenocarcinomatous transformation of mature teratoma</td>
<td>Good prognosis</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; GTCS, generalized tonic-clonic seizure; VP, ventriculoperitoneal.

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Mature Teratoma with Somatic-Type Malignancy

Diyora et al.

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(revealed a similarly well-defined multilobulated ex-ternal tumor in the region of the quadrigeminal plate, along with the pineal gland not separately visible.)
Extragonadal GCTs have no evidence of a primary tumors in the testis or ovary. Extragonadal GCTs can arise anywhere in the midline, including the retroperitoneum, anterior mediastinum, or along the craniospinal axis in the midline. CNS GCTs are grouped into three subgroups: germinomatous, nongerminomatous (yolk sac tumor, teratoma, embryonic carcinoma, endodermal sinus tumors, choriocarcinoma), and mixed GCTs. They comprise only 0.3 to 0.6% of all intracranial tumors. The most commonly proposed mechanisms for these tumors are KIT, KRAS/NRAS, and CBAL mutation. These tumors show male predominance with an overall male-to-female ratio being 3:1 with approximately over 90% incidence in a young population. Their pathophysiology is not clearly understood; however, there are two proposed theories: germ cell theory and embryonic theory. The germ cell theory hypothesizes that GCTs arise from primordial germ cells, which have migrated aberrantly during embryogenesis and later undergo malignant transformation. According to the embryonic theory, these tumors show from mixed migrational pluripotent germ cells. Another school of thought proposes that germinomas arise from germ cells. In contrast, other nongerminomatous GCTs, including teratomas, occur due to misfolding or misplacement of embryonic cells into the lateral mesoderm causing their entrapment in various parts of the CNS. The movement of the primordial germ cell migration, which coincides with the fetal hypothalamus maturation, is influenced by a few trophic molecules like growth factor β. It is believed that the hypothalamus may produce chemotropic factors like growth factor-β, which can cause mis-migration. Teratomas are a subtype of nongerminomatous GCTs, which by definition are tumors of multipotential cells derived from all three germ cell layers. They are hypothesized to arise from the misplacement of pluripotent germ cells. Teratomas with somatic-type malignancy is a generic designation of a teratomatous neoplasm with an additional malignant somatic tissue. The malignant component is usually a rhabdomyosarcoma or an undifferentiated sarcoma and, less commonly, a squamous cell carcinoma or an enteric-

Fig. 1 Computed tomography (CT) scan of the brain showing large heterogeneous midline mass containing irregular areas of high attenuation (calcification), low attenuation (fat), and intermediate attenuation (soft tissue). (A,B) It causes moderate asymmetric dilatation of the right lateral ventricle with a shift of the midline structures to the right. Magnetic resonance imaging (MRI) of the brain showing large well-defined, multilobulated extra-axial solid cystic lesion in the region of quadrigeminal cistern with the pineal gland not separately visible from the lesion. The solid component of the lesion appeared isointense on T1-weighted images in (C) axial view and (D) sagittal view, heterogeneously hyperintense on T2-weighted images in (E) axial view and (F) coronal view, with multiple foci of calcification. (G) The lesion was heterogeneously enhancing on postcontrast administration. The peripheral cystic component appeared iso-hypointense on T1-weighted images and heterogeneously hyperintense on T2-weighted images. (H) Diffusion tensor imaging (DTI) revealed displacement of bilateral corticospinal tracts, left superior longitudinal fasciculus, left inferior longitudinal fasciculus, and splenium.

Discussion

Extragonadal GCTs have no evidence of a primary tumors in the testis or ovary. Extragonadal GCTs can arise anywhere in the midline, including the retroperitoneum, anterior mediastinum, or along the craniospinal axis in the midline. CNS GCTs are grouped into three subgroups: germinomatous, nongerminomatous (yolk sac tumor, teratoma, embryonic carcinoma, endodermal sinus tumors, choriocarcinoma), and mixed GCTs. They comprise only 0.3 to 0.6% of all intracranial tumors. The most commonly proposed mechanisms for these tumors are KIT, KRAS/NRAS, and CBAL mutation. These tumors show male predominance with an overall male-to-female ratio being 3:1 with approximately over 90% incidence in a young population. Their pathophysiology is not clearly understood; however, there are two proposed theories: germ cell theory and embryonic theory. The germ cell theory hypothesizes that GCTs arise from primordial germ cells, which have migrated aberrantly during embryogenesis and later undergo malignant transformation. According to the embryonic theory, these tumors show from mixed migrational pluripotent germ cells. Another school of thought proposes that germinomas arise from germ cells. In contrast, other nongerminomatous GCTs, including teratomas, occur due to misfolding or misplacement of embryonic cells into the lateral mesoderm causing their entrapment in various parts of the CNS. The movement of the primordial germ cell migration, which coincides with the fetal hypothalamus maturation, is influenced by a few trophic molecules like growth factor β. It is believed that the hypothalamus may produce chemotropic factors like growth factor-β, which can cause mis-migration. Teratomas are a subtype of nongerminomatous GCTs, which by definition are tumors of multipotential cells derived from all three germ cell layers. They are hypothesized to arise from the misplacement of pluripotent germ cells. Teratomas with somatic-type malignancy is a generic designation of a teratomatous neoplasm with an additional malignant somatic tissue. The malignant component is usually a rhabdomyosarcoma or an undifferentiated sarcoma and, less commonly, a squamous cell carcinoma or an enteric-
type adenocarcinoma. Yolk sac tumor elements have also been considered progenitors of enteric-type adenocarcinoma from intracranial GCTs. Immunohistochemical examination plays a pivotal role in the diagnosis of TMT. Stains like vimentin, desmin, SMA, S-100, CD99, and GFAP antibodies are usually performed in the cases with sarcomatous transformation, whereas CK20, CK7, and p53 are performed in patients with carcinomatous transformation. Glypican-3 is used to rule out any yolk sac element.

Intracranial teratoma usually arises from midline structures, including the pineal region, quadrigeminal plate, wall of the third ventricle, suprasellar area, or cerebellar vermis. The pineal is the most common region where they are found. However, other less common locations from which intracranial GCT can arise include the cerebral hemispheres, ventricles, thalamus, basal ganglia, and medulla oblongata. There are a gamut of presenting features of these tumors, which are usually based on their location. They can present with only distressing localized or holocranial headaches or accompanied nausea and vomiting. They can cause visual disturbances like blurred vision, diplopia, or vertical gaze palsy. Not uncommonly, they can also present with GTCS or focal seizures. The ones in the suprasellar region can lead to dysfunction of the hypothalamus and pituitary gland, leading to features of diabetes insipidus, precocious puberty, developmental retardation, sexual precocity, isolated growth hormone deficiency hypopituitarism, and visual field defects like bitemporal hemianopia.

A clinical diagnosis is often based on imaging, tumor marker detection, and CSF cytology. A CT and a contrast MRI with spectroscopy are required to reach a diagnosis and for operative planning. In patients later diagnosed with TMT, it is prudent to rule out primaries elsewhere in the body by getting a PET CT. Intracranial teratomas can be large at the time of their presentation. Due to extreme variability in their content, imaging findings are also heterogeneous. Most of these lesions contain fat and calcification that is usually solid/clumplike. On MRI, they typically reveal lesions of mixed signal intensity due to their various components. On T1-weighted images, the lesion shows hyperintense, isointense, and hypointense signals due to fat/proteinaceous/lipid-rich fluid, soft tissue, and calcification/blood product, respectively. On T2-weighted images, the lesion shows mixed signals. Soft-tissue component usually enhances on intravenous gadolinium administration.

Detection of B-HCG and AFP in CSF and serum aids in detecting the tumor type and its further management. If possible, tumor markers should be detected in both CSF and serum, as it has been shown that the amount of β-hCG is substantially higher in the CSF, whereas that of AFP is slightly higher in the serum. A malignant teratoma would not present with a high concentration of AFP and β-hCG, which indirectly helps rule out other GCTs. CSF cytology should be routinely performed to rule out tumor dissemination into CSF. Patients with positive cytology have a poor prognosis.

Management is aimed at radical resection. They are chemo-resistant, and recurrence is common. Complete microsurgical resection of residual or recurrent tumors provides the best chance of prolonging survival. The location of the tumor decides the approach to the tumors. Excision is considered complete if more than 90% tumor is resected. An attempt should be made to excise as much tumor as possible because the tumor left with a malignant component leads to recurrence in the long term. In comparison to GCTs, NGGCTs are less radiosensitive. So chemotherapy and radiation therapy, with or without surgery, is usually required. In patients with teratoma with somatic-type malignancy, a search for the primary should be done. If no primary is found, the tumor bed should be irradiated to prevent a recurrence. When the tumors produce B-HCG or AFP markers, they can monitor treatment and early detection of recurrence.

The prognosis in a case of teratoma depends on its subtype. Mature teratomas containing well-differentiated elements of all three germ cell layers are associated with a good prognosis, with 10-year survival rates of more than 90%. In contrast, immature teratomas, with their undifferentiated components and the possibility of developing malignant tumors, have a less favorable prognosis with a 5-year survival rate of around 70%. Teratoma with somatic-type malignancy containing various components of conventional malignant tumors have a poor prognosis. Five-year survival rates are better for patients with mature teratoma.
than patients with teratoma with somatic-type malignancy. In patients with malignant transformation, a search for primary should be done. If no primary is found, the tumor bed should be irradiated to prevent a recurrence. They have an aggressive clinical course than mature or immature teratoma.

**Conclusion**

CNS teratoma is an uncommon tumor, and adenocarcinomatous transformation has made the tumor extremely rare as only six cases have been reported so far to the best of our
knowledge. Owing to the rarity of these lesions, their treatment strategy remains controversial. Patient age, biochemical markers, and histological diagnosis aid in their management. Radical resection, followed by adjuvant radiation, forms the cornerstone of its management.

Informed Consent
Patient’s informed consent was obtained for this study.

Conflict of Interest
None declared.

References