Case Report

rare tumors

Rare Tumors
Volume 13: 1–4

DOI: 10.1177/20363613211026501
journals.sagepub.com/home/rtu
SAGE

A rare giant mixed germ cell tumor of the pineal region with immature elements: Case report and review of the literature

Camille K Milton[1], Panayiotis E Pelargos[1], Nathaniel D Stetson[2], Manuel Maldonado-Vital[3], Kar-Ming A Fung[3] and Ian F Dunn[1]

Abstract

The diagnosis and management of mixed intracranial germ cell tumors may be complicated by the diversity present within this tumor category. Mixed germ cell tumors demonstrate variable natural histories which may be altered by the inclusion of even the most minute immature histological components. We report the case of an 18-year-old male who presented with a 3-month history of progressive headache and nausea leading to lethargy. Imaging revealed a giant pineal region mass extending superiorly from the roof of the fourth ventricle into the lateral ventricle, with resultant obstructive hydrocephalus. No spinal lesions were noted. Following gross total resection, the patient experienced marked improvement. Pathologic analysis identified an uncommon tumor composition: mature teratoma (96%), immature teratoma (2%), and germinoma (2%). Guided by the immature component, chemotherapy and radiation were added post-operatively to provide this patient with the greatest chance of long-term survival. Intracranial pathology, including germ cell tumors, should be included in the differential for any young patient presenting with new and progressive headache and nausea. This case emphasizes the benefit of a multimodal approach to mixed germ cell tumors of the pineal region and the importance of careful pathologic review of all submitted material.

Keywords

Pineal, mixed germ cell tumor, histology, germinoma, immature teratoma

Date received: 28 February 2021; accepted: 1 June 2021

Introduction

Primary intracranial germ cell tumors (GCTs) are rare tumors that show preference for pineal and suprasellar regions.[1] Primary intracranial GCTs constitute 33%–63% of all intracranial GCTs and 50%–75% of all pineal region tumors.[2] These tumors may be classified into germinomas and non-germinomatous GCTs (teratomas, choriocarcinomas, endodermal-sinus tumors, embryonal carcinoma, and mixed-GCTs).[1] The identification of management guidelines for mixed-GCTs is complicated by the fact that this category comprises distinct tumor-types with varied natural histories. We present the case of a young man with a giant mixed-GCT of an uncommon histological makeup: mature teratoma (96%), immature teratoma (2%), and germinoma

[1]Department of Neurosurgery, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[2]INTEGRIS Spine and Neurological Surgery, Oklahoma City, OK, USA
[3]Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

Corresponding author:
Ian F Dunn, Department of Neurosurgery, University of Oklahoma Health Sciences Center, 1000 N Lincoln Boulevard, Suite 4000, Oklahoma City, Oklahoma 73104, USA.
Email: ian-dunn@ouhsc.edu

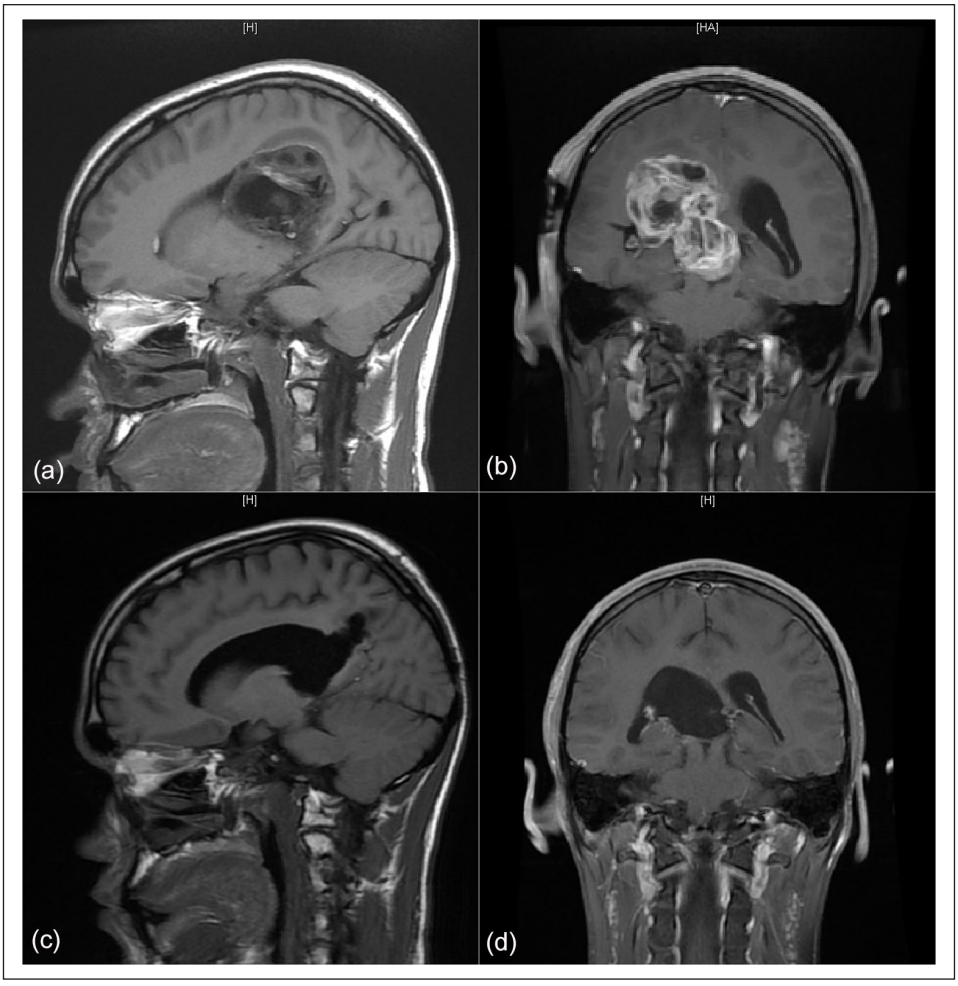

Figure 1. Preoperative sagittal (a) and coronal (b) T1 with contrast MRI demonstrating giant germ cell tumor of the pineal region. Postoperative sagittal (c) and coronal (d) T1 with contrast MRI following gross-total tumor resection.

(2%). His presentation, surgical treatment, and follow-up is described, and placed in context with current literature.

Case report

History

An 18-year-old male with a history of right-sided strabismus presented to an outside hospital with a 3-month history of headache and nausea. He returned home with antibiotic treatment for suspected sinusitis. The patient developed increasing fatigue, anorexia, hearing loss, and dizziness progressing to lethargy. Head-CT revealed a large pineal lesion with an obstructed right ventricle and hydrocephalus. He was stabilized with placement of an external ventricular drain (EVD) and transferred to our institution.

Examination

Bilateral horizontal nystagmus, left pronator drift, mild upgaze palsy, and three beats of clonus in bilateral lower extremities were observed. MRI showed a heterogeneously enhancing mass with areas of necrosis and cystic change and a maximum dimension of 6.9 cm. The lesion extended superiorly from the roof of the fourth ventricle into the right lateral ventricle, involving the pineal region (Figure 1). A mild leftward midline shift of 0.8 mm was observed. MRI-spine was normal. Serum HCG was within normal limits ($<$2.0 mIU/mL). Serum AFP was at the upper limit of normal (6.7 ng/mL). CSF HCG was mildly elevated at 4 IU/L and CSF AFP was markedly elevated at 23 ng/mL.

Operation and post-operative course

We performed a right parieto-occipital craniotomy with a trans-sulcal trans-ventricular approach. This approach was favored over occipital transtentorial or infratentorial supracerebellar approaches due to the lateral extension of the superior tumor component. Gross-total resection of the giant multiseptated mass was achieved. A second EVD was placed in the operating room and both drains were quickly weaned.

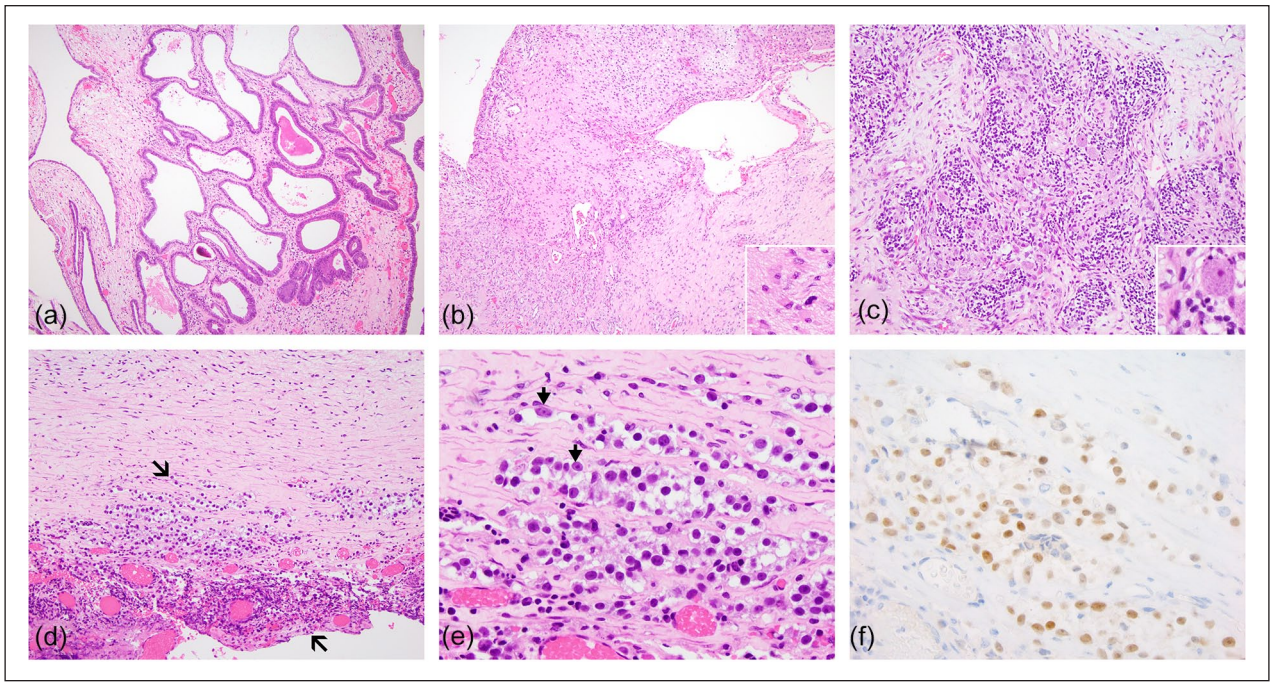

Figure 2. The histopathologic features of the resected mass were that of a tan-gray, semisolid, semicystic glial neoplasm exhibiting mitoses, and vascular proliferation. Mature teratoma with features of the gastrointestinal tract (a) makes up the bulk of the tumor with a minor glial component (b). There are small foci with features of ganglioneuroblastoma (c) which would classify this tumor as an immature teratoma. In a separate focus, there is an area with seminomatous component ((d) area between arrows). Prominent nucleoli are present ((e) small arrows) and these cells are positive for OCT 3/4 on immunohistochemistry (f) (original magnification: a to d are 20×; e and f, and all insets are 60×).

The patient tolerated the operation well. A temporary exaggeration of upgaze palsy with convergence nystagmus was noted. Post-operative MRI confirmed a complete resection (Figure 1).

Pathology

Pathology of the resected mass revealed a mixed-GCT with components of mature teratoma (96%), immature teratoma (2%), and germinoma (2%) (Figure 2).

Adjuvant treatment

Six of the six total cycles of induction chemotherapy (ifosfamide, etoposide, and mesna) were completed with omission of ifosfamide due to neurotoxicity during the final cycle. Chemotherapy was otherwise tolerated well throughout its course and was completed 5 months postoperatively. Proton craniospinal irradiation (p-CSI) was initiated 7 months postoperatively and was completed 9 months postoperatively. A total dose of 36 Gy in 20 fractions with 18 Gy in a 10 fraction boost to the pineal region was administered. The patient tolerated the p-CSI well, complaining only of mild nausea and decreased appetite. At latest follow-up, 14 months postoperatively, no evidence of new or progressive disease was found and all pre-operative symptoms had resolved.

Discussion

Mixed-GCTs represent approximately 10% of all CNS GCTs.[3] Diagnosis of primary intracranial mixed-GCTs is challenging. Due to their heterogeneous makeup, biopsies of inadequate size may lead to incomplete identification of tumor components.[4] Furthermore, neuroimaging characteristics and tumor marker profiles for all intracranial GCTs may be nonspecific.[5]

Mixed intracranial GCTs may be classified into two risk groups: an intermediate-prognosis group for mixed-GCTs composed of germinoma ± immature or mature teratoma and a poor-prognosis group for mixed-GCTs containing a component of embryonal carcinoma, yolk-sac tumor, or choriocarcinoma.[6,7] Pure germinomas may effectively be treated with chemotherapy and radiation alone. Excepting teratomas, which may be cured with surgery alone, non-germinomatous GCTs, including mixed-GCTs, frequently require a combined approach of surgical resection, chemotherapy, and radiation.[8–10]

Germinomatous and teratomatous elements are known to co-occur in mixed germ cell tumors. Matsutani et al.[6] retrospective series of 153 intracranial GCTs identified germinoma and teratoma elements in 21 of 49 mixed GCTs. The relative proportion of these elements was not reported. Furthermore, 27 of 36 mixed teratomas in the series contained immature elements.[6] However, neither

incidence nor treatment outcomes for mature teratomas with components of both germinoma and immature teratoma were described. Epidemiological studies of GCTs that followed Matsutani et al.[6] have evaluated mixed-GCTS as a single entity, omitting the individual histologic elements of these tumors.[3,5] Therefore, the incidence and natural history of mixed GCTs containing a predominant teratomatous component with smaller contributions of germinoma and immature teratoma is unknown.

An isolated report has described a third ventricular mixed-GCT containing a small component of immature teratoma with predominant mature elements.[11] The remaining histopathologic contributors to this tumor included germinoma, embryonal carcinoma, and choriocarcinoma.[11] The patient in this case presented with headache, nausea, and vomiting. Magnetic resonance imaging identified obstructive hydrocephalus and leptomeningeal dissemination of the tumor. Following subtotal resection the patient was treated with adjuvant chemotherapy and radiation.[11] Our case is distinguished from this previous report in several ways: tumor location, overall histopathological makeup of tumor, and the degree of resection. Nonetheless, both cases emphasize the fact that even minute components of immature teratoma in a mixed GCT must be taken into consideration during treatment planning.

Our case represents a novel example of a mixed-GCT of the pineal region containing predominant mature and minute immature teratoma components. The postoperative course illustrates the benefit of a multimodal approach to mixed GCTs of the pineal region. Gross total resection may not only lead to marked symptomatic resolution, but also enhances the ability of adjuvant radiation and chemotherapy to facilitate greater long-term survival.[12]

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Camille K Milton https://orcid.org/0000-0001-7883-5612

References

1. Kyritsis AP. Management of primary intracranial germ cell tumors. *J Neurooncol* 2010; 96: 143–149.
2. Hirato J and Nakazato Y. Pathology of pineal region tumors. *J Neurooncol* 2001; 54: 239–249.
3. Gittleman H, Cioffi G, Vecchione-Koval T, et al. Descriptive epidemiology of germ cell tumors of the central nervous system diagnosed in the United States from 2006 to 2015. *J Neurooncol* 2019; 143: 251–260.
4. Vasiljevic A, Szathmari A, Champier J, et al. Histopathology of pineal germ cell tumors. *Neurochirurgie* 2015; 61: 130–137.
5. Gao Y, Jiang J and Liu Q. Clinicopathological and immunohistochemical features of primary central nervous system germ cell tumors: a 24-years experience. *Int J Clin Exp Pathol* 2014; 7: 6965–6972.
6. Matsutani M, Sano K, Takakura K, et al. Primary intracranial germ cell tumors: a clinical analysis of 153 histologically verified cases. *J Neurosurg* 1997; 86: 446–455.
7. Sawamura Y. Current diagnosis and treatment of central nervous system germ cell tumours. *Curr Opin Neurol* 1996; 9: 419–423.
8. Fetcko K and Dey M. Primary central nervous system germ cell tumors: a review and update. *Med Res Arch* 2018; 6: 1719.
9. Murray MJ, Bartels U, Nishikawa R, et al. Consensus on the management of intracranial germ-cell tumours. *Lancet Oncol* 2015; 16: e470–e477.
10. Bruce JN and Stein BM. Surgical management of pineal region tumors. *Acta Neurochir (Wien)* 1995; 134: 130–135.
11. Demir MK, Yapicier O, Karakaya OF, et al. A primary third ventricle mixed germ cell tumor with leptomeningeal dissemination of immature teratoma component. *Childs Nerv Syst* 2019; 36: 629–633.
12. Ogawa K, Toita T, Nakamura K, et al. Treatment and prognosis of patients with intracranial nongerminomatous malignant germ cell tumors: a multiinstitutional retrospective analysis of 41 patients. *Cancer* 2003; 98: 369–376.