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CASE REPORT

Pure germinoma occurring 11 years after total pineal mature teratoma removal: a case report and review of the literature

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Abstract

Intracranial mature teratomas have good prognoses and are usually treated by total tumor resection. We report a rare case of a germinoma that occurred 11 years after total removal of a pineal mature teratoma. A 5-year-old boy presented with headache and nausea and was diagnosed with a pineal tumor and obstructive hydrocephalus on MRI. He underwent total removal of the lesion, which was pathologically diagnosed as a mature teratoma without any other germ cell tumor components. MR images after 11 years showed a newly developed pineal tumor, which was confirmed as a germinoma after neuroendoscopic biopsy. Chemoradiotherapy resulted in complete remission, without any symptoms. This case demonstrated possible late occurrence of germinoma even after total removal of a mature teratoma had been achieved. A long-term follow-up of 10 years or more should be planned for these patients.

Keywords Mature teratoma · Pure germinoma · Primordial germ cell · Germ cell tumor

Introduction

Mature teratomas are rare, accounting for 0.4–0.56% of primary brain tumors [2, 5]. They are classified as non-germinomatous germ cell tumors (NGGCTs), which include choriocarcinomas, yolk sac tumors, embryonal tumors, teratomas, and mixed germ cell tumors. The standard treatment for intracranial mature teratoma is surgery. The prognosis is good, even without adjuvant therapy, with a 5-year survival rate of 88–100% [7, 9, 11].

Here, we describe a patient with germinoma in the pineal region, 11 years after complete mature teratoma removal. We discuss the possible pathogenesis and management issues of this rare condition.

Case presentation

A 5-year-old boy with no relevant past medical history visited a local hospital complaining of headache and nausea. Magnetic resonance imaging (MRI) revealed a pineal region mass with obstructive hydrocephalus (Fig. 1). He was referred to our hospital. Serum levels of alpha fetoprotein (AFP) and beta subunit of human chorionic gonadotropin (β-HCG) were within normal ranges. He underwent endoscopic third ventriculostomy and subsequent tumor biopsy, which was histologically diagnosed as a mature teratoma. Two weeks later, he underwent gross total removal of the pineal tumor via an occipital tentorial approach, which was confirmed by postoperative MRI. The surgical specimen was a mature teratoma containing an intestine-like structure, bone, and adipose tissue, with no germinoma or any other germ cell tumor component (Fig. 1). The postoperative course was uneventful, and he was discharged without any further treatment regimen and with a follow-up plan including serial MRIs every other year (Fig. 2).

At 16, 11 years after the removal of the mature teratoma, a follow-up MRI showed a newly developed tumor in the pineal region, with contrast enhancement and marked peritumoral edema (Fig. 3), not observed in the previous MRI taken 2 years ago. Although he did not complain of any symptoms, he underwent tumor biopsy using neuroendoscopy. The third ventricle floor stoma was well patent, and a biopsy from a gray-reddish tumor pathologically revealed a two-cell pattern consisting of sheets of large cells and infiltrating small lymphocytes, suggestive of pure germinoma (Fig. 3c).

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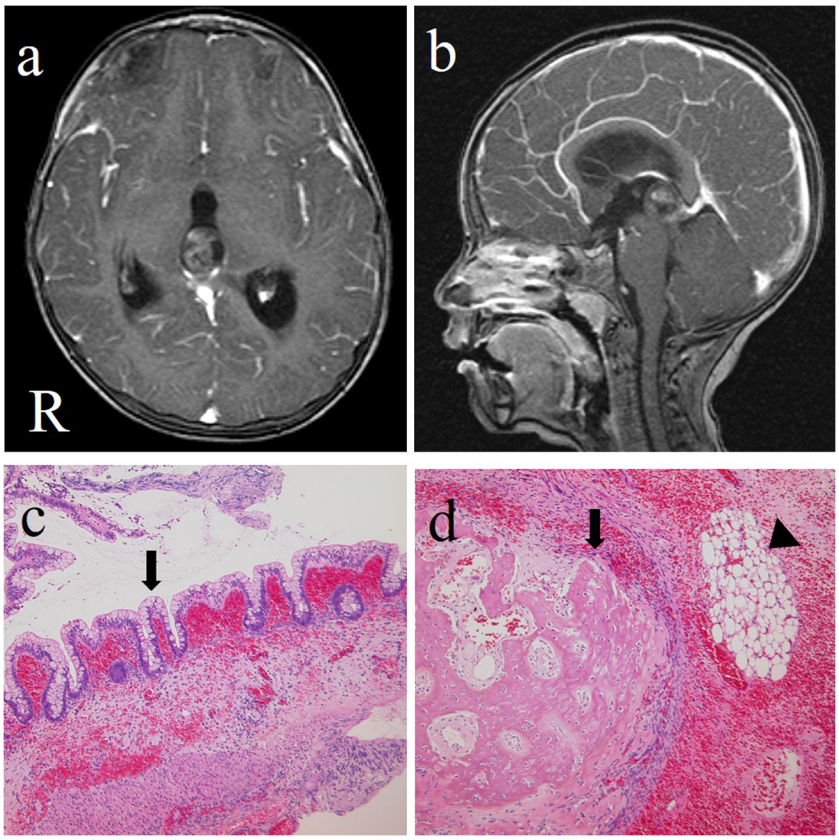

Fig. 1 An initial T1-weighted image with contrast showing a pineal tumor and obstructive hydrocephalus. The pineal tumor was heterogeneously enhanced (**a** axial, **b** sagittal). After total resection, the surgical specimen photomicrograph showed mature teratoma with an intestine-like structure (**c** arrow), bone (**d** arrow), and adipose tissue (**d** arrowhead) (hematoxylin and eosin stain: original magnification, × 100)

Immunohistochemical staining was positive for c-kit and placental alkaline phosphatase and negative for AFP and β-HCG.

After three courses of chemotherapy (carboplatin 450 mg/m^2: day 1 and etoposide 75 mg/m^2: days 1–3) followed by radiation therapy (whole ventricle proton radiation 30.6 GyE/17 Fr), the tumor achieved complete remission, with a low T2-weighted image intensity area remaining. He has no clinical symptoms or recurrence after 12 months of follow-up.

Discussion

Mature teratomas are rare germ cell tumors, commonly occurring in the pineal gland, followed by the suprasellar and parasellar regions. These tumors usually have clear margins, heterogeneous components, various degrees of enhancement, and a five-year overall survival rate of 88–100% [7, 9, 11]. It is well known that the current treatment protocol for mature teratoma is that if total removal is achieved, adjuvant therapy is unnecessary, since mature teratomas are resistant to

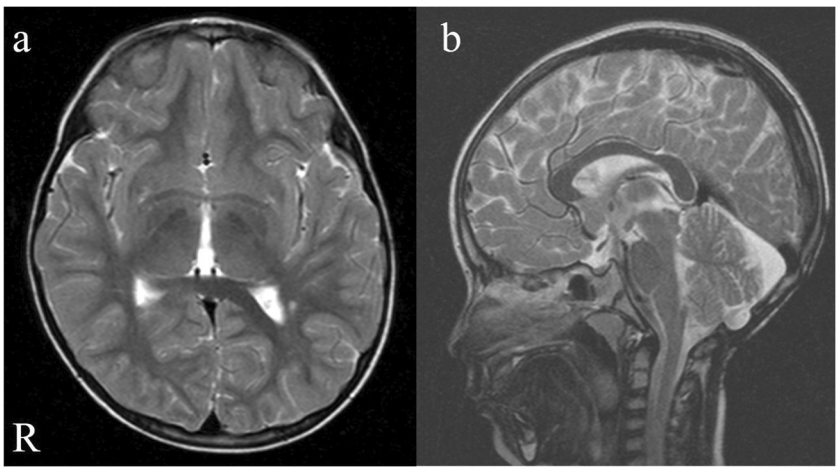

Fig. 2 Postoperative T2-weighted images (**a** axial, **b** sagittal) showing no tumor residue or recurrence

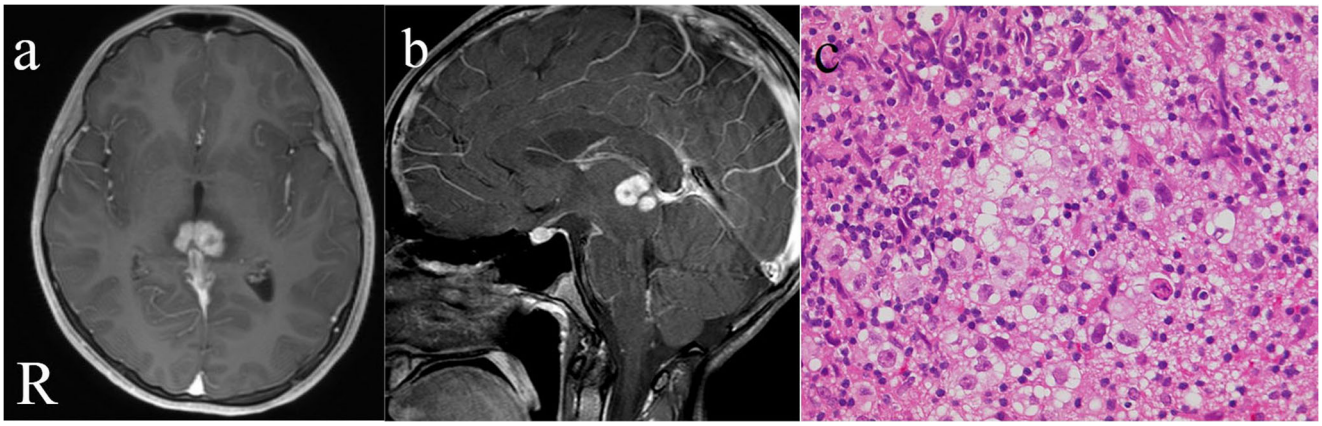

Fig. 3 T1-weighted MRI with contrast (**a** axial, **b** sagittal) 11 years after the removal of the initial teratoma, showing a pineal tumor with marked surrounding edema. The surgical specimen photomicrograph showed a two-cell pattern that consisted of sheets of large cells and infiltrating small lymphocytes (**c**), indicating a germinoma

chemotherapy and radiation [9]. A systemic analysis of 134 patients with mature teratoma showed that gross total removal is related to high disease-free survival and patients who received adjuvant therapy had a significantly longer overall survivals compared to those undergoing surgery alone [6]. Lee et al. reported a survival rate of 88% at 74 months in 31 patients with intracranial teratoma treated with chemoradiotherapy [7].

Although uncommon, mature teratomas can recur, probably due to local recurrence of residual malignant components or metachronous germ cell tumors. Germ cell tumors that contain different tissues are not uncommon [10]. Even if surgical specimens are pathologically diagnosed as "pure" mature teratoma, minor malignant components might exist, which might increase in size later. Sawamura et al. found that cisplatin-based chemotherapy was effective for mature teratoma with suspicious immature components [11]. The development of germ cell tumors could also be de novo [3]. Primary intracranial germ cell tumors are believed to originate from primordial germ cells located along the midline, which can metachronously develop germ cell tumors in the central nervous system. Hormonal stimulation at puberty may affect these dormant residual tumor cells or primordial germ cells [4, 8]. More recently, the study of genome-wide profiles in intracranial germ cell tumors [1] has reported that pure germinomas, unlike other germ cell tumors, present with low DNA methylation. The new molecular-based approach might help unveil the origin of the tumor in future studies.

In our case, the first tumor in the pineal region was a mature teratoma and was completely resected. All specimens were re-examined, and immunohistochemical analyses were also performed, but no components to hint to a germinoma or other NGGCTs were found. The tumor recurred, although there was no evidence of any growth on serial MRIs for 11 years. A few studies have reported the late development of different histological germ cell tumors after total mature teratoma removal (Table 1). Utsuki et al. reported mature teratoma recurrences as yolk sac tumors 7 years after total resection [12]. Another study reported a disseminate germinoma that occurred 21 years after the removal of a disseminated pineal immature teratoma [8]. To the best of our knowledge, this is the first case of late germinoma development after complete resection of a mature pineal teratoma. All three patients in Table 1 did not receive adjuvant therapy and were followed up by serial MR images.

Some questions remain regarding this case. (1) Is the recurrence mechanism residual or metachronous? Although careful reexamination ruled out the presence of any germinoma component in the original tumor, a small microscopic focus of germinoma cells might have been missed. This raises the question as to whether germinoma could remain silent for such a long time without chemotherapy or radiation. Germinoma has a good 10-year survival rate of 92.7% [9], and regrowth of residual tumor usually occurs soon after the initial treatment. (2) Should all mature teratomas be treated with

Table 1 Summary of cases with late germ cell tumor recurrences after pineal teratoma resection

Author, year	Age at initial onset (year), sex	Pathology of initial tumor	Initial treatment	Pathology of second tumor	Interval between initial and second tumor
Utsuki et al. 2007 [12]	9, M	Mature teratoma	Total resection	Yolk sac tumor	7 years
Mano et al. 2016 [8]	3, M	Immature teratoma	Total resection	Germinoma	21 years
Present case	5, M	Mature teratoma	Total resection	Germinoma	11 years

adjuvant therapy to prevent "late recurrence," even after complete resection? Chemotherapy and radiation have a wide range of toxicities, especially in childhood, and the indications for adjuvant therapy should be weighed carefully. Although adjuvant therapy has shown to result in higher mean overall survival rates, survival outcomes were reportedly multifactorial [6]. A large multicenter study is necessary to clarify these issues.

We reported a patient with germinoma that occurred 11 years after total removal of a mature pineal teratoma. Even if total removal of the mature teratoma is achieved, a long-term follow-up of 10 years or more should be planned in these patients. Role of chemotherapy and radiation for completely resected mature teratoma is still controversial.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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