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Review article

Atypical teratoid/rhabdoid tumor of the sellar region in adult women: Is it a sex-related disease?

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ABSTRACT

Atypical teratoid/rhabdoid tumor (AT/RT) is a highly malignant embryonal tumor in children and a rare entity. Although adult AT/RT is extremely rare, some cases of adult-onset AT/RT in the sellar region have been described. Here, we report an adult patient with AT/RT of the sellar region in whom it was difficult to make a definitive diagnosis and the clinical course was aggressive. This is the first report of autopsy findings that could confirm the clinical characteristics of this rare unresolved pathology, and will contribute to the improvement of prognosis. In addition, a literature review was performed to clarify this exceptionally rare condition. Interestingly, all reported adult patients with sellar AT/RT, along with the present case, were female. This raises the possibility of its being a sex-related disease. However, further studies are required to come to a definitive conclusion.

1. Introduction

Atypical teratoid/rhabdoid tumor (AT/RT) is a very aggressive rare intracranial embryonal malignancy of the central nervous system (CNS), which is considered one of the most challenging pathologies for neurosurgeons. The 2016 WHO Classification of Tumors of the CNS defined this tumor as "Grade IV," which requires characteristic molecular defect for accurate diagnosis [1]. This neoplasm is most often seen in infants and young children [2]. In this study, we report an adult woman with AT/RT of the sellar region in whom autopsy findings confirmed the clinical characteristics of this rare unresolved pathology. Based on our review of the literature of all reported adult cases of sellar AT/RT, this study raises the question of whether it a sex-related disease.

2. Case report

2.1. History and examination

A previously healthy 42-year-old Japanese woman presented to a local hospital with slight headache. Magnetic resonance imaging (MRI) showed an intrasellar mass; conservative therapy was recommended and accepted (Fig. 1a). Two months later, the patient suffered severe headache, vertigo, and visual disturbance, which were rapidly aggravated. Physical examination showed superior temporal hemianopia, left oculomotor and abducens nerve palsy, and left facial pain with V1 distribution. MRI revealed rapid enlargement of the intrasellar mass (19 × 20 × 5 mm) that invaded into the left cavernous sinus and compressed the optic chiasma (Fig. 1b–d). The tumor showed reduced and delayed enhancement with gadolinium than the normal pituitary gland on dynamic MRI. Serum hormone values were within normal limits. There was no elevation of serum tumor markers, including carcinoembryonic antigen, carbohydrate antigen 19-9, squamous cell carcinoma antigen, alpha-fetoprotein, cancer antigen 125, or carbohydrate antigen 15-3.

2.2. First operation and histopathological studies

The tumor was considered a nonfunctioning pituitary adenoma and resection was performed via endoscopic transsphenoidal surgery (ETSS). Intraoperatively, the tumor was slightly more fibrous than a typical pituitary adenoma. Histopathological examination indicated medullary proliferation of tumor cells with polygonal nuclei and eosinophilic cytoplasm admixed with apparent residual pituitary glandular cells. Tumor nuclei showed a variety of shapes,

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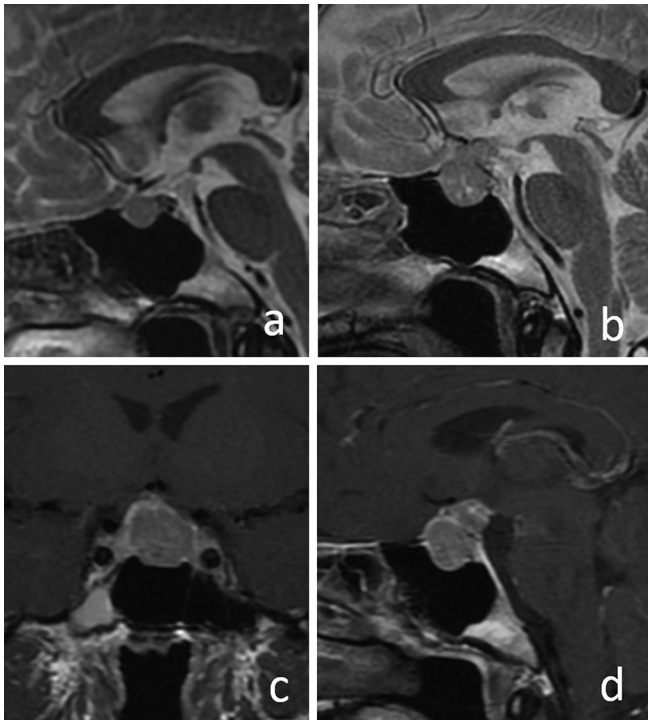

Fig. 1. Magnetic resonance imaging (MRI) of 2 months before admission demonstrating a sellar mass which is considered as presence of pituitary adenoma (a). Preoperative MRI showing a significant rapid enlargement over two months; less enhancing pituitary tumor with gadolinium. The tumor compresses the optic chiasma and invades into left cavernous sinus. Normal gland is shifted to the right side (b–d).

including ovoid, round, spindle, and pleomorphic appearances. Occasionally, a distinct nucleolus was observed. Many mitotic figures were seen in the tumor (Fig. 2a and b). The proliferation labeling index, measured using MIB-1 monoclonal antibody to Ki67, was 30% (Fig. 2c). As many tumor cells were positive for cytokeratin antigen (Fig. 2d), the tumor was considered a pituitary carcinoma.

2.3. Postoperative course

Stereotactic radiosurgery to the periphery was performed twice, consisting of 16 Gy and 14 Gy, respectively, following surgical resection. After resection and radiosurgery, the tumor shrunk and the patient's symptoms gradually improved except left abducens nerve palsy (Fig. 3a and b). Temozolomide maintenance chemotherapy (150 or 200 mg/m^2/day on days 1–5, in 28-day cycles) was administered.

2.4. Follow-up

Six months following the first surgery, the patient was readmitted to our hospital with consciousness disturbance and severe headache. Neuroimaging indicated ventriculomegaly attributed to bleeding from the recurrent tumor, which eroded the surrounding skull base and encased the left internal carotid artery. Serial computed tomography (CT) scans showed continued rapid tumor growth with progressive bone destruction (Fig. 4a–d).

2.5. Second operation and immunohistochemical evaluation

Second tumor resection via ETSS followed by ventriculoperitoneal shunt was performed. Postoperatively, conventional radiotherapy was delivered to the residual mass with a total dose of

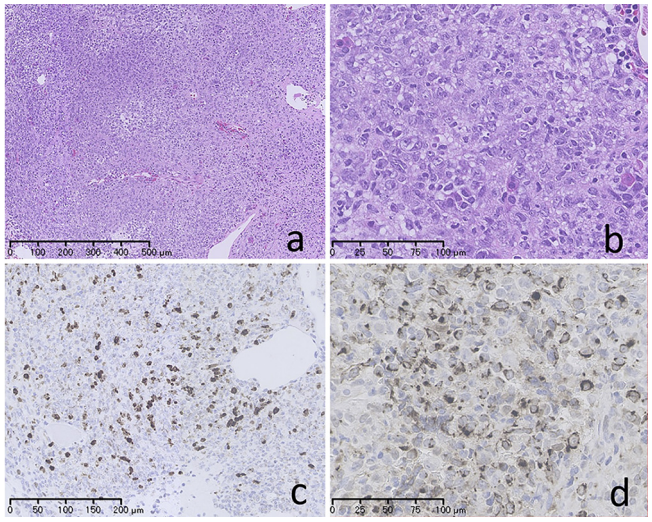

Fig. 2. Histopathological findings demonstrating medullary proliferation of tumor cells with variety shaped nuclei and many mitotic figures. H & E staining (a and b). The proliferation labelling index, measured by MIB-1 monoclonal antibody to the Ki67, was 30% (c) and Cytokeratin AE1/3 was positive (d).

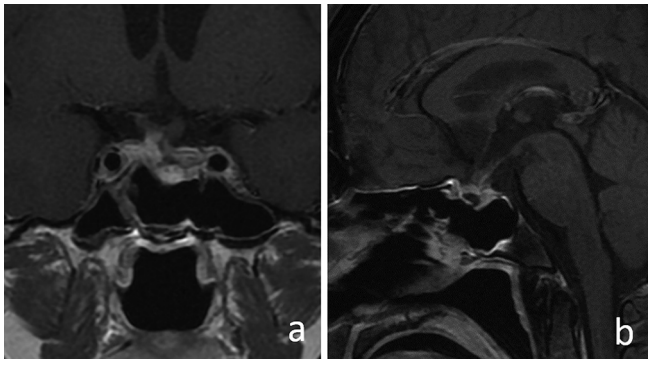

Fig. 3. Postoperative MRI after completing the stereotactic radiosurgery showing sufficient mass resection with adequate tumor control (a and b).

60 Gy and weekly paclitaxel (80 mg/m^2/day on days 1, 8, 15, cycl e = 28 days) was administered. Histological examination of the specimens revealed the same features as observed previously. We realized that some of the tumor cells had rhabdoid features characterized by ample eosinophilic cytoplasm and eccentric nuclei (indicated by arrows in Fig. 5a). Immunohistochemical studies demonstrated the polyphenotypic characters, showing epithelial and mesenchymal differentiation (Fig. 5b–d). INI (SMARCB1) expression was clearly negative in tumor cells, whereas it was positive in endothelial cells (Fig. 6a). On the other hand, BRG1 (SMARCA4) was expressed in both tumor cells and endothelial cells (Fig. 6b). Fluorescence *in situ* hybridization (FISH) analysis using *INI1* probe (RP11-1087B15) and *PDGFB* probe (RP11-434E5), which are probes for 22q, indicated deletion of both sites in tumor cells (Fig. 6c), while it showed non-deletion of both sites in normal pituitary cells. DNA sequencing of tumor tissue showed nonsense mutation c.592T > C (p.Gln198x) in the coding region. On the other hand, no mutation was identified at the same site in normal pituitary cells (Fig. 6d). The tumor was finally classified as atypical teratoid/rhabdoid tumor (AT/RT) (WHO grade IV).

2.6. Follow-up

Systemic pain and severe headache with nuchal rigidity appeared on the 10th week after the second surgery, necessitating

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