Received: 7 April 2021 | Accepted: 14 August 2021

DOI: 10.1111/pin.13159

CASE REPORT

Pathology International WILEY

# A case of an atypical teratoid/rhabdoid tumor with distinctive histology in the pineal region in an adult patient

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**Abstract**

A 31-year-old man suffered from headaches and presented at a hospital after the symptom worsened. Obstructive hydrocephalus and a pineal tumor were identified, and he was transferred to our hospital for further investigation and treatment. Cranial computed tomography revealed a hypodense mass lesion on the right of the pineal region, and calcifications and enlargement of the lateral and third cerebral ventricles were also evident. Blood tests were negative for all tumor markers. Laparoscopic biopsy and third-ventricle fenestration were performed that day as an emergency surgery to treat the obstructive hydrocephalus. Postoperative cranial magnetic resonance imaging revealed a solid tumor that was hypointense on T1-weighted imaging, hyperintense on T2-weighted imaging, and heterogeneously enhanced by Gd. Subsequently, the tumor increased in size, and craniotomy and tumorectomy were performed. Histologically, the tumor proliferated as round or short spindle-shaped cells in a myxoid matrix, forming arrays that surrounded the blood vessels. As a few cells with eosinophilic cytoplasm were also present and immunostaining for INI-1 was negative, the patient was diagnosed with atypical teratoid/rhabdoid tumor (AT/RT). AT/RT of the pineal region in adults is rare, and herein, we report the morphological characteristics of this case and reviewed the relevant literature.

**KEYWORDS**

adult, atypical teratoid/rhabdoid tumor (AT/RT), craniotomy, headache, obstructive hydrocephalus, pineal region

## INTRODUCTION

Atypical teratoid/rhabdoid tumor (AT/RT) is an exceptionally malignant childhood tumor of the central nervous system, and it was first proposed as a disease concept by Rorke et al.[1] in 1996. It appears as rhabdoid cells, exhibits diverse tendencies to differentiate, and is classified as grade IV according to the World Health Organization (WHO) classification. Epidemiologically, it most often occurs in children under 3 years of age,

**Abbreviations:** αSMA, α-smooth muscle actin; AT/RT, teratoid/rhabdoid tumor; CT, computed tomography; DMT, desmoplastic myxoid tumor; EMA, epithelial membrane antigen; GFAP, glial fibrillary acidic protein; INI-1, integrase interactor 1; MRI, magnetic resonance imaging; Olig2, oligodendrocyte transcription factor 2; WHO, World Health Organization.

affecting a slightly higher number of males with a tendency to be more common in Caucasians.[2,3] According to a survey by Lau et al.,[3] adults accounted for 3 out of 174 cases (1.7%), and the pineal gland was extremely small in six cases (3.4%). We treated an adult patient with AT/RT of the pineal region that exhibited distinctive histology. Herein, we report this case together with a review of relevant literature. This was an extremely rare case in which the age at onset, site, and histological presentation were all atypical of AT/RT.

## CLINICAL SUMMARY

A 31-year-old man presented to our hospital with a chief complaint of headache. His medical history was not significant, and he had no relevant medication history. He and his family had no history of malignancy. The patient had suffered from dull, non-pulsatile headaches for 1 month before the admission. His symptom worsened 3 days before admission, and the pain became extreme, limiting his mobility; therefore, he visited a hospital. Cranial computed tomography (CT) scan revealed obstructive hydrocephalus and a pineal tumor; thus, he was transferred to our hospital for further examination and treatment.

On arrival, a cranial CT (Figure 1a) scan revealed a hypodense mass lesion on the right of the pineal region. Calcifications and enlargement of the lateral and third cerebral ventricles were also evident. Blood tests were negative for all tumor markers. Endoscopic biopsy and third-ventricle fenestration were performed that day as an emergency surgery to treat the obstructive hydrocephalus. Postoperative CT (Figure 1b) scan showed that the ventricle had decreased in size, and the patient's headache was also significantly ameliorated. Postoperative cranial magnetic resonance imaging (MRI) revealed a solid tumor that was hypointense on T1-weighted imaging, hyperintense on T2-weighted imaging, and heterogeneously enhanced by Gd (Figure 1c–e). The tumor subsequently increased in size, and craniotomy and tumorectomy were performed. After surgery, treatment with a modified IRS-III protocol was selected. However, cerebrospinal fluid dissemination was observed 4 months after the biopsy, and the patient died in 13 months. Informed consent was obtained from the patient.

## PATHOLOGICAL FINDINGS

In the initial biopsy, areas of small cells that formed arrays that encircled the surrounding blood vessels were observed, but only a small part of the lesion was sampled, and a definitive diagnosis was not reached (Figure 2a). After tumor removal, histological examination revealed the proliferation of relatively small tumor cells against the background of a large amount of myxoid matrix. The tumor cells formed arrays that surrounded the blood vessels via the proliferation of round to short spindle-shaped cells that were loosely bound together (Figure 2b). A few small rhabdoid cells were also present (Figure 2c).

Alcian blue staining revealed a mucus matrix in the background of the tumor (Figure 2d). Immuno histochemical staining was performed with formalin-fixed paraffin-embedded tumor sections. Table 1 summarizes the antibodies used and the staining conditions. Some antibodies were activated by heat treatment at 96°C for 40 min using a water bath. In immunohistochemical staining, although the tumor cells were diffusely positive for vimentin (Figure 3a), they were negative for glial fibrillary acidic protein (GFAP), S-100, CD34, and oligodendrocyte transcription factor 2 (olig2). A few tumor cells were also positive for epithelial membrane antigen (EMA) or α-smooth muscle actin (αSMA) (Figure 3b,c), and approximately 10% for Ki-67. The tumor cells were also negative for integrase interactor 1 (INI-1) staining, which was conducted simultaneously (Figure 3d). From these findings, the patient was diagnosed with AT/RT in the pineal region.

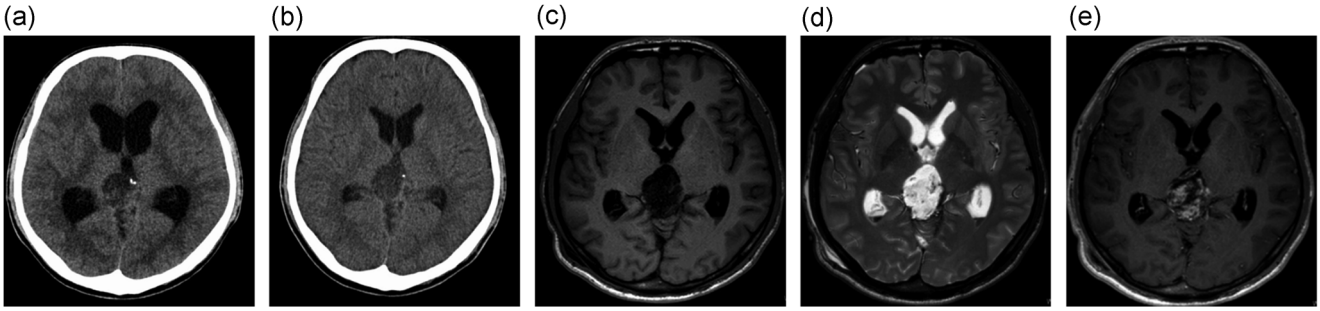


**FIGURE 1** Imaging results. (a) Cranial CT scan on admission. A hypodense mass lesion can be seen in the pineal region. (b) CT scan after the third cerebral ventricle fenestration. The size of the ventricle had decreased. (c–e) Cranial MRI scan. The mass was hypointense on T1-weighted imaging (c). On T2-weighted imaging, it was hyperintense, with punctate hypointensities in its interior (d). It was heterogeneously enhanced by Gd (e). CT, computed tomography; MRI, magnetic resonance imaging

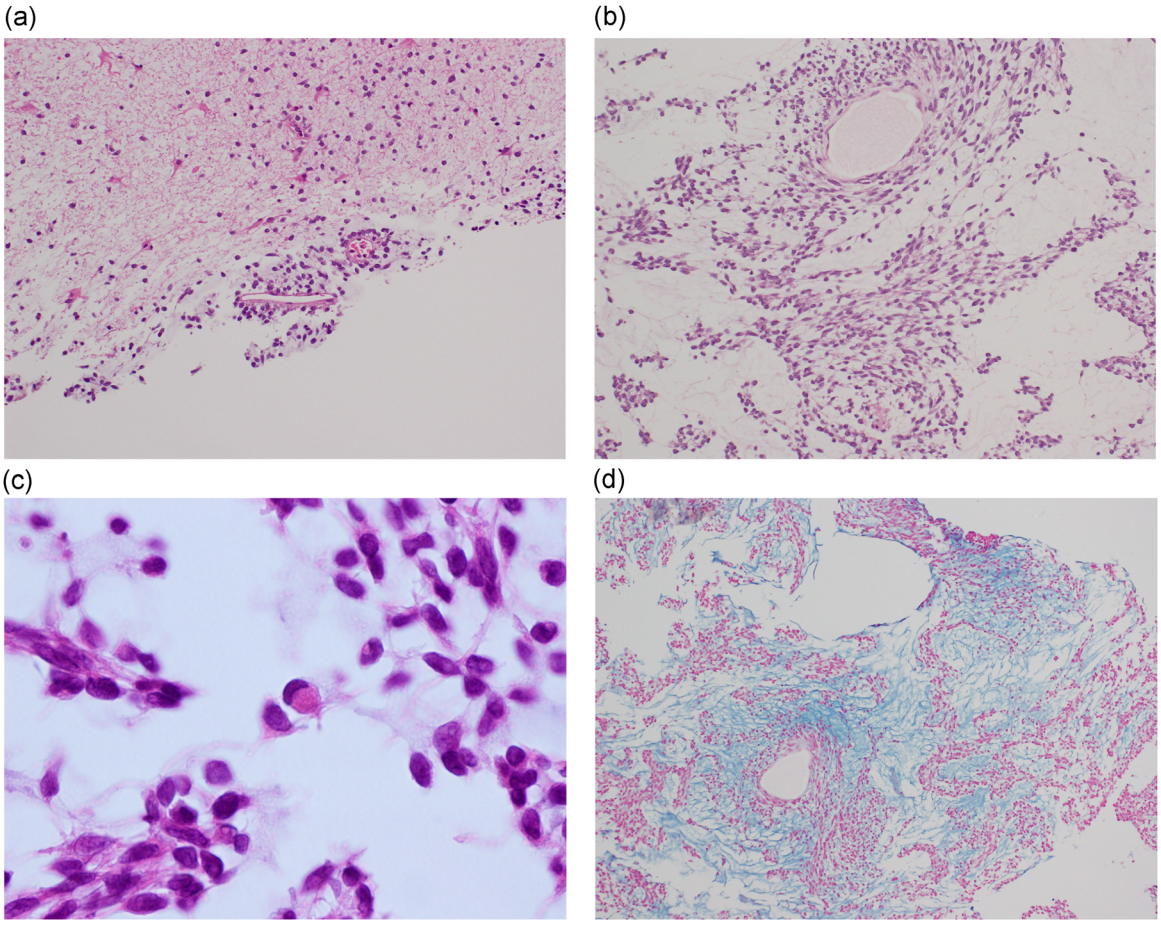


**FIGURE 2** HE staining and special staining. (a) HE of initial biopsy. A few small tumor cells surrounding the blood vessels were evident. (b) Resected specimen. Circular to short spindle-shaped tumor cells proliferated in regions around the blood vessels. The myxoid matrix can also be discerned in the background. (c) A few tumor cells with eosinophilic cytoplasm were also present (arrow). (d) Alcian blue staining. A large amount of mucus matrix can be seen in the background. HE, hematoxylin and eosin

**TABLE 1** Antibodies used for immunohistochemical staining

| Antibody | Clone | Dilution rate | Manufacturer | Location | Activation |
|---|---|---|---|---|---|
| INI-1 | 25/BAF47 | 1:50 | BD Biosciences | San Jose, CA, USA | Citric acid buffer (pH 6) |
| Vimentin | V9 | – | Agilent Dako | Santa Clara, CA, USA | Distilled water |
| EMA | E29 | – | Agilent Dako | Santa Clara, CA, USA | – |
| αSMA | 1A4 | 1:500 | Agilent Dako | Santa Clara, CA, USA | – |
| GFAP | 6F2 | 1:2000 | Agilent Dako | Santa Clara, CA, USA | Distilled water |
| CK (CAM5.2) | CAM5.2 | – | BD Biosciences | San Jose, CA, USA | – |
| NFP | 2F11 | 1:200 | Agilent Dako | Santa Clara, CA, USA | Distilled water |
| Ki-67 | MIB-1 | 1:200 | Agilent Dako | Santa Clara, CA, USA | Citric acid buffer (pH 9) |

Abbreviations: αSMA, α-smooth muscle actin; CK, cytokeratin; EMA, epithelial membrane antigen; GFAP, glial fibrillary acidic protein; INI-1, integrase interactor 1; NFP, neurofilament protein.

## DISCUSSION

A typical teratoid/rhabdoid tumors are rare tumors, accounting for only approximately 1%–2% of childhood brain tumors.[4,5] It is a highly malignant brain tumor that is classified as grade IV according to the WHO classification. In most cases, it appears before the age of 3 years, but it also rarely occurs in adults. It may occur in various supratentorial and infratentorial locations, but most cases are in the posterior cranial fossa; in the

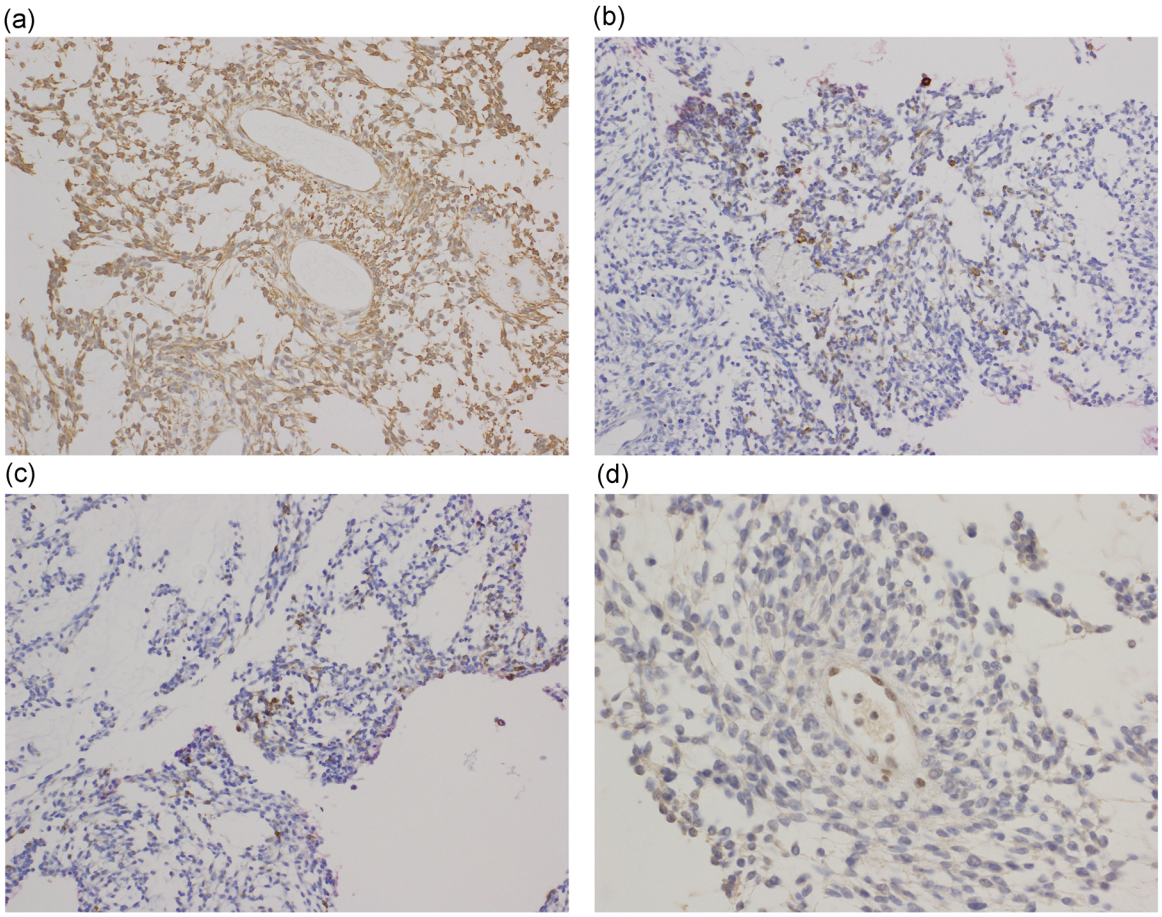


**FIGURE 3** Immunohistochemical staining. (a) Vimentin. Diffuse positive staining was apparent. (b) EMA. Some tumor cells were stained positive (approximately 3%). (c) αSMA. A few positive-stained cells were present (< 1%). (d) INI-1. The tumor cells were negative. αSMA, α-smooth muscle actin; EMA, epithelial membrane antigen; INI-1, integrase interactor 1

supratentorial region, it tends to be found in the cerebral hemispheres. It commonly occurs in the frontal lobe in adults, and its occurrence in the pineal region is exceptionally rare. It has been reported that the frequency of adult-onset AT/RT is approximately 1.7% of AT/RT cases. Furthermore, according to a survey by Mathkour et al.,[6] only 9 of the 85 adult-onset AT/RTs occurred in the pineal gland, establishing its rarity.

Morphologically, it is characterized by predominantly undifferentiated elements, a diverse variety of histological presentations, and the appearance of rhabdoid cells. These cells possess unevenly distributed nuclei and a large amount of eosinophilic cytoplasm; they typically contain eosinophilic inclusion bodies within their cytoplasm. In terms of molecular genetics, they are characterized by the inactivation of the *SMARCB1* (*INI1*) gene and that of the *SMARCA4* (*BRG1*) gene in extremely rare cases. SMARCB1 and SMARCA4 are nuclear proteins that are expressed in cells throughout the body. Immunohistochemical staining revealed the lack of INI1 and BRG1 expression, reflecting the inactivation of these genes. Another characteristic is that a wide range of different cell lineage markers is expressed in varying proportions, with cells staining positive for vimentin, EMA, and αSMA in many cases and sometimes expressing cytokeratin, GFAP, and neurofilament protein.

Atypical teratoid/rhabdoid tumor of the pineal region in adults was first reported in 1999 by Sugita et al.[7] as a pineal malignant rhabdoid tumor; thereafter, only nine cases have been reported to date, making our patient 10th in the list (Table 2).[6–14] Considering the radiographic images, adult pineal AT/RT examined by Kanoto et al.[15] in 2015 was considered to be the same as the case reported by Kuge et al.[11] in 2012; therefore, it was counted as one case. The age of these patients ranged from 19 to 45 years and comprised four men and six women. On immunohistochemical staining, 7/7 patients were positive for vimentin, 10/10 for EMA, and 8/10 for αSMA. Approximately 60% of the patients were positive for GFAP (5/8) and cytokeratin (3/5), and 25% of the patients (1/4) were positive for neurofilament protein. INI-1 expression was not observed in 9/9 cases.

Overall, rhabdoid cells were unclear in our patient, and the main growth pattern consisted of comparatively

**TABLE 2** Reported adult cases of AT/RT in the pineal region

| Year | Author | Age (years) | Sex | INI-1 | Vimentin | EMA | αSMA | GFAP | CK | NFP |
|---|---|---|---|---|---|---|---|---|---|---|
| 1999 | Sugita et al.[7] | 27 | M | N/A | + | + | + | − | − | − |
| 2006 | Ingold et al.[8] | 45 | F | − | + | + | + | N/A | + | N/A |
| 2010 | Takei et al.[9] | 33 | F | − | + | + | − | + | + | + |
| 2011 | Shonka et al.[10] | 33 | F | − | N/A | + | + | N/A | N/A | N/A |
| 2012 | Kuge et al.[11] | 20 | F | − | + | + | + | − | N/A | − |
| 2014 | Yang et al.[12] | 40 | F | − | + | + | − | + | + | N/A |
| 2017 | Liebigt et al.[13] | 19 | M | − | N/A | + | + | + | N/A | N/A |
| 2020 | Monteiro et al.[14] | 41 | F | − | + | + | + | + | N/A | N/A |
| 2020 | Mathkour et al.[6] | 29 | M | − | N/A | + | + | + | N/A | N/A |
| 2021 | Present case | 31 | M | − | + | + | + | − | − | − |

Abbreviations: αSMA, α-smooth muscle actin; AT/RT, atypical teratoid/rhabdoid tumor; CK, cytokeratin; EMA, epithelial membrane antigen; F, female; GFAP, glial fibrillary acidic protein; INI-1, integrase interactor 1; M, male; N/A, not available; NFP, neurofilament protein.

small, short spindle-shaped tumor cells proliferating around the blood vessels against the background of a mucus matrix. From the morphological perspective, we first considered the possibility of pilomyxoid astrocytoma or another form of glioma. However, the neuroepithelial markers of GAFP, olig2, and S-100 were all negative on immunohistochemical staining, and therefore, glioma was excluded. AT/RT was included in the differential diagnosis because vimentin, EMA, and αSMA were all positive to varying extents, and the tumor contained a few small eosinophilic cells. This diagnosis became definitive when screening for INI-1, revealing the lack of INI-1 expression. AT/RT may be considered when rhabdoid cells account for the majority of tumor cells or if the growth pattern consists of classic medulloblasts or PNET-type undifferentiated cells, but the presence of a large amount of mucus matrix in the background and a growth pattern that superficially resembles that of glioma are both atypical of AT/RT, and it was difficult to reach a definitive diagnosis. Recently, Thomas et al.[16] reported desmoplastic myxoid tumor (DMT), SMARCB1-mutant as an INI-1-negative tumor that develops in the pineal gland from adolescence to adulthood. Histologically, the tumor cells are small to medium sized, oval to spindle shaped, and epithelioid like. They are characterized by highly desmoplastic stromal components and mucoid substances. Hence, AT/RT of the pineal region in adults, consisting of small short spindle-shaped cells with abundant mucus matrix as in the present case, must be carefully distinguished from DMT, SMARCB1-mutant. Clinically, DMT, SMARCB1-mutant has a better prognosis than AT/RT, and no metastasis or dissemination has been reported to date.[16–18] However, in this case, cerebrospinal fluid dissemination occurred 4 months after the initial surgery, the disease progressed rapidly, and the patient died in 13 months. Histologically, although there were similarities in the cell images of hematoxylin and eosin staining, the desmoplastic change was unclear and contained a small amount of rhabdoid cells. In addition, in the nine cases of DMT[16–18] reported to date, six out of eight cases were CD34-positive, and in seven of the nine cases, Ki-67 level was 5% or less. However, in the present case, CD34 was negative and Ki-67 was as high as approximately 10%. Hence, these are the clinical pathologies that should be noted in AT/RT occurring in the pineal region in adults, and they are different from those of DMT, SMARCB1-mutant.

As AT/RT occurring in the pineal gland is extremely rare, even in pediatric cases,[3] there are only a few case reports.[19,20] According to a report of Meyers et al.,[21] out of 17 cases, one showed the occurrence of tumor in the pineal gland and two from the pineal gland to the dorsal midbrain, which also spread to the cerebellum. In general, AT/RT may partially exhibit proliferation of spindle-shaped cells and the presence of mucus matrix. However, as there are no reports of such morphologies, caution should be exerted during differentiation. To the best of our knowledge, reports on AT/RT with abundant spindle-shaped cells are extremely rare, and the only case report that focused on and emphasized its morphological images is in an adult patient.[22] The patient had a lesion in the left occipital lobe with abundant spindle-shaped cells that exhibited a characteristic histology showing nuclear palisading and perivascular pseudorosettes. On the contrary, in the present case, the lesion was fully composed of short spindle-shaped cells and mucus matrix, which can be considered a very rare morphological image. However, no clear nuclear palisading or perivascular pseudorosettes were observed.

In conclusion, we treated an adult patient with AT/RT in the pineal region that exhibited distinctive histology. This case apprised us of the difficulty in reaching a definitive diagnosis as pathologists.

## ACKNOWLEDGMENTS

This manuscript was presented as a poster at the 105th Annual Meeting of the Japanese Society of Pathology on May 14, 2016. We would like to express our thanks to Dr. Takashi Komori of the Department of Laboratory Medicine and Pathology of Tokyo Metropolitan Neurological Hospital and Dr. Junko Hirato of the Department of Diagnostic Pathology of Tomioka General Hospital for their valuable advice in the diagnosis of this patient.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## AUTHOR CONTRIBUTIONS

Masatomo Doi and Junki Koike performed histological evaluation and drafted the manuscript and figures. Motohiro Chosokabe, Saeko Naruki, Shinya Tajima, and Akira Endo performed histological evaluation. Hisao Nakamura performed image analysis and provided image data. Yasuyuki Yoshida, Takashi Matsumori, and Yuichiro Tanaka provided clinical information of the patient. All authors contributed to discussions and agreed on the final version of the submitted manuscript.

## REFERENCES

1. Rorke LB, Packer RJ, Biegel JA. Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: definition of an entity. J Neurol Surg. 1996;85(1):56–65.
2. Ostrom QT, Chen Y, M de Blank P, Ondracek A, Farah P, Gittleman H, et al. The descriptive epidemiology of atypical teratoid/rhabdoid tumors in the United States. 2001–2010. Neurooncol. 2014;16(10):1392–9.
3. Lau CS, Mahendraraj K, Chamberlain RS. Atypical teratoid rhabdoid tumors: a population-based clinical outcomes study involving 174 patients from the Surveillance, Epidemiology, and End Results database (1973–2010). Cancer Manag Res. 2015;7:301–9.
4. Rickert CH, Paulus W. Epidemiology of central nervous system tumors in childhood and adolescence based on the new WHO classification. Childs Nerv Syst. 2001;17(9):503–11.
5. Wong TT, Ho DM, Chang KP, Chang KP, Yen SH, Guo WY, et al. Primary pediatric brain tumors: statistics of Taipei VGH, Taiwan (1975–2004). Cancer. 2005;104(10):2156–67.
6. Mathkour M, Carsky K, Chabot AB, Chabot AB, Werner C, Berry JF, et al. Adult pineal region atypical teratoid rhabdoid tumor: a case for aggressive surgical and chemoradiation management with comprehensive literature review. World Neurosurg. 2020;142:117–27.
7. Sugita Y, Takahashi Y, Hayashi I, Morimatsu M, Okamoto K, Shigemori M. Pineal malignant rhabdoid tumor with chondroid formation in an adult. Pathol Int. 1999;49(12):1114–8.
8. Ingold B, Moschopulos M, Hutter G, Hutter G, Seeger H, Röthlisberger B, et al. Abdominal seeding of an atypical teratoid/rhabdoid tumor of the pineal gland along a ventriculoperitoneal shunt catheter. Acta Neuropathol. 2006;111(1):56–9.
9. Takei H, Adesina AM, Mehta V, Powell SZ, Langford LA. Atypical teratoid/rhabdoid tumor of the pineal region in an adult. J Neurol Surg. 2010;113(2):374–9.
10. Shonka NA, Armstrong TS, Prabhu SS, Prabhu SS, Childress A, Choi S, et al. Atypical teratoid/rhabdoid tumors in adults: a case report and treatment-focused review. J Clin Med Res. 2011;3(2):85–92.
11. Kuge A, Sato S, Sakurada K, Takemura S, Kayama T. Atypical teratoid rhabdoid tumor located in the pineal region following prophylactic irradiation for acute lymphoblastic leukemia. Brain Tumor Pathol. 2012;29(3):177–81.
12. Yang M, Chen X, Wang N, Wang N, Zhu K, Hu YZ, et al. Primary atypical teratoid/rhabdoid tumor of central nervous system in children: a clinicopathological analysis and review of literature in China. Int J Clin Exp Pathol. 2014;7(5):2411–20.
13. Liebigt S, Florschütz A, Arndt N, Stock K, Renner C. Atypical teratoid/rhabdoid tumor of the pineal region in a young adult male patient: case report and review of the literature. J Neurol Surg A. 2017;78(1):92–8.
14. Monteiro J, Santiago B, Manilha R, Viegas C, Oliveira A, Cunha E, et al. Adult atypical teratoid/rhabdoid tumor in the pineal region: case report and literature review. World Neurosurg. 2020;134:428–33.
15. Kanoto M, Toyoguchi Y, Hosoya T, Kuchiki M, Sugai Y. Radiological image features of the atypical teratoid/rhabdoid tumor in adults: a systematic review. Clin Neuroradiol. 2015;25(1):55–60.
16. Thomas C, Wefers A, Bens S, Bens S, Nemes K, Agaimy A, et al. Desmoplastic myxoid tumor, SMARCB1-mutant: clinical, histopathological and molecular characterization of a pineal region tumor encountered in adolescents and adults. Acta Neuropathol. 2020;139(2):277–86.
17. Matsumura N, Goda N, Yashige K, Yashige K, Kitagawa M, Yamazaki T, et al. Desmoplastic myxoid tumor, SMARCB1-mutant: a new variant of SMARCB1-deficient tumor of the central nervous system preferentially arising in the pineal region. Virchows Arch. Published online January 9, 2021. https://doi.org/10.1007/s00428-020-02978-3
18. Wang YE, Chen JJ, Wang W, Zhang AL, Zhou W, Wu HB. A case of desmoplastic myxoid tumor, SMARCB1 mutant, in the pineal region. Neuropathology. 2021;41:37–41.
19. Gendle C, Karthigeyan M, Salunke P, Gupta K. Pineal atypical teratoid rhabdoid tumor in a 5-month-old child. Pediatr Neurosurg. 2020;55(6):404–8.
20. Tan X, Xiao M, Jiang W, Yue C, Qu L, Zhao G. Paediatric atypical teratoid/rhabdoid tumour of the pineal region mimicking a meningioma: a case report and literature review. Br J Neurosurg. 2021;16:1–4.
21. Meyers SP, Khademian ZP, Biegel JA, Chuang SH, Korones DN, Zimmerman RA. Primary intracranial atypical teratoid/rhabdoid tumors of infancy and childhood: MRI features and patient outcomes. AJNR Am J Neuroradiol. 2006;27(5):962–71.
22. Horiguchi H, Nakata S, Nobusawa S, Nobusawa S, Uyama S, Miyamoto T, et al. Adult-onset atypical teratoid/rhabdoid tumor featuring long spindle cells with nuclear palisading and perivascular pseudorosettes. Neuropathology. 2017;37(1):52–7.

**How to cite this article:** Doi M, Koike J, Yoshida Y, Nakamura H, Chosokabe M, Naruki S, et al. A case of an atypical teratoid/rhabdoid tumor with distinctive histology in the pineal region in an adult patient. Pathology International. 2021;71:777–782. https://doi.org/10.1111/pin.13159