

An Adult Case of Sellar Atypical Teratoid/Rhabdoid Tumor Presenting with Lung Metastasis, Harboring a Compound Heterozygous Mutation in *INI1*

Norito FUKUDA,¹ Masakazu OGIWARA,¹ Satoshi NAKATA,² Mitsuto HANIHARA,¹
Tomoyuki KAWATAKI,¹ Masataka KAWAI,³ Sumihito NOBUSAWA,²
Hideaki YOKOO,² and Hiroyuki KINOUCHI¹

¹Department of Neurosurgery, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Chuo, Yamanashi, Japan

²Department of Human Pathology, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

³Department of Human Pathology, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Chuo, Yamanashi, Japan

Abstract

A typical teratoid/rhabdoid tumors (AT/RT) are highly malignant embryonal tumors in children that are associated with inactivation of the *integrase interactor 1 (INI1)* gene. Several adult cases of AT/RT have been reported, which were characterized by the sellar occurrence and predominantly occurred in females with *INI1* mutation variants. However, clinical and genetic features are poorly understood in this unusual entity. We experienced a case of a 45-year-old female with sellar AT/RT presenting diplopia, who underwent subtotal removal of the tumor by the endoscopic endonasal transsphenoidal approach. Pathological diagnosis was AT/RT with *INI1* inactivation on immunohistochemistry. Subsequently, multiple lung metastases were confirmed on fluorodeoxyglucose positron emission tomography (FDG-PET). Although she received postoperative chemoradiotherapy, she died of cerebrospinal fluid dissemination. Autopsy revealed cerebrospinal dissemination and lung metastasis of AT/RT. Biallelic alterations in the *INI1* gene were identified by direct sequencing, harboring on different alleles (compound heterozygous mutations) was observed, which is the potential genetic pattern in adult AT/RT. Literature review indicated that lung metastasis frequently occurs in sellar AT/RTs, which is accompanied by cavernous sinus invasion. These observations suggested that cavernous sinus invasion causes haematogenous metastasis to the lung in sellar AT/RT. We discuss clinical and pathological features in adult sellar AT/RT to improve understanding of this unique entity.

Keywords: adult AT/RT, compound heterozygous mutation, *INI1*, lung metastasis, staghorn appearance

Introduction

Atypical teratoid/rhabdoid tumors (AT/RT) are extremely aggressive neoplasms of the central nervous system (CNS) that most often affect children under the age of 3 years.¹⁾ The main genetic hallmark of AT/RT is a mutation or deletion of *INI1/SWI/SNF-related matrix-associated actin-dependent regulator*

of chromatin subfamily B member 1 (SMARCB1).²⁾ Recently, several adult cases of AT/RT have been reported; the sellar region was the most commonly occurring site and patients were predominantly middle-aged women.^{3,4)} Moreover, current genetic studies have revealed that adult sellar AT/RT demonstrates different alterations in *INI1*.^{3,4)} These observations indicate that adult sellar AT/RT could be a distinct disease entity. However, clinical and genetic features are poorly understood in this unusual entity.

Here, we present a case of sellar AT/RT in a 45-year-old female that metastasized to the lung with rapid progression. Genetic analysis indicated a compound heterozygous mutation in *INI1*, which

Received April 23, 2020; Accepted September 11, 2020

Copyright© 2021 by The Japan Neurosurgical Society This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives International License.

is a relatively rare genetic alteration pattern in infants. Literature review of adult sellar AT/RTs demonstrated that lung metastasis frequently occurs, all of which were accompanied by cavernous sinus invasion. We discuss the pathogenesis of lung metastasis and the *INI1* mutation pattern based on the detection of pathological autopsy findings and whole-genome sequencing in this case.

Case Report

Clinical summary

A 45-year-old female presented with bilateral ptosis and diplopia, which had worsened within a few weeks before visiting our institution. Neurological examination revealed right oculomotor nerve palsy, right trigeminal hypesthesia, and bilateral abducens nerve palsy. Magnetic resonance imaging (MRI) revealed a heterogeneously enhanced mass lesion mainly located in the intra-suprasellar region, invading into the bilateral cavernous sinus, pituitary stalk, and hypothalamus (Fig. 1A). Panhypopituitarism was observed on blood biochemical examination. The patient did not develop diabetes insipidus during the course. Under the preoperative differential diagnosis of pituitary carcinoma, pituitary apoplexy, or metastatic pituitary tumor, the patient underwent surgical removal by the endoscopic endonasal transsphenoidal approach with posterior ethmoid sinus fenestration. The tumor was fibrous, firm, and hemorrhagic. It was removed with residual tumor in the lateral portion of the cavernous sinus (Fig. 1B). The pathological diagnosis was classic AT/RT showing a highly cellular component of rhabdoid cells with mitosis. Although her symptoms improved just after surgery, right oculomotor nerve palsy gradually worsened and MRI showed regrowth of the residual tumor (Fig. 1C). She underwent intensity-modulated radiotherapy (total dose of 66 Gy with 33 fractions) as local radiation and temozolomide (TMZ) medication (75 mg/m² daily for 42 days) as chemotherapy. The tumor size decreased after chemoradiation therapy (Fig. 1D); however, the computed tomography (CT) scan revealed multiple lesions in bilateral lungs (Fig. 1E). Lung lesions showed accumulation in fluorodeoxyglucose positron emission tomography (FDG-PET) (Fig. 1K) and CT-guided needle biopsy revealed metastasis of AT/RT. She subsequently received radiotherapy for the lung lesion. A few days later, she presented with bilateral leg pain and gadolinium-enhanced MRI of the spine demonstrated dissemination along the spinal cord and L4-5 spinous process metastasis (Figs. 1F and 1G). Therefore, systemic antineoplastic therapy with ifosfamide (900 mg/m²), cisplatin

(20 mg/m²), and etoposide (60 mg/m²) (ICE) was applied. After the first cycle of ICE chemotherapy, the metastatic lung tumor and cerebrospinal fluid dissemination were ameliorated (Figs. 1H–1J), but the primary sellar lesion was unchanged. Five weeks after the first cycle of ICE chemotherapy, her leg pain again worsened due to dissemination around the cauda equina. Finally, disturbance of consciousness rapidly progressed and the patient passed away 5 months after the initial diagnosis.

Pathological findings

Histological examination revealed a densely cellular neoplasm, which was composed of small- to medium-sized cells with vesicular nuclei that had prominent nucleoli (Figs. 2A and 2B). Additionally, hemangiopericytoma-like staghorn vasculature within the dense, diffuse proliferation of jumbled cells, and a small number of scattered rhabdoid cells suggested characteristic histology of sellar AT/RT but not common findings of AT/RT. Rare rhabdoid cells with eosinophilic cytoplasm including hyaline inclusions, discrete cell borders, and eccentric nuclei (Fig. 2B) were found among other tumor cells with eosinophilic, pale, clear, or vacuolated cytoplasm. Frequent mitotic and apoptotic changes, but not necrosis, were noted in examined sections.

Immunohistochemical examination demonstrated that tumor cells were negative for *INI1* compared with endothelial cells as a positive internal control (Fig. 2C). Diffuse and strong immunoreactivity for vimentin, CD31, CD34, and alpha-smooth muscle actin was observed in the tumor cells. Scattered tumor cells were immunopositive for cytokeratin AE1/AE3 and epithelial membrane antigen. Immunostaining for glial fibrillary acidic protein and synaptophysin was negative. Mindbomb E3 ubiquitin protein ligase 1 (MIB-1) labeling index was approximately 70%.

A systemic pathological autopsy was performed to investigate the pathology of dissemination and metastasis. The autopsy revealed dissemination around the brain stem, spinal cord, and cauda equina. Lung pathology demonstrated multiple metastases and vascular invasion (Figs. 2D–2F). Similar to CNS lesions, rhabdoid cells with eccentric nuclei and eosinophilic cytoplasm were observed and were clearly metastasized (Fig. 2E). Dissemination to the brainstem was suggested as a cause of consciousness disturbance.

Molecular genetic analysis for *INI1* alterations

Genomic deoxyribonucleic acid (DNA) was extracted from formalin-fixed, paraffin-embedded sections as previously described and then amplified and

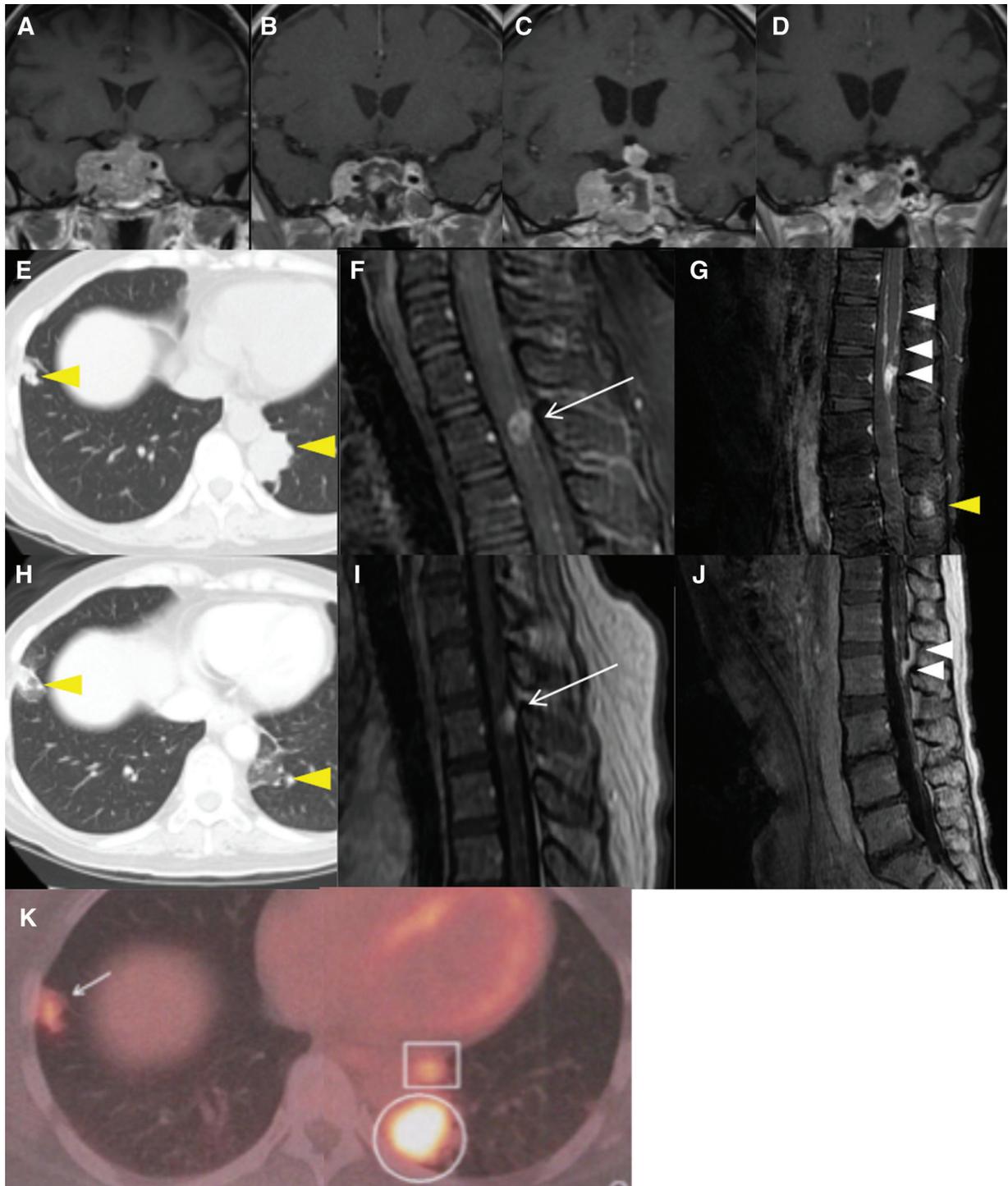


Fig. 1 Coronal T1-weighted MR images with contrast enhancement before (A) and after (B) surgery. Two weeks after surgery, the enhancing mass lesion was increased (C). After initial chemoradiation therapy, the enhancing mass lesion was decreased (D). An enhanced CT image (E) showed several nodular metastases in axial slices of both lungs (yellow arrowheads). Sagittal T1-weighted spinal MR images (F, G) revealed an enhanced mass lesion at the Th2 level (arrow, F). The surface of the spinal cord was almost enhanced, suggesting cerebrospinal fluid dissemination (white arrowheads, G). Bone metastasis was seen at the L4-5 spinous process (yellow arrowhead, G). After ICE therapy, the metastatic lung lesion and cerebrospinal fluid dissemination were decreased (yellow arrowheads H, arrow I, white arrowheads J). FDG-PET (K) showed accumulation in the lung tumor (arrow and circle). Hilar lymph node also showed increased accumulation (square). CT: computed tomography, FDG-PET: fluorodeoxyglucose positron emission tomography, ICE: ifosfamide, cisplatin, and etoposide, MR: magnetic resonance.

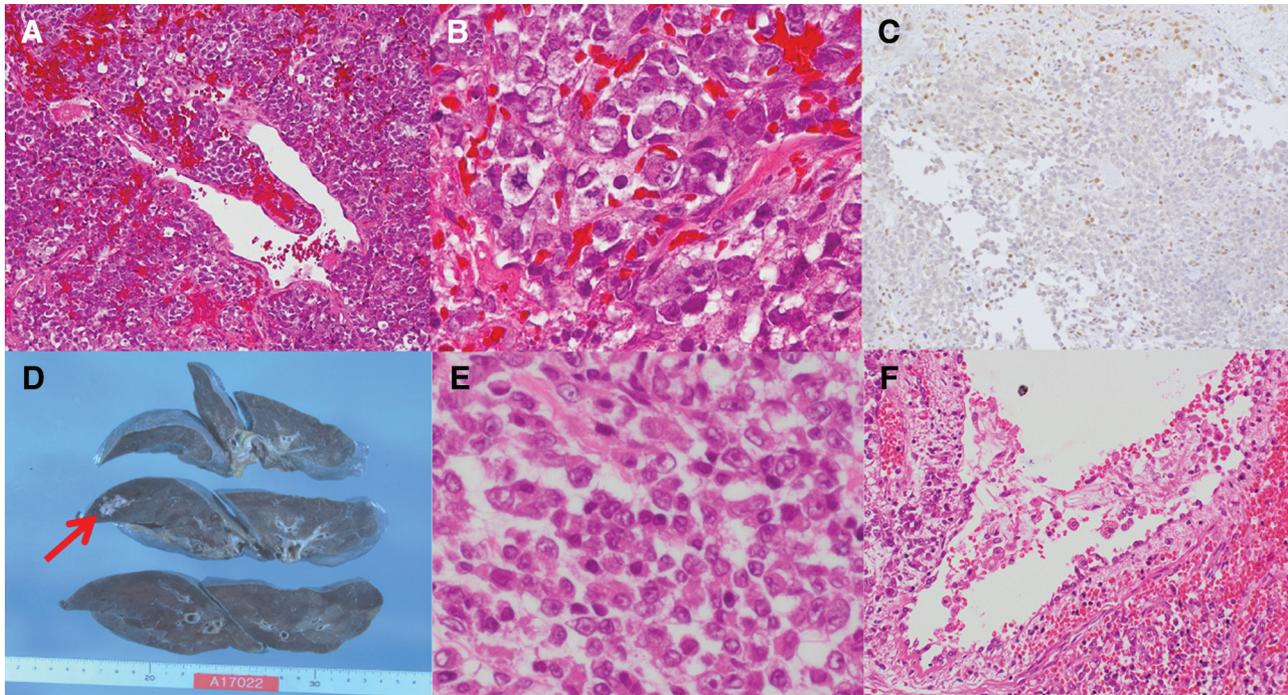


Fig. 2 Photomicrographs of the tumor. (A and B) The tumor was predominantly composed of dense, diffuse proliferation of small- to medium-sized cells with vesicular nuclei that had prominent nucleoli. Thin-walled branching vessels were observed (A). Rare rhabdoid cells were admixed within (B). (C) Immunohistochemistry. Tumor cells were negative for INI1, whereas endothelial cells were positive for INI1 as an internal control (C). (D–F) Systemic pathological autopsy. The tumor could be seen in the lung (red arrow) (D). Metastasis of sellar AT/RT (E) and vascular invasion (F) were detected in lung pathology. Haematoxylin and eosin staining (A, B, E, F). Original magnification: A, C, D, F: 100 \times ; B, E: 400 \times . AT/RT: atypical teratoid/rhabdoid tumors.

sequenced using primers for exons 1–9 of the *INI1* gene.⁴⁾ Two different mutations were detected, presumably on different alleles (compound heterozygous mutations): one mutation was c.144 delC in exon 2, and the other mutation was c.819_820 insT in exon 7 (Fig. 3A). Copy number changes in exons of the *INI1* gene and flanking genes were analyzed by multiplex ligation-dependent probe amplification (MLPA) analysis using the SMARCB1 MLPA test kit P258-C1 (MRC-Holland, Amsterdam, The Netherlands), as previously described,⁵⁾ and no copy number change was observed (Fig. 3B).

Discussion

We report a case of adult sellar AT/RT presenting with lung metastasis and cerebrospinal fluid dissemination and confirmed compound heterozygous mutation in *INI1*. To our knowledge, this is the first sellar AT/RT case evaluated by systemic pathological autopsy including lung metastasis and dissemination. We describe two important points from the present case, lung metastasis, and compound heterozygous mutation of *INI1*.

Only 24 cases of sellar AT/RT have been reported to date. We summarize all reported cases along with the present case in Table 1.^{4–19)} The mean age of patients was 44.3 (20–69) years,^{4–19)} and there were no pediatric cases. All cases except one were female, and the present case was also an adult female. We speculated an epigenetic mechanism by methylation of the X chromosome or an association with female hormones as in gynecologic cancer.^{1,20)} However, the reason for the female predominance is not well understood.

Pediatric AT/RT is likely to show tumor dissemination to the whole CNS, especially to the spinal cord. However, extraneural metastasis is a rare event for intracranial tumors including AT/RT.^{21,22)} We found that 3 of 25 patients (9%) with sellar AT/RT had lung metastasis (Table 1).^{4–19)} Sellar AT/RT may tend to elicit extraneural metastasis compared with pediatric AT/RT. Sellar AT/RT often invades into the cavernous sinus. In previous reports, invasion of the cavernous sinus was seen in 9 of 11 cases, and all cases with lung metastases showed invasion of the cavernous sinus (Table 1). Thus, malignant tumor cells of the cavernous sinus may have the ability to spread to the lung or other organs as haematogenous

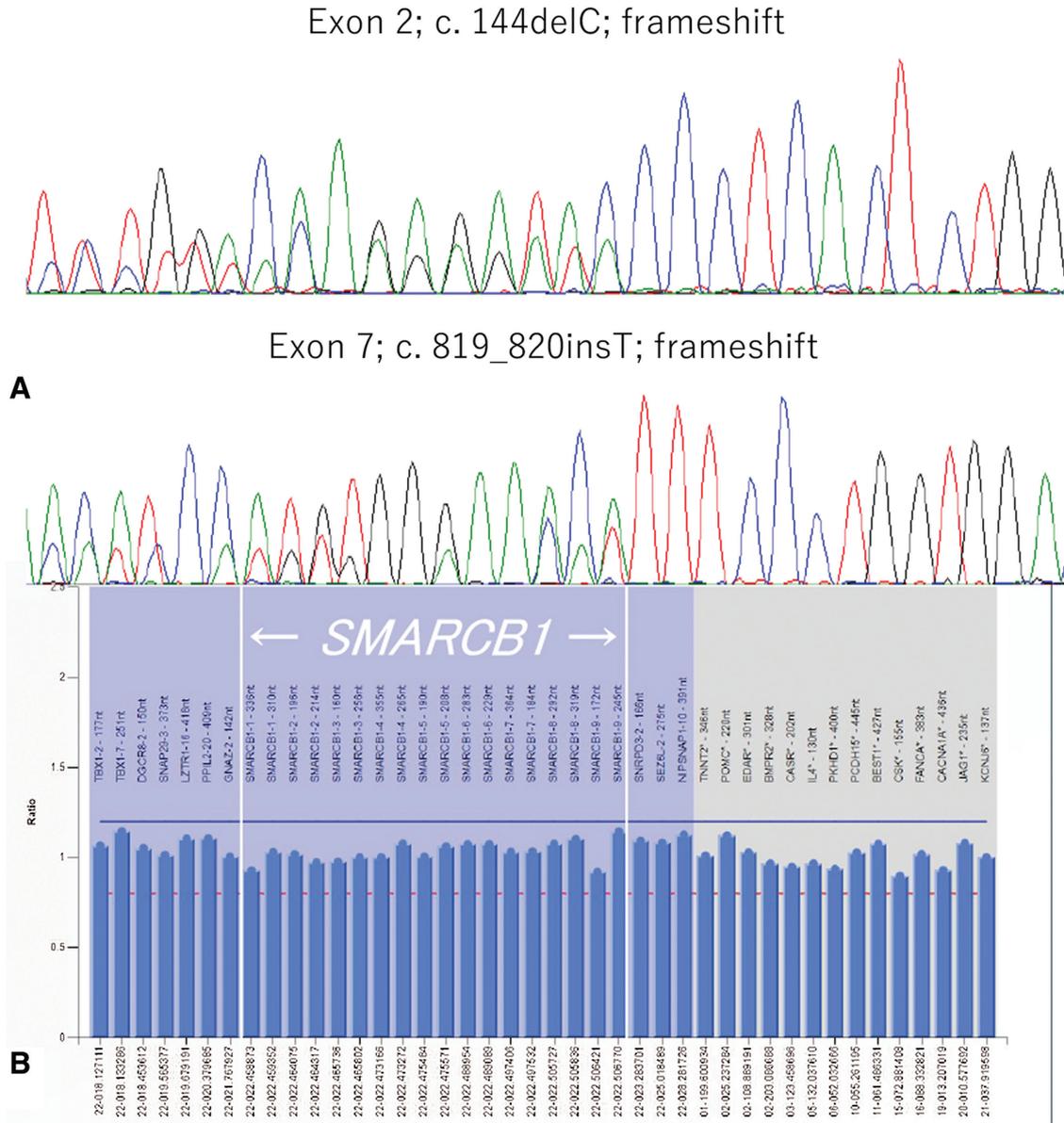


Fig. 3 Molecular genetic analyses. (A) Multiplex ligation-dependent probe amplification analysis revealed that there are no copy number changes in the *IN11* gene and flanking genes. (B) Sanger sequencing detected two different coding sequence mutations; one mutation was c.144 delC in exon 2, and the other mutation was c.819_820 insT in exon 7.

metastasis. Therefore, the patients with AT/RT invasion of the cavernous sinus might be better to receive multi-agent chemotherapy and radiation therapy as soon as possible after the diagnosis.

We speculated that intensive treatment after surgical resection might suppress remote metastasis. In the literature, 11 cases underwent local radiotherapy and one case was treated with craniospinal radiotherapy. Eight cases survived more than 30 months. Four of these cases received ICE-based chemotherapy and the median overall survival was 27.5 months (Table 1). In the present case, the

patient was treated with TMZ, a DNA alkylating agent used for malignant glioma that has been suggested to have a tumor suppression effect for AT/RT.^{4,23,24} TMZ and radiotherapy significantly reduced the primary tumor; however, these treatments could not prevent dissemination to the spinal cord and cauda equina or metastasis to the lungs and spinal bone. Therefore, we should have adopted ICE-based chemotherapy and radiotherapy initially after the diagnosis. In addition, spinal radiotherapy is also considered if spinal cord dissemination is observed.

Table 1 Clinical and pathological characteristics of sellar atypical teratoid/rhabdoid tumor

Authors and year	Age (years), sex	Surgery	Radiation	Chemotherapy	Cavernous invasion	Metastatic site	Autopsy	Survival (month)	<i>SMARCB1</i> Sequencing
Kuge A et al., 2000 ¹⁰⁾	31, F	Subtotal	Local, posterior fossa	1st: CDDP + VP-16, 2nd: MTX	-	-	-	28	NA
Raisanen J et al., 2005 ¹⁷⁾	20, F	No detail	Yes (no detail)	Yes (No detail)	NA	-	-	Alive at 28	c.118 delC (exon2)
Raisanen J et al., 2005 ¹⁷⁾	31, F	No detail	Yes (no detail)	NA	NA	-	-	9	NA
Arita K et al., 2008 ⁷⁾	56, F	Subtotal	SRS, local, spine	No	+	Spinal cord	-	23	c.370_371 delA (exon4) + c.528_529 delC (exon5)
Las Heras F et al., 2010 ¹¹⁾	46, F	No detail	NA	NA	NA	-	-	Not described	NA
Schneiderhan et al., 2011 ¹⁸⁾	61, F	Total	NA	NA	-	-	-	3	c.91G>T p. (Glu31) (exon 1) + c.538_563 del p. (Ala 180Hisfs22) (exon 5)
Schneiderhan et al., 2011 ¹⁸⁾	57, F	No detail	Yes (no detail)	ADM+CDDP	+	-	-	Alive at 6	NA
Moretti C et al., 2013 ¹²⁾	60, F	Subtotal	Local	1st: ADM + VNB 2nd: CBDCA	+	Lung	-	30	NA
Park HG et al., 2014 ¹⁶⁾	42, F	Subtotal	Craniospinal	Multiagent	+	-	-	Alive at 24	NA
Shitara S et al., 2014 ¹⁹⁾	44, F	Partial	Yes (no detail)	ICE	+	Spinal cord, lung	-	17	No aberrations
Biswas S et al., 2015 ⁸⁾	48, F	Total	No	VDC, ICE	NA	-	-	Died	c.146C>G (exon2) + c.629+2T>G (intron5)
Nobusawa S et al., 2016 ⁴⁾	69, F	Subtotal	Local	TMZ	+	-	-	Alive at 37	c.795 + 1 delG (intron6) + c.150 dupC p. (Trp51Leufs20) (exon2)
Nakata S et al., 2017 ³⁾	26, F	No detail	Local, spine	1st: MTX, 2nd: ICE	NA	-	-	33	c.544C>T (exon5) + c.681_697del (exon6)
Nakata S et al., 2017 ³⁾	21, F	No detail	Local	ICE	NA	-	-	35	No aberrations
Almalki MH et al., 2017 ⁶⁾	36, F	Total	Local	ICE	+	-	-	Alive at 37	NA
Johann PD et al., 2018 ⁹⁾	66, M	No detail	NA	NA	NA	-	-	Alive at 54	No aberrations
Johann PD et al., 2018 ⁹⁾	20, F	No detail	NA	NA	NA	-	-	120	c.118 delC p. (Arg40Glu fs16) (exon2)
Johann PD et al., 2018 ⁹⁾	48, F	No detail	NA	NA	NA	-	-	Alive at 4	No aberrations

Table 1 Continued

Authors and year	Age (years), sex	Surgery	Radiation	Chemotherapy	Cavernous invasion	Metastatic site	Autopsy	Survival (month)	SMARCB1 Sequencing
Johann PD et al., 2018 ⁹⁾	46, F	No detail	NA	NA	NA	–	–	0	c.818_886 del p. (Ile273_Leu295del) (exon7)
Nishikawa A et al., 2018 ¹³⁾	42, F	Total	Local	Paclitaxel	+	Spinal cord	Systemic	11	c.592T>C (p.Gln198x)
Paolini MA et al., 2018 ¹⁵⁾	31, F	Subtotal	No	No	NA	–	–	2	SMARCB1 homozygous deletion
Paolini MA et al., 2018 ¹⁵⁾	36, F	Subtotal	Yes (no detail)	Yes (No detail)	NA	–	–	Alive at 22	c.785del, p.V262AfsX5
Paolini MA et al., 2018 ¹⁵⁾	47, F	Subtotal	Local	Yes (3 agent)	NA	–	–	Alive at 62	c.472C>T, p.R158X
Paolini MA et al., 2018 ¹⁵⁾	65, F	Subtotal	Local	Yes (4 agent)	NA	Spinal cord	–	23	c.773C>A, p.S258X
Present	45, F	Subtotal	Local, lung	1st: TMZ, 2nd: ICE	+	Lung, spinal cord, bone	Systemic	5	c.144 delC (exon2) + c.819_820 insT (exon7)

NA: not assessed.

In the present case, we detected a compound heterozygous mutation in *INI1*. Although the genetic mutation pattern has not been well clarified, AT/RTs have been associated with a specific genetic alteration, that is, mutation of the *INI1* gene located on chromosome 22q11.2.²⁵⁾ The *INI1/hSNF5* gene encodes a component of the *SWI/SNF* chromatin remodeling complex and interacts with sequence-specific DNA binding proteins such as *cellular myelocytomatosis oncogene (c-Myc)* and *Epstein-Barr virus encoded nuclear antigen2*.²⁾ This genetic hallmark of AT/RT, either mutation or deletion of both copies of the *INI1/hSNF5* gene, is detected in approximately 70% of tumors. Genetic analysis has recently revealed that the prevalence of compound heterozygous mutations and splice-site mutations is significantly higher in sellar AT/RT than in pediatric AT/RT.¹⁾ Only 1 of 116 cases (<1%) of pediatric AT/RT with detectable biallelic *INI1* alterations harbored this type of mutation.²⁶⁾ In contrast, 6 of 18 cases (33%) of sellar AT/RT exhibited compound heterozygous mutations (Table 1).

A recent study categorized pediatric AT/RT into three molecular subgroups, AT/RT—tyrosine, AT/RT—sonic hedgehog and AT/RT-MYC, by DNA methylation patterns.²¹⁾ In unsupervised hierarchical cluster analysis of DNA methylation profiles, sellar AT/RT clustered with AT/RT-MYC.²¹⁾ Analysis of

DNA methylation array intensity data revealed that only one case of sellar AT/RT had characteristic features of pediatric ATRT-MYC, that is, major copy number losses affecting the *SMARCB1* region.²¹⁾ These results suggest that sellar AT/RTs in adults form a clinically distinct entity with a different mutational spectrum but share epigenetic similarities with pediatric AT/RTs of the AT/RT-MYC subgroup.⁹⁾ However, it is unclear how this classification affects clinical biology and therapeutic application. The relation between compound heterozygous mutations in *INI1* and specific methylation patterns should be studied in the near future.

We reported the case of an adult female with sellar AT/RT who underwent systemic pathological autopsy and exhibited metastasis and dissemination. The patient had a compound heterozygous mutation in *INI1*, suggesting that adult AT/RT is a different pathological condition than pediatric AT/RT, including site and prognosis. Because the autopsy revealed cerebrospinal fluid dissemination and lung metastasis, aggressive chemoradiotherapy following maximum surgical resection should be considered.

Conflicts of Interest Disclosure

All authors have no conflict of interest.

References

- 1) Johann PD, Erkek S, Zapatka M, et al.: Atypical teratoid/rhabdoid tumors are comprised of three epigenetic subgroups with distinct enhancer landscapes. *Cancer Cell* 29: 379–393, 2016
- 2) Biegel JA: Molecular genetics of atypical teratoid/rhabdoid tumor. *Neurosurg Focus* 20: E11, 2006
- 3) Nakata S, Nobusawa S, Hirose T, et al.: Sellar atypical teratoid/rhabdoid tumor (AT/RT): a clinicopathologically and genetically distinct variant of AT/RT. *Am J Surg Pathol* 41: 932–940, 2017
- 4) Nobusawa S, Hirato J, Sugai T, et al.: Atypical teratoid/rhabdoid tumor (AT/RT) arising from ependymoma: a type of AT/RT secondarily developing from other primary central nervous system tumors. *J Neuropathol Exp Neurol* 75: 167–174, 2016
- 5) Francis NJ, McNicholas B, Awan A, et al.: A novel hybrid CFH/CFHR3 gene generated by a microhomology-mediated deletion in familial atypical hemolytic uremic syndrome. *Blood* 119: 591–601, 2012
- 6) Almalki MH, Alrogi A, Al-Rabie A, Al-Dandan S, Altwairgi A, Orz Y: Atypical teratoid/rhabdoid tumor of the sellar region in an adult with long survival: case report and review of the literature. *J Clin Med Res* 9: 216–220, 2017
- 7) Arita K, Sugiyama K, Sano T, Oka H: Atypical teratoid/rhabdoid tumour in sella turcica in an adult. *Acta Neurochir (Wien)* 150: 491–495; discussion 496, 2008
- 8) Biswas S, Wood M, Joshi A, et al.: Exome sequencing of an adult pituitary atypical teratoid rhabdoid tumor. *Front Oncol* 5: 236, 2015
- 9) Johann PD, Bens S, Oyen F, et al.: Sellar region atypical teratoid/rhabdoid tumors (ATRT) in adults display DNA methylation profiles of the ATRT-MYC subgroup. *Am J Surg Pathol* 42: 506–511, 2018
- 10) Kuge A, Kayama T, Tsuchiya D, et al.: Suprasellar primary malignant rhabdoid tumor in an adult: a case report. *No Shinkei Geka* 28: 351–358, 2000. (Japanese)
- 11) Las Heras F, Pritzker KP: Adult variant of atypical teratoid/rhabdoid tumor: immunohistochemical and ultrastructural confirmation of a rare tumor in the sella turcica. *Pathol Res Pract* 206: 788–791, 2010
- 12) Moretti C, Lupoi D, Spasaro F, et al.: Sella turcica atypical teratoid/rhabdoid tumor complicated with lung metastasis in an adult female. *Clin Med Insights Case Rep* 6: 177–182, 2013
- 13) Nishikawa A, Ogiwara T, Nagm A, et al.: Atypical teratoid/rhabdoid tumor of the sellar region in adult women: Is it a sex-related disease? *J Clin Neurosci* 49: 16–21, 2018
- 14) Nobusawa S, Nakata S, Hirato J, et al.: Atypical teratoid/rhabdoid tumor in the sella turcica of an elderly female with a distinct vascular pattern and genetic alterations. *Virchows Arch* 469: 711–715, 2016
- 15) Paolini MA, Kipp BR, Sukov WR, et al.: Sellar region atypical teratoid/rhabdoid tumors in adults: Clinicopathological characterization of five cases and review of the literature. *J Neuropathol Exp Neurol* 77: 1115–1121, 2018
- 16) Park HG, Yoon JH, Kim SH, et al.: Adult-onset sellar and suprasellar atypical teratoid rhabdoid tumor treated with a multimodal approach: a case report. *Brain Tumor Res Treat* 2: 108–113, 2014
- 17) Raisanen J, Biegel JA, Hatanpaa KJ, Judkins A, White CL, Perry A: Chromosome 22q deletions in atypical teratoid/rhabdoid tumors in adults. *Brain Pathol* 15: 23–28, 2005
- 18) Schneiderhan TM, Beseoglu K, Bergmann M, et al.: Sellar atypical teratoid/rhabdoid tumours in adults. *Neuropathol Appl Neurobiol* 37: 326–329, 2011
- 19) Shitara S, Akiyama Y: Atypical teratoid/rhabdoid tumor in sellar turcica in an adult: A case report and review of the literature. *Surg Neurol Int* 5: 75, 2014
- 20) Gharwan H, Bunch KP, Annunziata CM: The role of reproductive hormones in epithelial ovarian carcinogenesis. *Endocr Relat Cancer* 22: R339–363, 2015
- 21) Athale UH, Duckworth J, Odame I, Barr R: Childhood atypical teratoid rhabdoid tumor of the central nervous system: a meta-analysis of observational studies. *J Pediatr Hematol Oncol* 31: 651–663, 2009
- 22) Varan A, Sari N, Akalan N, et al.: Extraneural metastasis in intracranial tumors in children: the experience of a single center. *J Neurooncol* 79: 187–190, 2006
- 23) Takahashi K, Nishihara H, Katoh M, et al.: Case of atypical teratoid/rhabdoid tumor in an adult, with long survival. *Brain Tumor Pathol* 28: 71–76, 2011
- 24) Wang CH, Hsu TR, Wong TT, Chang KP: Efficacy of temozolomide for recurrent embryonal brain tumors in children. *Childs Nerv Syst* 25: 535–541, 2009
- 25) Betz BL, Strobeck MW, Reisman DN, Knudsen ES, Weissman BE: Re-expression of hSNF5/INI1/BAF47 in pediatric tumor cells leads to G1 arrest associated with induction of p16ink4a and activation of RB. *Oncogene* 21: 5193–5203, 2002
- 26) Torchia J, Golbourn B, Feng S, et al.: Integrated (epi)-genomic analyses identify subgroup-specific therapeutic targets in CNS rhabdoid tumors. *Cancer Cell* 30: 891–908, 2016

Corresponding author: Hiroyuki Kinouchi, MD, PhD
 Department of Neurosurgery, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, 1110 Shimokato, Chuo, Yamanashi 409-3898, Japan.
e-mail: hkinouchi@yamanashi.ac.jp