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LETTER TO THE EDITOR

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Abdominal seeding of an atypical teratoid/rhabdoid tumor of the pineal gland along a ventriculoperitoneal shunt catheter

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Atypical teratoid/rhabdoid tumor (AT/RT) is a rather novel malignant central nervous system (CNS) neoplasm of uncertain origin, which was first defined as an entity in 1987 [5]. The vast majority of AT/RTs occur in infants or children below 5 years of age and only few AT/RTs in adults have been reported [3, 6]. Most AT/RTs arise in the posterior fossa, the cerebral hemispheres and the suprasellar region, but can also occur in the spinal cord and the pineal region. In the latter, AT/RT has been reported only once [10]. Histopathologically, AT/RT is composed of rhabdoid cells with or without areas of epithelial, mesenchymal and/or primitive neuroectodermal differentiation. Fluorescence in situ hybridization (FISH) and loss of heterozygosity studies revealed deletions of chromosome 22 in 75–90% of AT/RTs with inactivation of the *INI1/hSNF5* gene and, consequently, lack of INI1 protein expression similar to rhabdoid tumors of other organs such as kidney [1, 6]. Despite the aggressive treatment with surgery, chemo- and radiotherapy, AT/RTs have an unfavorable prognosis with early recurrence and short median survival times [8].

An otherwise healthy 45-year-old-woman presented with visual disturbances. Cranial magnetic resonance imaging (MRI) displayed a tumor mass in the pineal region, which was resected. Histological examination revealed a neoplasm with high cellularity, numerous mitotic figures and a predominantly rhabdoid appearance of the tumor cells (Fig. 1a, b). Immunohistochemical analysis revealed strong reactivity for vimentin in almost all, and focal positivity for smooth muscle actin (SMA), cytokeratins and epithelial membrane antigen (EMA) in some tumor cells (Fig. 1c–f). FISH analysis using probes to the breakpoint cluster region (BCR) on chromosome 22q11.2 showed a single BCR signal in tumor cells, while two signals of the ABL locus on chromosome 9 were present. This result suggested deletion of the *INI1/hSNF5* gene, which is located close to the BCR locus on chromosome 22q11.2 (Fig. 1h). This conclusion was supported by the loss of *INI1/hSNF5* protein expression in tumor cells, whereas non-neoplastic CNS cells displayed a nuclear INI1 signal (Fig. 1g). Histological, immunohistochemical and FISH results were consistent with the diagnosis of AT/RT, which was confirmed by the Brain Tumor Reference Center of the German Society of Neuropathology and Neuroanatomy.

Postoperative radio- and chemotherapy was performed. Due to development of occlusive hydrocephalus, a ventriculoperitoneal (VP) shunt catheter was inserted. Six months after the initial diagnosis, the tumor recurred locally. Gross total resection was achieved and histological and immunohistochemical analysis re-confirmed the initial diagnosis of an AT/RT.

One month after re-craniotomy, the patient was admitted to the hospital with progressive loss of

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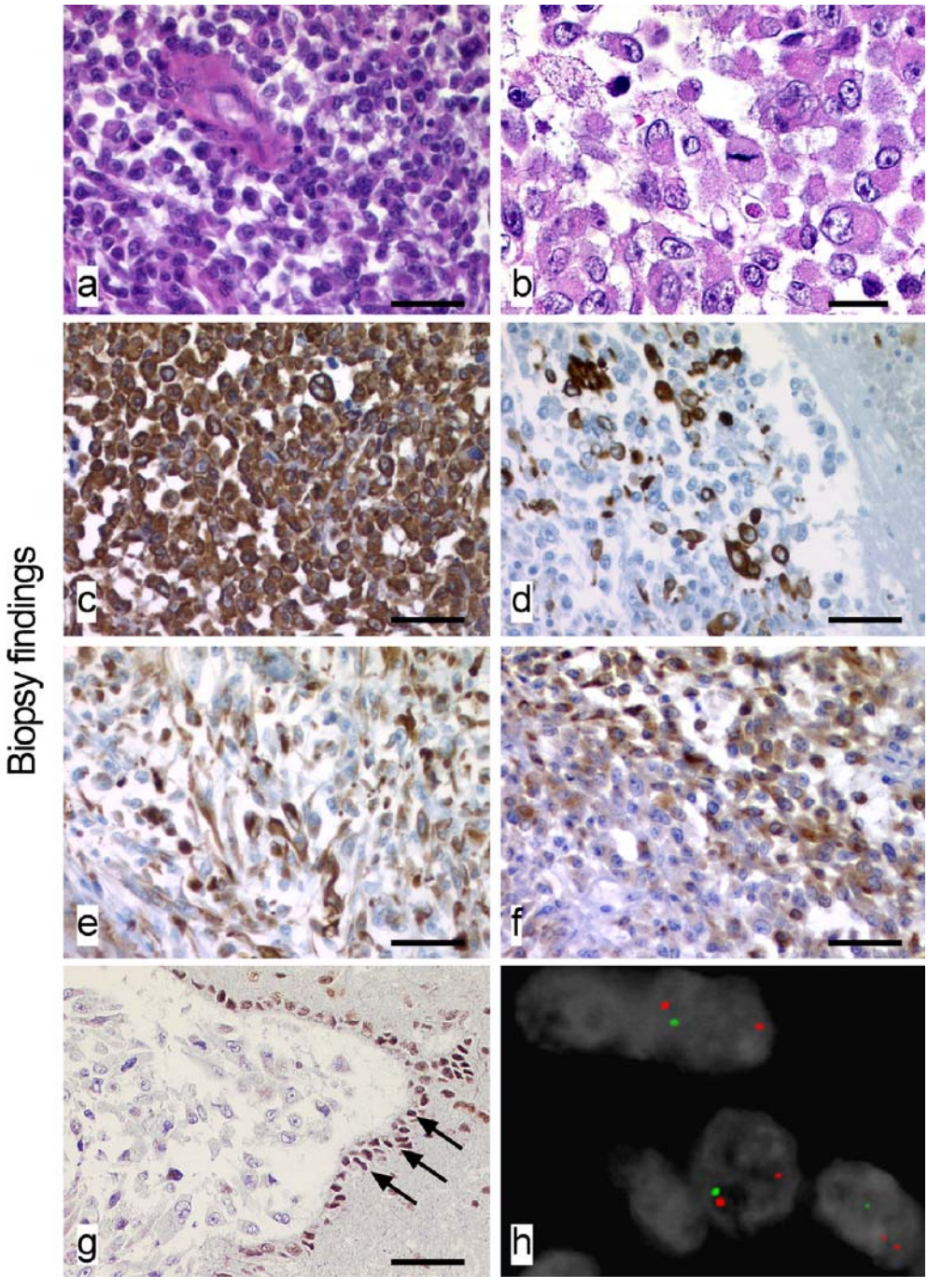

Fig. 1 Biopsy findings: Morphological appearance of a highly cellular, partly rhabdoid tumor in the pineal region (HE; **a, b**). Immunohistochemical staining reveals strong reactivity for vimentin (**c**) and focal positivity for SMA (**d**), cytokeratins (clone AE1–3; **e**) and EMA (**f**), while INI1 protein expression is lacking (internal positive control: ependymal cells, *arrows*; **g**). FISH depicting two signals of the ABL locus (*red*), but only one BCR signal (*green*) in tumor cells (**h**) (*HE* hematoxylin and eosin, *FISH* fluorescence in situ hybridization). *Bars* **a**, **c–g** 50 μm; **b** 20 μm

consciousness and a non-convulsive status epilepticus. MRI scan revealed recurrent tumor in the pineal region with brainstem infiltration and leptomeningeal dissemination, while there were no tumor cells detectable in the cerebrospinal fluid. The patient died 12 days later with palliative therapy. At autopsy, tumor tissue was found in the pineal region with infiltration of the third and fourth ventricles, the cerebellum, both oculomotor nuclei and the mesencephalon, where an acute hemorrhage was evident (Fig. 2a, b). Tumor cells also extended into Virchow-Robin spaces and leptomeninges and infiltrated along the cavity in which the VP shunt catheter had been placed (Fig. 2c). Upon opening the peritoneal cavity, multiple intra-abdominal tumor nodules in liver, spleen and on the peritoneal surface were found (Fig. 2d). Histological, immunohistochemical and genetic analyses of the metastases revealed an identical pheno- and genotypic pattern as for the primary CNS tumor, indicative of a metastatic spread of the AT/RT to the abdominal cavity (Fig. 2e–h).

Extraneural metastases of primary brain tumors occur very rarely. They originate from gliomas, menin-

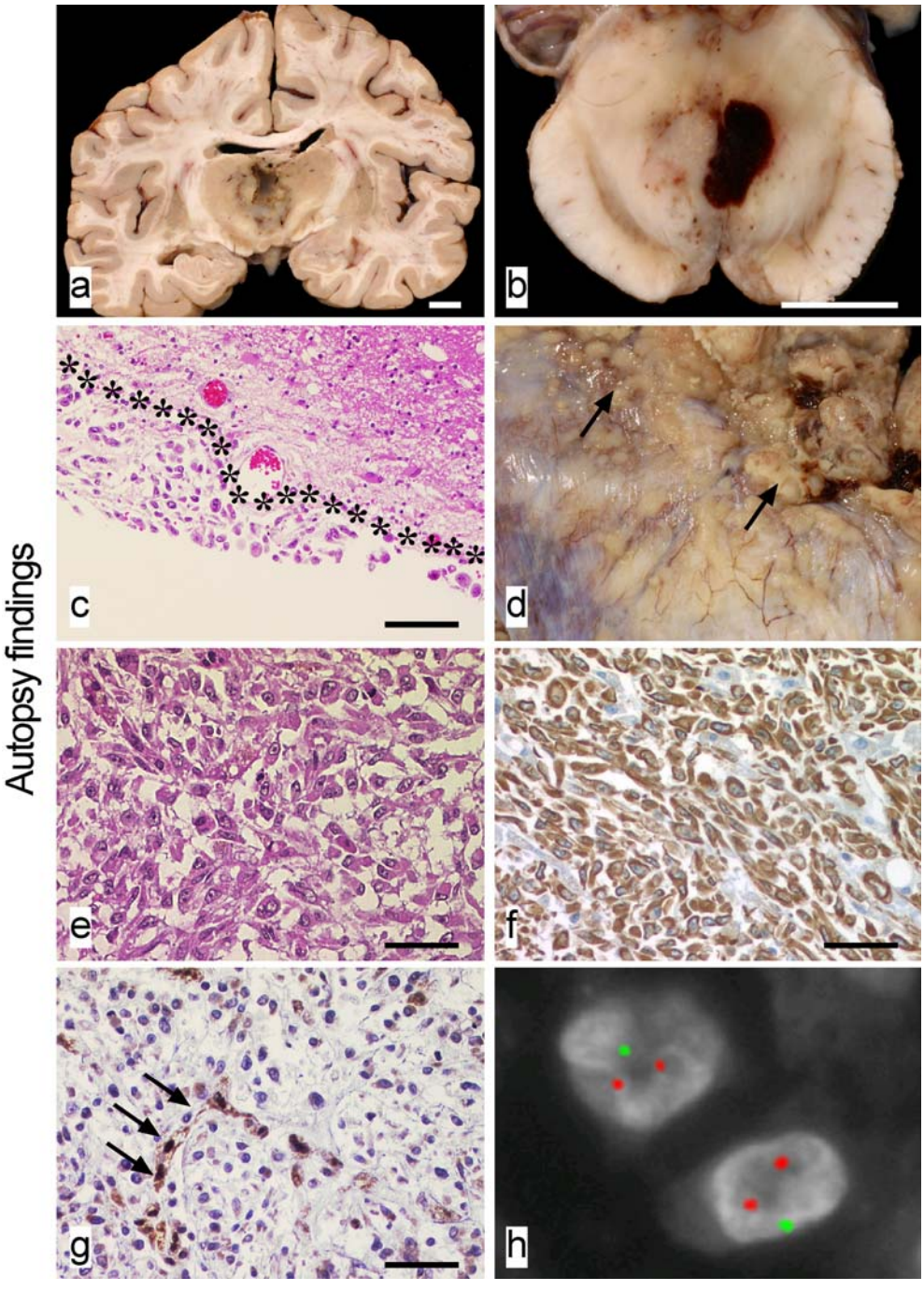

Fig. 2 Autopsy findings: Coronal section of the brain around the pineal region depicting the operation cavity filled with fibrin and recurrent tumor tissue (**a**) and acute hemorrhage due to tumor infiltration in the mesencephalon (**b**). Tumor cell growth along the shunt cavity in the CNS (HE). *Asterisks* indicate border between brain tissue and tumor cells (**c**). Macroscopic appearance of multiple solid abdominal metastases (*arrows*) in the peritoneal cavity (**d**). Liver metastasis with similar morphological appearance as the primary CNS tumor (HE; **e**) and analogous immunohistochemical pattern including reactivity for vimentin (**f**) and lack of INI1 expression (internal positive control: endothelial cells, *arrows*; **g**). FISH depicting two signals of the ABL locus (*red*), but only one BCR signal (*green*; **h**). *Bars* **a**, **b** 1 cm; **c, e–g** 50 μm

geal tumors, ependymomas and medulloblastomas [9], and may propagate via cerebrospinal fluid, blood and lymphatic vessels or through direct infiltration of adjacent structures. Spread via VP shunt catheters, inserted to control tumor-related occlusive hydrocephalus, has been limited to few patients with various types of CNS tumors, including medulloblastomas and germinomas [7]. As for AT/RTs, metastatic spread to extraneural sites is very rare. So far only one child with lung metastasis and one infant with spread to the peritoneal cavity due to a VP shunt catheter has been reported [2, 4]. While the surface of certain catheters—in our case silicone elastomer—may influence tumor cell migration to some extent, it is also feasible that malignant tumor cells with a perivascular growth pattern in general have a higher likeliness to migrate along (natural or artificial) tube-like structures.

In conclusion, we report the first case of a VP shunt-related spread of an AT/RT in the adult. Thus, despite being a very rare phenomenon, VP shunts must be considered as potential route for iatrogenic transmission of AT/RTs into the periphery.

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