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BRIEF COMMUNICATION

Synchronous congenital malignant rhabdoid tumor of the orbit and atypical teratoid/rhabdoid tumor—feasibility and efficacy of multimodal therapy in a long-term survivor

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Among infant malignancies, congenital tumors, especially those of the central nervous system (CNS), constitute a rather unique subgroup. Poor survival rates (28% in CNS tumors) may be attributed to the aggressive biology as well as specific therapeutic limitations innate to the young age of affected patients. Our patient developed synchronous congenital tumors: an atypical teratoid/rhabdoid tumor (AT/RT) localized in the right lateral ventricle of the brain and a malignant rhabdoid tumor (MRT) in the soft tissue of the right orbit. A de novo germline chromosomal deletion in 22q encompassing the *SMARCB1* gene was detected, prompting the diagnosis of a de novo rhabdoid tumor predisposition syndrome 1 (RTPS1). The patient was reported to the European Rhabdoid Registry (EU-RHAB) and treated according to the *Rhabdoid 2007* recommendation. Despite the very young age of the patient, the initially desperate situation of RTPS1, and the synchronous localization of congenital rhabdoid tumors, intensive chemotherapy was well tolerated; the child is still in complete remission 5 years following diagnosis. In conclusion, RTPS1 with congenital synchronous MRTs is not necessarily associated with a detrimental outcome. Intensive multidrug chemotherapy, including high dose chemotherapy, may be feasible and justified.

Keywords Atypical teratoid/rhabdoid tumor, rhabdoid tumor predisposition syndrome 1, synchronous congenital tumors, multimodal therapy

Congenital tumors are a very rare and specific subgroup of infant malignancies.(1) The aggressive behavior of the tumors combined with the specificities of an infant organism limit the therapeutic options that are, in most cases, multidrug approaches and surgery. Especially in congenital rhabdoid tumors, survival rates are rather poor (e.g., Isaacs reported only 10% survivors (2)). Like other rhabdoid tumors, congenital rhabdoid tumors can arise in various locations. Here, we describe a patient with a synchronous congenital rhabdoid tumor localized in the central nervous system (CNS) (an atypical teratoid/rhabdoid tumor (AT/RT)) and a malignant rhabdoid tumor (MRT) in the soft tissue around the orbit. The patient was reported to the European Rhabdoid Registry (EU-RHAB), which is the first European registry of rhabdoid tumors. EU-RHAB registers rhabdoid tumors of any anatomical site and proposes a consensus therapy.

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Material and methods

Immunohistochemical staining of the *SMARCB1/INI1* status of the tumor as well as its molecular analysis is part of the routine evaluation of every rhabdoid tumor reported to EU-RHAB. If available, a genetic analysis of the blood for detection of a potential germline mutation completes the assessment of the tumor. All analyses are performed at the EU-RHAB reference centers at the University Hospital in Kiel and the University Medical Center Hamburg-Eppendorf.

Results

Case report

The female newborn was delivered at full term (birth weight 3.1 kg, birth size 50 cm) without complications, following an unremarkable pregnancy, as the first child of healthy parents. At birth, a periorbital mass infiltrating the periorbital musculature and the right orbit was encountered (Figure 1A; the mass had not been obvious on prenatal ultrasonograph). Interventional embolization of the tumor vasculature was performed 2 days after birth, followed by gross total resection (GTR) 3 days later (Figure 1B). Histopathologic examination established the diagnosis of MRT, and the case was reported to EU-RHAB. Chemotherapy according to the *Rhabdoid 2007* protocol employing vincristine, cyclophosphamide, and doxorubicin (VCD) followed by ifosfamide, carboplatin, and etoposide (ICE) started 16 days after birth of the infant (therapeutic schedule: first, VCD 100%; second, VCD 100%; third, ICE 66%; fourth, ICE 80%; fifth, VCD 80%; and sixth, VCD 70%). Chemotherapy was generally well tolerated. The infant developed recurrent fever of unknown origin because of the chemotherapy-induced neutropenia but recovered rapidly. At the age of 4½ months, the patient developed relapsing vomiting. Magnetic resonance imaging of the brain revealed a tumor located within the right lateral ventricle with beginning blockage of the foramen of Monro (Figure 2). On GTR, a neuropathologic diagnosis of AT/RT was established. In retrospect, a discrete opacity had already been present on earlier magnetic resonance imaging studies at the location of the now obvious intracerebral lesion. No recurrent orbital tumor growth was detected. Chemotherapy was adapted and started with ICE 80% and four doses of methotrexate (MTX) intrathecally. No tumor cells were detected in the cerebrospinal fluid (CSF). The 7-month-old infant received tandem high dose chemotherapy (HDCT) with peripheral blood stem cell rescue employing carboplatin and etoposide (66% of scheduled dose) followed by cyclophosphamide and thiotepa (100% of scheduled dose) 2 months later. At the age of 10

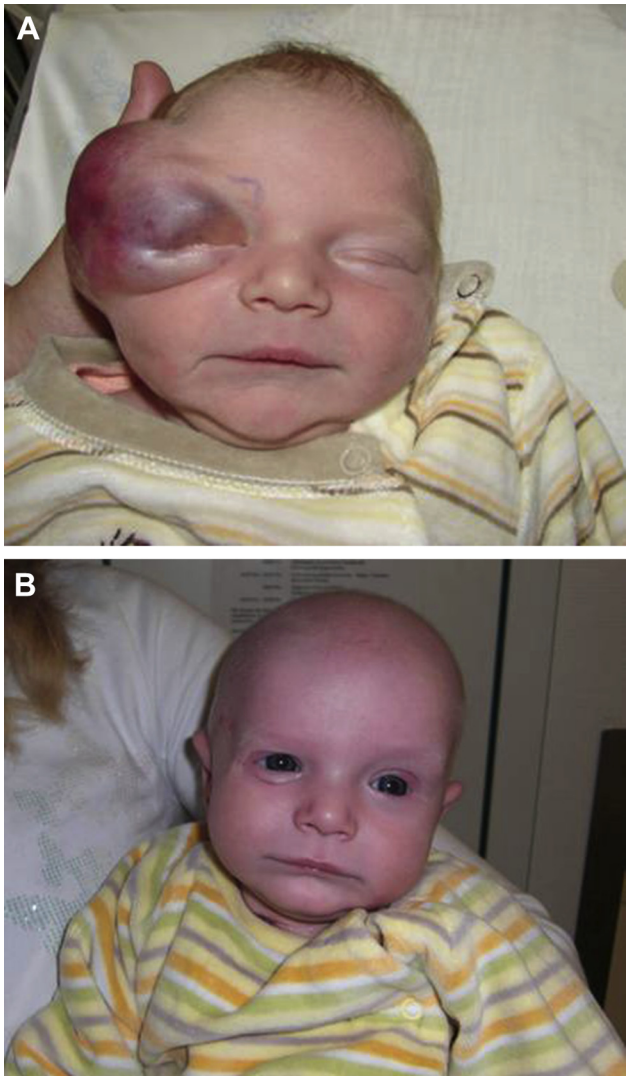

Figure 1 The congenital malignant rhabdoid tumor presented as a periorbital mass. (A) A photograph of the patient with the periorbital mass as it presented at birth. (B) A photograph of the patient after complete resection of the periorbital mass.

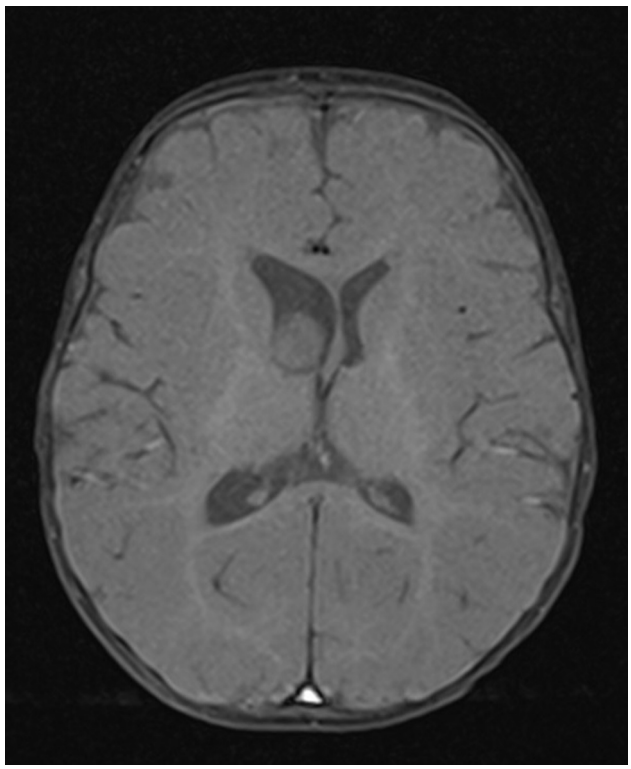

Figure 2 A magnetic resonance image of the AT/RT.