Effective treatment of recurrent orbital Rhabdoid Tumor with Predisposition Syndrome 1

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Abstract

Rhabdoid tumor with predisposition syndrome 1 is a highly aggressive, rare genetic condition in young children. We report an 18-month-old child with bleeding from a second local recurrence of an orbital rhabdoid tumor. Due to the rarity of the syndrome there are no generally accepted treatment approaches, especially in tumor recurrences. As a rescue therapy, our patient received a combination of transarterial embolization and interstitial brachytherapy (BT). From the initiation of our treatment until his death, he experienced neither recurrent bleeding nor local tumor recurrence. The combination of embolization and BT might offer a safe palliative approach and could be considered as a possible alternative at an earlier stage.

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Abstract:

Rhabdoid tumor with predisposition syndrome 1 is a highly aggressive, rare genetic condition in young children. We report an 18-month-old child with bleeding from a second local recurrence of an orbital rhabdoid tumor. Due to the rarity of the syndrome there are no generally accepted treatment approaches, especially in tumor recurrences. As a rescue therapy, our patient received a combination of transarterial embolization and interstitial brachytherapy (BT). From the initiation of our treatment until his death, he experienced neither recurrent bleeding nor local tumor recurrence. The combination of embolization and BT might offer a safe palliative approach and could be considered as a possible alternative at an earlier stage.

Key words: orbit, embolization, brachytherapy, rhabdoid tumor Predisposition Syndrome 1

Introduction:

Rhabdoid tumor predisposition syndrome 1 (RTPS1) is a rare genetic condition characterized by pathogenic variants in the SMARCB1 gene. RTPS1 leads to highly aggressive soft tissue tumors, which may occur in the brain and spinal cord, kidneys and liver, but can occasionally originate from the orbit and carries a high potential for local recurrence and metastasis. It occurs predominantly in infants and young children [1, 2] and represents less than 1% of pediatric soft tissue malignancies [3]. Primary therapy consists of excision, followed by adjuvant chemotherapy and radiotherapy. Due to the rarity of orbital rhadoid tumor (oRT), there is little reliable data on effective treatment approaches, especially in cases of tumor recurrence. Here, we report an effective combination of embolization and interstitial brachytherapy (BT) in a child with RTPS1 and a second local recurrence of an oRT with hemorrhage.

Case presentation

Our 18-month-old patient with recurrent oRT of the right side presented to our hospital with rapid tumor growth and profuse bleeding from the right orbital cavity. Magnetic Resonance Imaging (MRI) revealed extensive tumor recurrence in the orbit with infiltration of the adjacent bony structures of the maxillary sinus the nasal cavity, ethmoid cells, and frontal base, as well as intracranial extension via the right optic canal (Fig.1 A).

13 months prior to this presentation, he had undergone surgical resection of the tumor, chemotherapy according to the European Rhabdoid Registry (EU-RHAB) and proton radiotherapy of 54 Gray (Gy). One year later, the first local recurrence was observed and the patient underwent tumor resection followed by orbital exenteration.

A significant drop in hemoglobin level (75 g/l) was noted on admission, requiring transfusions of packed red blood cells. Considering the patient's medical history and previous treatments, tumor location and skin toxicity in the right maxillary and periorbital regions after proton therapy, a combined approach consisting of transarterial embolization and subsequent BT was chosen to achieve hemostasis and local tumor control.

Due to the young age, the treatment was performed under general anesthesia. Diagnostic angiography showed a predominantly medial tumor blush via the nasal ethmoid branches and the infraorbital artery; therefore, these vessels were embolized with precipitating hydrophobic injectable liquid (PHIL) 25% after exclusion of collaterals, particularly to the internal carotid artery (ICA). (Fig.2 A).

One hour later, after CT marking for BT, a total of twelve plastic tubes and four Onco-Smarts catheters were implanted in the cheek, caudal and lateral to the orbital cavity, to completely cover the clinical target volume (CTV) (Fig 2.B,C,D and E). We applied a total dose of 28 Gy (7x 4Gy) over four days, 2 fractions per day with minimum intervals of 6 hours by using a 192Ir source taking into account the dose of the proton therapy completed 7 months earlier.

The first fraction was administered on the same day of embolization and implantation, and the remaining six sessions were conducted on the following days without complications.

Regular wound checks showed intact skin without development of macroscopic tumor progress and bleeding.

On 6-week follow up, MRI showed a significant decrease in the size of the tumor in the right orbit (Fig. 1B). Unfortunately, the patient died 2 months after the procedure due to new distant metastases.

Discussion:

Orbital rhabdoid tumors were first described by Rootman in 1989 [4]. The management of RTs is a major challenge in oncology due to its rarity, aggressive behavior and lethality. In a large study conducted from 2005 to 2014 by the European Pediatric Soft Tissue Sarcoma Study Group (EpssG), out of 100 patients, only 1 had a malignant oRT [5]. According to the literature, the presence of the RTSP1 gene, metastases and inability to perform gross total resection are considered unfavorable prognostic factors, placing patients in the high risk group (5-year, OS 32.5± 6.2%). High risk patients are faced with a dismal course and novel

treatment methods are desperately needed for these patients [6, 7]. In a published report from the SIOPE Host Genome Working Group, RTPS 1 has high penetration early in life and is associated with low survival. In addition, among 99 RT patients from the EU-RHAB median overall survival after relapse and progression was 18 weeks, and only 20% were alive one year after relapse and progression. [8].

In our patient, vascular invasion of the tumor and the acute decline in hemoglobin had significantly increased his risk of mortality; therefore, selective intraarterial embolization was performed to prevent further hemorrhage. However, tumor desvacularization is not considered a definite treatment, so BT was started on the same day to achieve a better outcome.

Our pre-interventional embolization effectively reduced the blood supply to the tumor by closing two feeders with Phil 25%. Liquid embolic agents can effectively interrupt vascular tumor supply within a relatively short time even in orbital tumors [9]. Safe and extensive embolization was possible in our case due to previous exenteration of the orbit, so no dangerous collaterals to the ophthalmic artery had to be respected.

Compared to EBRT (External Beam Radiation Therapy), a higher dose can be administered with interstitial BT, while sparing adjacent structures, resulting in better local tumor control and fewer side effects [10]. Due to the short duration of therapy and late toxicity, it is a possible alternative to EBRT in young children.

In a study conducted on a group of 18 children and young adults with relapse of head and neck rhabdomyosarcoma (RMS) with prior EBRT, Vaawerk et al. described the salvage Ablative surgery, MOuld technique brachytherapy and surgical REconstruction (AMORE) approach as an efficient local therapy [11]. Furthermore, as a second-line therapy in young patients with relapsed or refractory orbital RMS, Zloto et al., recommended local radiotherapy or complete wide surgery [12].

To date, several BT techniques have been reported with effective local control and excellent results [13, 14, 15, 16]. In our case, we chose a combination of implants, plastic tubes and Onco-Smarts catheter to achieve perfect dose distribution as well as better protection and handling during the long-term anesthesia in the pediatric ICU.

This approach was ideal in our case because it allowed us to immediately stop the bleeding and decrease the tumor size in a short period of time; thus, the therapy improved the quality of life of our patient in a palliative situation. Because of its minimally invasive nature and the simultaneous achievement of two treatment goals, this procedure could also be considered as a possible alternative at an earlier stage.

Conflicts of Interest: Ansgar Berlis declares as potential conflict of interest proctoring for MicroVention. The other authors have no conflicts of interest to disclose.

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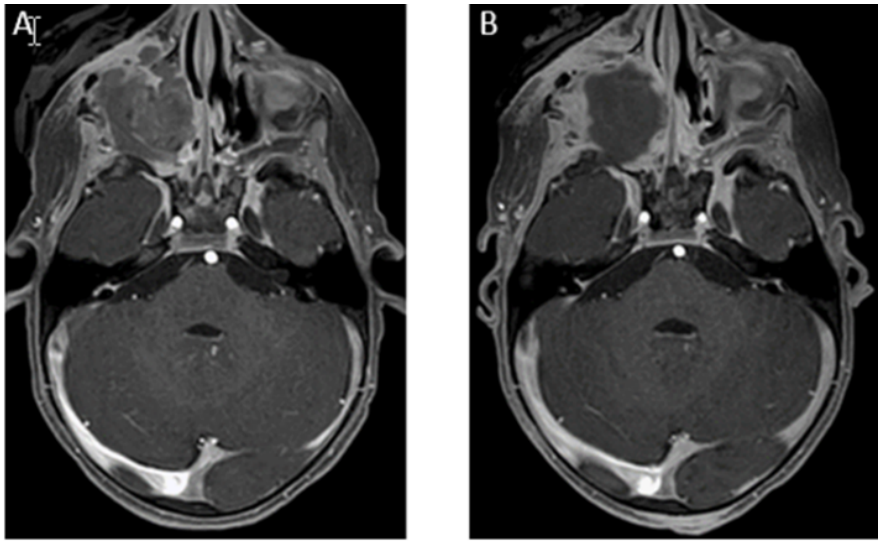
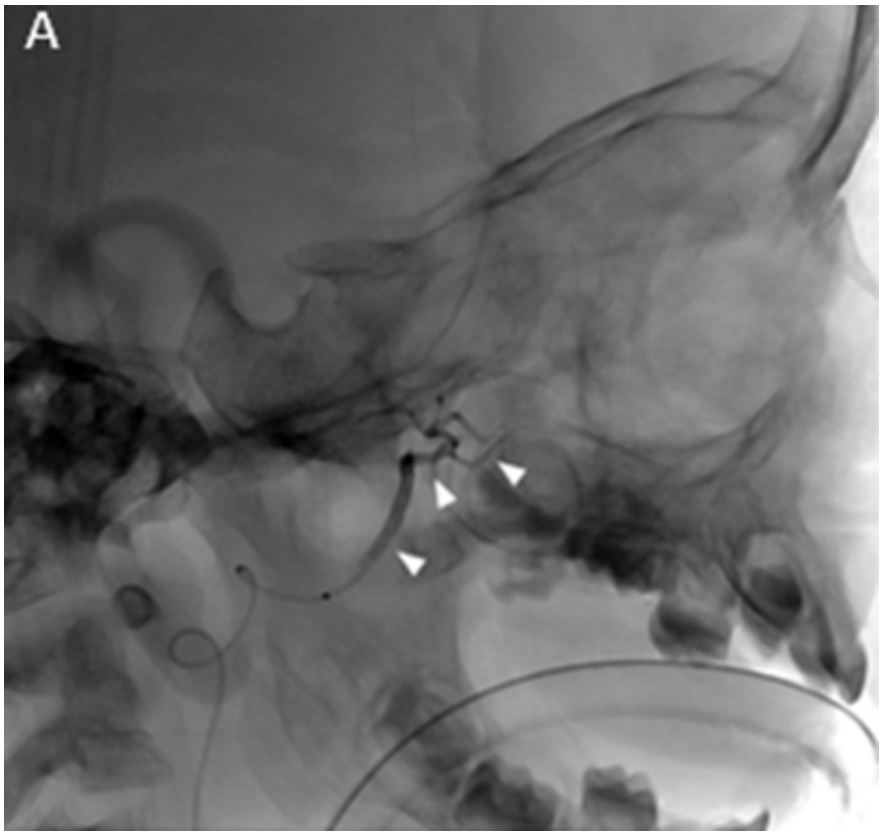


Figure 1. (A) MRI of recurrent tumor in the right orbit. (B) MRI follow-upafter 6 weeks, which showed decrease in tumor size and extensive necrosis.



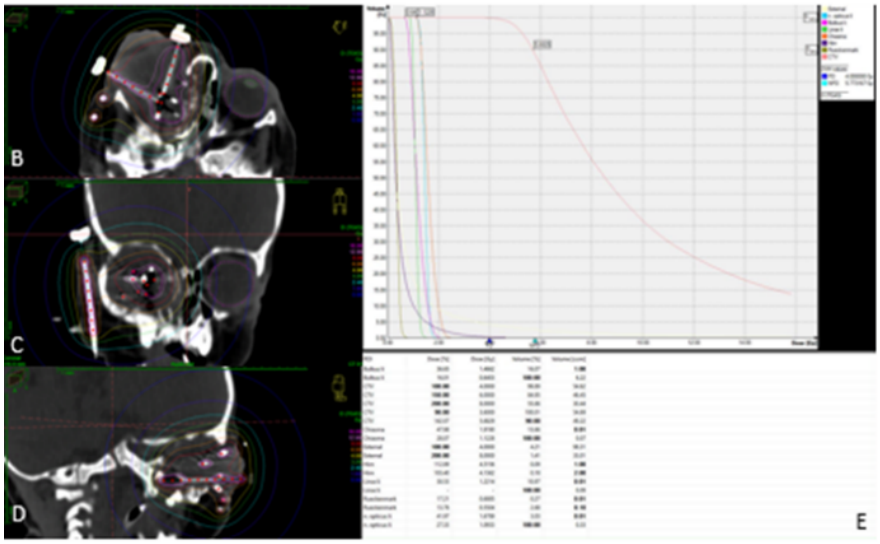


Figure 2. (A) Lateral radiograph after embolization demonstrating embolic material in the infraorbital branch of the right maxillary artery (arrow heads). (B,C andD) Position of implanted Tubs and Oncosmarts catheters and dose distrubutaion.(E) Dose-volume histogram.

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