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Persistent mass after treatment for orbital rhabdomyosarcoma

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ABSTRACT

Purpose: To report a case of orbital rhabdomyosarcoma and highlight the treatment approach to the dilemma of a residual mass.

Observations: An eleven-year-old boy was diagnosed with Stage 1, Group III embryonal rhabdomyosarcoma in the orbit. After completing a 24-week treatment regimen of chemotherapy and radiation, imaging showed a large persistent mass with erosion through the medial wall. It was uncertain whether the erosion was due to radiation osteonecrosis or to advancing tumor, creating a treatment dilemma for the providers. A repeat biopsy was planned. During the procedure, the mass was completely excised due to ease of removal, and the biopsy showed completely treated tumor. MRI surveillance at four years follow up showed that the patient remains tumor-free.

Conclusions and Importance: Rhabdomyosarcoma was once a disease with a very poor outcome, but advances in imaging, chemotherapy, and radiation therapy have improved the prognosis of these patients. What was once a surgical disease treated with morbid resection is now predominantly a medical disease diagnosed with biopsy and treated with chemotherapy and radiation. However, such patients may have a residual mass after completing treatment. This situation presents a challenge, as it may not be clear whether the persistent mass is active tumor or treated tumor. This report describes the presentation and management of such a case in the orbit and demonstrates that a residual orbital mass may remain and represent completely treated tumor.

1. Introduction

Rhabdomyosarcoma (RMS) is a rare pediatric cancer with an incidence of approximately 300 cases per year in the United States.[1] It commonly involves the orbit, as RMS is the most common primary orbital malignancy in children, with about 35 cases diagnosed each year.[2]

Decades ago, orbital RMS was a disease with poor outcomes, but advances in imaging, chemotherapy, and radiation therapy have improved prognosis.[1] The previous treatment strategy was complete surgical resection which often incorporated disfiguring exenteration. Prognosis was poor, with 3-year survival rates of 25%.[3,4] In 1972, the Intergroup Rhabdomyosarcoma Studies Group (IRSG) was formed under the National Cancer Institute to investigate new therapies for RMS.[5] This group launched major clinical trials that demonstrated improved outcomes for patients treated with chemotherapy and radiation. Mutilating surgery became less common, and prognosis for orbital RMS has since improved to a 5-year survival rate of 94% for the embryonal histologic subtype.[6]

Chemotherapy and radiation regimens for orbital RMS are guided by tumor stage and IRSG grouping classification.[7] Due to the proximity of an orbital mass to the eye and other vital structures, complete excision may not be possible, and incisional biopsy with debulking may be performed. In the following reported case, a post-treatment residual mass remained after chemotherapy and radiation, raising the question whether the persistent mass was active tumor or treated residual tumor.

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2. Case report

An 11-year-old male presented with a 3-week history of progressive right eye injection, periorbital swelling, and decreased extraocular movement. During this time, the patient denied pain, but he reported that his eye felt "different." Exam revealed proptosis with a large reddish inferomedial mass visible in the fornix. An MRI of the brain and orbit demonstrated a 2.7 × 2.2 × 3.3 cm enhancing intraconal mass in the right orbit deforming the globe (Fig. 1). An incisional biopsy revealed a friable, unencapsulated mass with prominent vascularity. The tumor was composed of small round blue cells with dense and loose areas of cellularity (Fig. 2). The dense areas contain several cells with ovoid nuclei and abundant polarized eosinophilic cytoplasm with blunted edges, consistent with so-called "strap" cells of skeletal muscle differentiation, amid mostly poorly differentiated tumor cells with scant cytoplasm ("small round blue cells"). Immunohistochemical stains (expression of myogenin and MyoD1) confirmed skeletal muscle differentiation. FISH testing was negative for rearrangement of FOXO1 (13q14) locus. The overall histologic features are diagnostic of embryonal rhabdomyosarcoma.

The patient's tumor was classified as Stage 1, Group III embryonal RMS. A 24-week treatment regimen of chemotherapy (8 three-week cycles of vincristine, cyclophosphamide, and dactinomycin) was initiated with a cumulative cyclophosphamide dose of 4.8 g/m^2. Radiation therapy with a total dose of 50.4 Gy was initiated emergently at the same time as chemotherapy due to rapid regrowth of the mass after biopsy. Five months after the initiation of treatment, CT scan of the orbit showed a large persistent 2.9 × 2.4 × 1.6 cm mass with erosion through the medial wall (Fig. 3). It was uncertain whether this erosion was due to radiation osteonecrosis or to advancing tumor. The persistent size and bone erosion concerned the oncologist, who requested a repeat biopsy.

After tumor board discussion, a combined surgical approach was undertaken with an ENT surgeon first performing endoscopic exploration of the ethmoid sinuses and medial orbit. The sinus and medial wall tissue appeared normal, so the medial periorbita was left intact. Next, via a transconjunctival and transcaruncular approach, the orbital surgeon carefully dissected and completely excised the tumor due to the ease of its removal. The specimen had a more cohesive consistency with less vascularity compared to the original tumor.

Histologically, the specimen consisted of differentiated rhabdomyomatous cells with abundant cytoplasm and small nuclei, reminiscent of a benign mature rhabdomyoma. Many of these cells show pyknotic or crenated nuclei and dense pink cytoplasm, features consistent with apoptotic or karyorrhectic (non-viable) differentiated tumor cells. The cells are embedded in an abundant largely acellular fibroblastic matrix. No poorly differentiated tumor cells or mitotic figures (i.e. residual viable embryonal rhabdomyosarcoma) are identified (Fig. 4). A post-surgical MRI showed residual peripheral enhancement consistent with surgical change. MRI surveillance at four years follow up showed that the patient remains tumor free (Fig. 5).

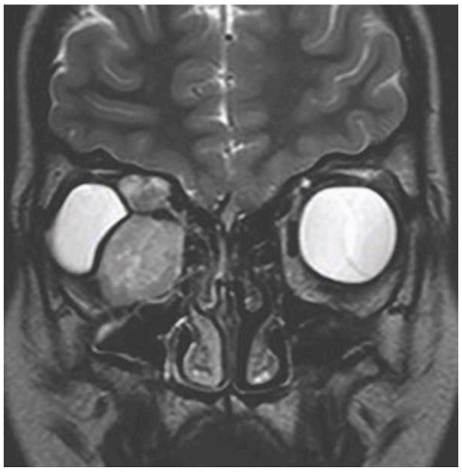

Fig. 1. MRI of the brain and orbit in coronal view at presentation reveals a 2.7 × 2.2 × 3.3 cm enhancing intraconal mass in the right orbit deforming the globe.

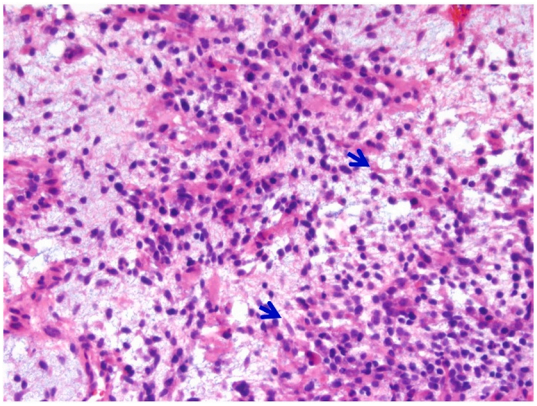

Fig. 2. Photomicrograph of pre-treatment tumor on hematoxylin and eosin (H&E) stain shows dense and loose areas of cellularity, characteristic of embryonal rhabdomyosarcoma. Occasional scattered cells with "strap" cell morphology (arrows), ovoid nuclei with abundant polarized cytoplasm with blunted ends, indicative of skeletal muscle differentiation, were present amid numerous poorly differentiated tumor cells with scant cytoplasm (200x magnification).

3. Discussion

Residual masses after chemotherapy and radiation are common in all sites of RMS. Retrospective investigation of clinical trial participants of RMS in all sites have demonstrated that patients who have a complete response to chemotherapy have a similar event free survival as those with a partial response, suggesting that residual masses overall in RMS do not portend a worse outcome.[8,9] However, their management remains controversial in the literature and in practice.[8–10]

Reports of residual orbital RMS are limited. Older studies of children with residual orbital masses on imaging recommend that tumor resection or orbital exenteration is indicated. In this study, 4 of 7 patients had stable imaging while 3 had progression, but the authors hypothesized that surgical intervention was indicated for all because the status of the tumor could not be known without tissue.[11] More recent investigations suggests biopsy of a residual orbital mass only if there is a clear indication of tumor regrowth as shown by clinical and imaging findings.[6] The authors cite the risk of complications from re-biopsy of a small orbital tumor and difficulty in pathological interpretation of the residual tumor.[6] A more recent report notes that a residual mass in orbital RMS is present in about one-third of patients after standard treatment. Some of these can take years to completely resolve on imaging. Observation can be a reasonable approach with a low threshold to re-biopsy for signs of growth.[12]

In this case, the persistent mass was of significant size, similar to the pre-treatment tumor at presentation. In addition, imaging showed bony erosion, causing concern of an incomplete response to chemotherapy and radiation treatment. Based on these findings, a second incisional biopsy was planned, but the entire mass was excised due to ease of removal. Pathology showed complete treatment response, and no further treatment was indicated.

4. Conclusions

This case report demonstrates that despite adequate treatment for orbital rhabdomyosarcoma, a residual mass may remain in the orbit and

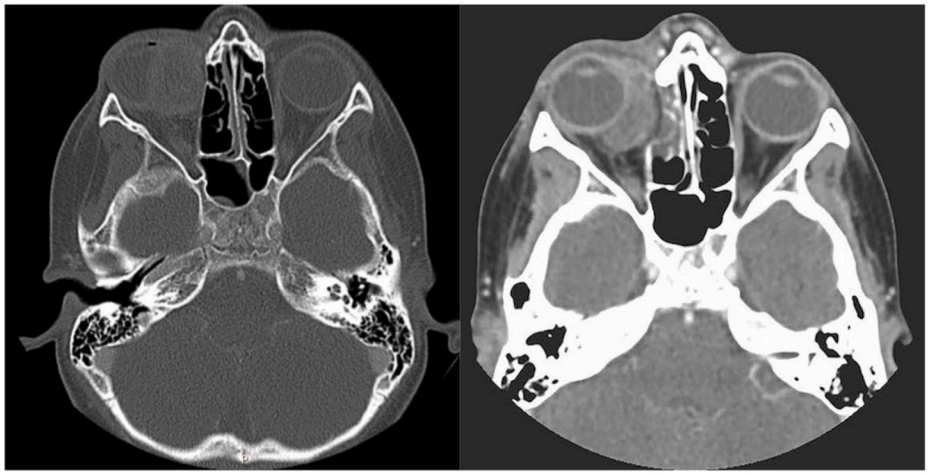

Fig. 3. CT of the orbit shows a large persistent 2.9 × 2.4 × 1.6 cm mass with erosion through the medial wall. A preoperative CT scan shows intact bone.

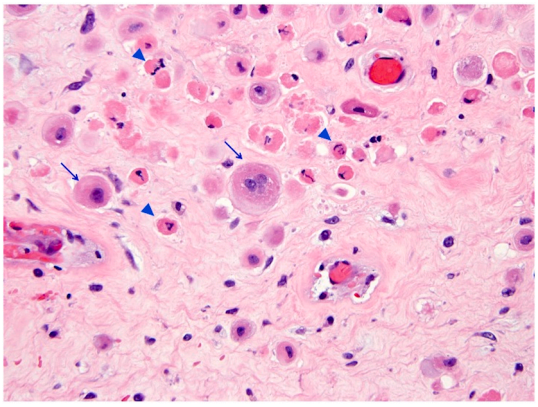

Fig. 4. Photomicrograph of post-treatment tumor on H&E stain shows differentiated rhabdomyomatous cells with abundant cytoplasm (arrows) and frequent apoptotic (non-viable) forms (arrowheads) (100x magnification) in an abundant largely acellular fibroblastic matrix. No undifferentiated or poorly differentiated rhabdomyosarcoma cells were identified throughout the tissue sections.

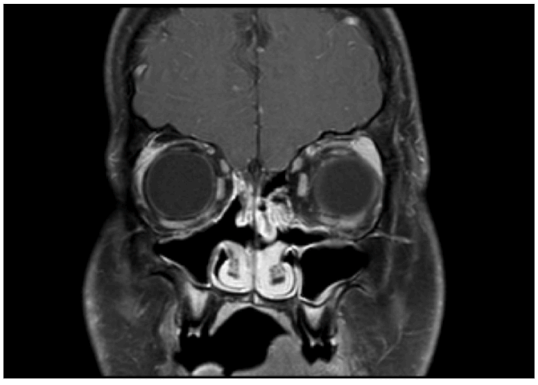

Fig. 5. MRI of the brain and orbit in coronal view shows no evidence of tumor after 4 years.

can represent completely treated tumor composed entirely of mature rhabdomyoblasts. To avoid biopsy, sequential imaging as well as PET scan uptake may give information to guide clinical decision making in these patients.[8,9] However, PET avidity as a surrogate for recurrent or refractory disease remains unclear and close proximity to the brain, which is a PET avid organ, makes interpretation challenging.[10] Further studies may aid in management by assessing the functional imaging characteristics of inactive masses compared to active masses as well as the expected time frame for these residual masses to resolve without surgery.

Patient consent

The patient and the patient's legal guardian consented to publication of the case in writing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

Dr. Sobel is a consultant for Guidepoint. The other authors have no financial disclosures.

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