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Exenteration and Custom Implant Brachytherapy as a Treatment for Recurrent Primary Extraskkeletal Orbital Ewing Sarcoma

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Abstract

A 6-year-old boy initially presented to an outside hospital with a right orbital mass with biopsy positive for translocation involving EWS RNA-binding protein 1 gene and imaging consistent with primary extraskkeletal Ewing sarcoma (ES). There was no evidence of metastatic disease. Patient underwent gross tumor resection and adjuvant chemotherapy (VAdriaC/IE) followed by postoperative 45-Gy proton beam radiation. After 19 months, a solitary infield local recurrence occurred, which was unsuccessfully surgically resected. Thereafter, treatment commenced with irinotecan and temozolomide, and the patient presented to the center of the authors. MRI showed locally recurrent disease without evidence of metastatic disease. Right orbital exenteration was performed, and an orbital mold was fashioned to deliver brachytherapy. There were no complications. The patient had no evidence of recurrent disease at 37-month follow up. This is the first report of orbital implant brachytherapy for recurrent primary ES of the orbit, and an additional report of primary extraskkeletal ES of the orbit, which is a rare primary orbital tumor.

CASE REPORT

Ewing sarcoma (ES), first described by James Ewing in 1921,¹ is a poorly differentiated neoplasm that is considered to be the least differentiated form of the primitive neuroectodermal tumor/ES family of tumors and is the second most common pediatric bone tumor comprising 3% of all pediatric malignancies.^{2,3} These small round cell neoplasms of neuroectodermal origin have a continuum of neurogenic differentiation with peripheral

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neuroepithelioma being the most differentiated and ES representing the least differentiated form.² The cell of origin is controversial; however, current accepted hypotheses propose the progenitor to be a mesenchymal stem cell or early primitive neuroectodermal cell with the ability for multilineage differentiation, resulting in varying degrees of neuroectodermal phenotypic features.^{4,5} Cytogenetic studies have revealed the presence of a recurring, characteristic translocation most commonly involving chromosomes 11 and 22 and the EWS gene.^{6,7}

Ewing sarcoma classically involves the shaft of tubular long bones, ribs, and pelvis and is rare to arise primarily in the orbit, first reported by Harbert and Tabor in 1950.^{3,8–11} Primary extraskeletal or extraosseous (soft tissue) orbital ES is rare with only 3 cases reported in the literature.^{12–14} Recurrent ES carries a poor prognosis¹⁵ with no past reports of successful treatment of recurrent primary ES of the orbit, which often progresses rapidly and has a propensity to metastasize.^{9,10,16,17} The authors report a case of primary extraskeletal ES of the orbit in a 6-year-old boy and successful treatment using a unique multimodal treatment approach. This case report is in compliance with the Health Information Portability and Accountability Act and followed the principles of the Declaration of Helsinki.

CLINICAL HISTORY

A 6-year-old boy with recurrent extraskeletal (extraosseous or soft tissue) ES (biopsy positive for EWS-FLI-1 mutation and CD99) of the orbit was referred for additional therapy. Previously, he had undergone gross tumor resection of a primary extraosseous orbital mass with no evidence of metastatic disease and adjuvant chemotherapy (VAdriaC/IE; vincristine + doxorubicin+ cyclophosphamide+ ifosfamide+ etoposide) followed by postoperative 45-Gy proton beam radiation. After an interval of 19 months, a solitary in-field local recurrence occurred. The child underwent a “piecemeal debulking” surgery, with operative report stating the mass “crumbled” as it was being removed. Thereafter, treatment commenced with irinotecan and temozolomide, and the patient presented to the center of the authors.

CLINICAL COURSE

On examination, Snellen visual acuity was 20/50 in the right with external examination significant for 1.5 mm of ptosis with increased retropulsion of the right eye. A scar was noted above the lash line of the right upper eyelid from the 2 previous orbitotomies. There were no palpable regional lymph nodes on physical examination. Repeat MRI confirmed an extraosseous superolateral right orbital mass with involvement of the adjacent lacrimal gland and superior rectus/levator extraocular muscle complex, which was not hypermetabolic on contemporaneous positron emission tomography scan. Systemic work-up showed no evidence of metastatic disease. Given the recurrence occurred within the prior proton radiotherapy field, the likelihood of cure with radiation alone was low and the risk of complications high; likewise, the prospects for cure with orbital surgery and/or third line chemotherapy were low. The tumor board unanimously favored a combined modality approach incorporating both surgery and radiation.

The authors performed a noneyelid sparing orbital exenteration with removal of an intact periosteum and creation of a custom intraoperative orbital mold. Intraoperatively, the intact periosteum further supported the radiographic origin of this tumor as extraskeletal (soft tissue) rather than arising primarily from bone. No consideration was given to sparing the eyelids, given the initial orbitotomy was performed through the superior eyelid and the high risk of recurrence along this tract.

Following exenteration (Fig. A), a polyvinylsiloxane material (Affinis, Coltène/Whaledent Inc., Cuyahoga Falls, OH, U.S.A.) was injected into the orbital defect (Fig. B) to create an impression. The primary area of disease was highlighted with a tissue marker (Fig. B, inset). The impression was used to fashion a clear polymethylmethacrylate (Lucitone Clear, DENTSPLY Prosthetics, York, PA, U.S.A.) implant (Fig. C). The polymethylmethacrylate mold was loaded with 18 catheters within 2 mm of the surface containing 73 I-125 model 6711 seeds with 275 units total air kerma strength activity (Fig. C, inset). Two weeks after the exenteration, the mold was placed into the orbit (Fig. D) and secured with a silk suture (Fig. D, inset). The implant delivered 5000 cGy to a high-risk region and 3600 cGy to a low-risk region to a depth of 5 mm over 72 hours. There were no complications from the exenteration or brachytherapy. There is slow but continued epithelialization of orbital socket. There is no evidence of contralateral cataract, retinopathy, secondary tumors, or adverse central nervous system effects. The patient has no evidence of recurrent local or systemic disease at 37-month follow up.

DISCUSSION

This is a report of a rare orbital tumor, primary extraskeletal ES of the orbit, and the first curative treatment reported for recurrent primary ES of the orbit using an innovative, multimodal approach. This technique has been previously reported by us to treat recurrent rhabdomyosarcoma of the orbit.¹⁸ ES most commonly affects the long bones of limbs, the ribs, and the pelvis, infrequently arises primarily in the head and neck (1%–4% of all ES), and is rare to involve the orbit with the mandible and maxilla more likely to be affected.¹⁶ Primary extraskeletal (soft tissue) orbital ES is very rare with this case adding to the small number previously reported in the literature.^{12–14} More commonly, orbital ES represents metastases from a distant site.^{3,10,19,20} The addition of chemotherapy to local resection and radiation therapy for the treatment of ES has improved survival.^{14,16} A review of 22 cases of primary orbital ES found 7 patients died within an average of 17.1 months and none survived for more than 5 years.⁹ To date, approximately 25 cases of primary orbital ES have been reported; however, no reports comment on favorable treatment of recurrent disease. The technique described in this report requires the multidisciplinary efforts of ophthalmologists, radiation oncologists, pediatric oncologists, dentists, radiation physicists, radiologists, and nurses. Theoretical complications of this treatment technique include movement of the implant during delivery of the brachytherapy, which was mitigated in this case by placement of a silk suture, orbital hypoplasia, persistent communication with the sinus, and incomplete epithelialization of the orbital socket. It offers clinicians a treatment option for recurrent sarcomas of the orbit, particularly with regard to rhabdomyosarcoma of the orbit, which is more common than ES and over the past decade has shown increased rates of local recurrence with the de-escalation of systemic chemotherapy.²¹

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Fig.

Surgical procedure: orbital exenteration with implant brachytherapy. **A**, Right orbit status after exenteration. **B**, Polyvinylsiloxane material injected into orbital socket to form impression, and (**inset**) area with most extensive disease was highlighted intraoperatively. **C**, Processed clear polymethylmethacrylate mold with 18 mock catheters in position, and (**inset**) carrier loaded with actual I-125 radiation catheters. **D**, Insertion of custom brachytherapy implant into orbit, which was secured with a silk suture (**inset**).