Mohs Micrographic Surgery for Primary Cutaneous Ewing Sarcoma

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Abstract
Primary cutaneous Ewing sarcoma (PCES) is an exceedingly rare neoplasm with less than 100 cases reported in the literature. Herein we present a case of PCES that developed in a 45-year-old male and was successfully managed with Mohs Micrographic Surgery (MMS) and adjuvant radiation therapy without chemotherapy. The patient had no evidence of recurrence in the past 24 months of follow-up. We believe this to be the first reported utilization of MMS in the management of PCES.

Case Report
A 45-year-old male presented with a three-month history of an asymptomatic, enlarging lesion on the left anterior shoulder. The lesion was a dome-shaped, red nodule measuring one-centimeter in diameter. Histopathology demonstrated a malignant small round cell neoplasm (Figure 1) with strong, diffuse CD99-positivity. Other immunohistochemical markers, including S100, HMB-45, CK20, CD56, chromogranin, and desmin were all negative, ruling-out entities such as melanoma, Merkel cell carcinoma, and neuroblastoma. With exclusion of other diagnoses, morphologic and immunohistochemical findings were consistent with Ewing sarcoma.

Upon follow-up (Figure 2A), no lymphadenopathy was noted on examination. Pre-operative positron emission tomography – computed tomography (PET-CT) did not detect any abnormalities in the lymph nodes or internal organs, and bone marrow aspiration was negative for involvement. After ruling-out an internal source of metastasis, the final diagnosis was primary cutaneous Ewing sarcoma (PCES).

The patient was presented with various treatment options, and ultimately Mohs micrographic surgery (MMS) with adjuvant radiation was selected as the ideal therapeutic approach. The patient underwent MMS with clearance of tumor margins in one stage (Figure 2B). Permanent sections confirmed eradication of the tumor. The defect was closed in a linear manner (Figure 2C) in order to preserve the architecture for future imaging and potential sentinel lymph node biopsy (SLNB).

Radiotherapy to the tumor bed was performed with a single dose of 55.80 Gy, without concurrent radiation of the ipsilateral axillary and supravacular lymph node basins. We elected not to pursue adjuvant chemotherapy due to a lack of systemic involvement and recent reports suggesting that risks of treatment sequelae outweigh the risk of recurrence of tumors that are adequately excised. The patient has been examined every three months and surveyed with an annual MRI for the past two years. The patient has exhibited no evidence of recurrence over the past 24-months post-operatively (Figure 2D). We report the first case of PCES successfully managed with MMS and adjuvant radiation with no evidence of recurrence.

Discussion
PCES belongs to the family of neuroectodermal tumors that includes Ewing sarcoma, primitive neuroectodermal tumor (PNET), and Askin tumor of the chest wall (1). The osseous form of Ewing sarcoma is the second most common primary bone tumor of children and adolescents. Despite intensive chemotherapy approaches, Ewing sarcoma of the bone carries a poor prognosis, with five-year survival rates averaging 60.2% (2). In contrast, PCES, while much rarer, carries a more favorable prognosis compared to its osseous counterpart, with ten-year survival rates reaching 91% (1). This difference in prognosis can be attributed to earlier detection and a smaller tumor burden resulting in lower rates of metastasis. Recent studies also suggest that distinct cells of origin and different cooperative mutations may alter the metastatic potential of extraskeletal variants of Ewing sarcoma, though these theories require further analysis (2).

All forms of Ewing sarcoma exhibit similar biology. Tumors are composed of small round basophilic cells that express CD99 – a product of the MIZ2 gene – in a characteristic membranous pattern (3). A chromosomal translocation t(11;22) between the EWSR1 gene on chromosome 22 and the FLI1 gene results in a fusion oncogene (1). Notably, this translocation is not specific to Ewing sarcoma; however, after ruling-out other CD99-positive entities, Ewing sarcoma remains as a diagnosis of exclusion.

Given the rarity of PCES, management recommendations have been extrapolated from experience in treating Ewing sarcoma of the bone. First-line therapy is extensive surgical removal followed by several rounds of multi-agent chemotherapy, and adjuvant radiotherapy for inadequate excised tumors (5). Given the dearth of cases and knowledge about PCES, we question the utility of such an aggressive strategy in the treatment of a localized cutaneous tumor. A recent publication described a large PCES limited to the foot with no systemic involvement that was successfully excised with 1.5 cm margins and no adjuvant chemoradiation (4). Further, a review of 61 patients by Delaplace, et al. emphasized the increased morbidity and mortality in patients treated with systemic chemotherapy, and suggested a less toxic treatment approach, given the epidemiological and prognostic differences between PCES and Ewing sarcoma of the bone (1). Collier et al. found a 90% survival rate among PCES patients who received excision and chemotherapy, while patients who had excision alone had a survival rate of 85.7% (5). These new data suggest that chemotherapy may not be necessary for tumors that can be managed with local therapy. However, without adequate local control, survival dropped to 66.7% in chemotherapy patients and 0% survival in those without chemotherapy, highlighting the importance of local tumor control (5).

Given these recent data suggesting a more conservative management approach to PCES, we believed MMS to be ideal for our patient. We achieved clearance of tumor margins in one stage and permanent sections confirmed tumor eradication. In concert with oncology, we elected to incorporate a single dose of post-operative radiotherapy to further ensure local tumor suppression. We chose not to pursue chemotherapy given the recent data suggesting that the risk of long-term sequelae of chemotherapy may outweigh the risk of recurrence or metastasis for small tumors that are completely excised.

Conclusions
To our knowledge, this is the first case of PCES successfully treated with MMS. After two years of follow-up, our patient remains disease-free. We believe this confirms our hypothesis that PCES should be approached differently from its osseous counterpart. Further cases will be necessary to determine if MMS is an appropriate therapeutic modality in the management of PCES.

References