Ewing Sarcoma of the 9th Rib Subsequent to Pediatric Leukemia: A Case Series

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Ewing Sarcoma of the 9th Rib Subsequent to Pediatric Leukemia: A Case Series

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Abstract

- Ewing Sarcoma is an aggressive malignancy that accounts for approximately 2% of cases of childhood cancer, most commonly occurring in adolescent and young adult patients.
- We report two pediatric patients in northeast Pennsylvania, who developed secondary Ewing Sarcoma of the 9th rib within 5 years of primary childhood leukemia diagnoses.

Introduction

- Ewing sarcoma (EWS) features:
  - High-grade sarcoma described as a small round cell tumor of bone and soft tissue.[1,2]
  - Hematogenous spread, with lung, bone, and bone marrow being the most common metastasis.
  - Rarely reported as a secondary malignant neoplasm after treatment of childhood cancer.
- Secondary neoplasms occur more frequently among females, patients older at time of cancer diagnosis, and those treated with radiation therapy.[3]
- Further investigation of secondary EWS is warranted to identify potential risk factors and emphasize the importance of surveillance cancer screening.

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Case Descriptions

PATIENT 1

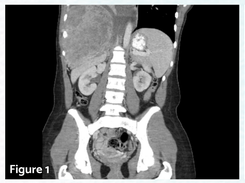
- 15-year-old female with prior history of precursor B cell ALL treated on study AALL0932 (cumulative 75 mg/m2 of anthracyclines) in remission now 46 months off therapy who presented with right-sided chest pain and dyspnea.
- CT scan obtained was notable for malignant mass (Fig. 1)

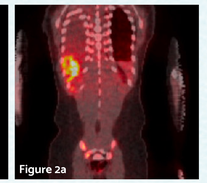
CLINICAL COURSE

- Biopsy revealed a small round blue cell tumor consistent with EWS.
- Flow cytometry was notable for EWSRI (22q12) gene rearrangement.
- PET/CT scan revealed localized disease (Fig. 2a, 2b).
- Treated on study AEWS0031 (regimen B2) as well as proton radiation (5580 cGy).

PATIENT FOLLOW-UP

- 14 months later patient endorsed new right-sided chest and wrist pain with new findings on surveillance PET/CT (Fig. 3).
- Biopsy confirmed relapsed EWS positive for EWSR1 rearrangement.
- Underwent 7 cycles of individualized salvage therapy with temozolomide and irinotecan with progression of her right lung mass.
- Enrolled in the pediatric MATCH (Molecular Analysis for Therapy Choice) trial (COG APEC1621) with no match identified.
- Significant progression and underwent palliative radiation with 60% decrease in tumor size.





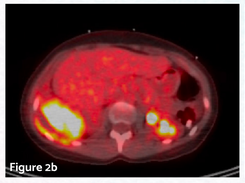


Figure 1: CT scan with large malignant mass in the right inferior hemithorax involving the right chest wall and possibly the hemidiaphragm.

Figure 2: PET/CT scan
(A) Fused coronal image revealing radiotracer uptake in the right ninth rib consistent with active malignancy.
(B) Fused axial image with similar uptake in the right ninth rib.

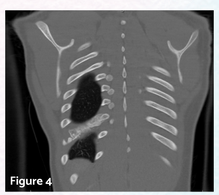
Figure 3: New metabolically active tumor within a 7.3x8.2x7cm soft tissue mass in the central and posterior aspects of the right lung. Previous lesions stable and no other areas of radiotracer uptake.

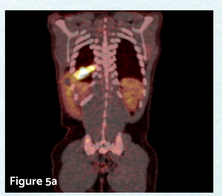
PATIENT 2

- 14-year-old male with prior history of AML non-M3 subtype treated on study AAML1031 protocol (received cumulative 492 mg/m2 of anthracyclines) in remission now 5 months off therapy who presented with worsening back pain.
- CT scan obtained was notable for expansive lesion concerning for malignancy (Fig. 4).

CLINICAL COURSE

- Biopsy revealed a small round blue cell tumor.
- Flow cytometry suspicious for a non-hematolymphoid tumor consistent with EWS.
- PET/ CT revealed localized disease (Fig. 5a, 5b).
- Treated on study AEWS0031 including radiotherapy and underwent wide surgical excision of the tumor with negative margins, but viable tumor on the pleural margin.
- Completed treatment without evidence of disease on follow-up imaging.





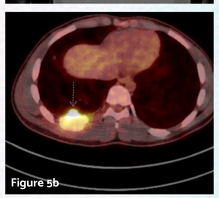


Figure 4: CT scan revealing expansile permeative lesion with periosteal reaction involving the right posterior 9th rib

Figure 5: PET/CT scan
(A) Fused coronal image revealing radiotracer uptake similar to patient 1.
(B) Fused axial image with similar uptake.

Discussion

- This case series illustrated two pediatric patients with findings of secondary EWS of the rib within 5 years of treatment completion for primary leukemia.
- According to the CCSS, incidence of EWS after ALL was 1/49 (2%) and AML was 2/49 (4%) in 5-year survivors.
- Childhood cancer survivors have a nine-fold increased risk of developing secondary sarcoma compared to rates of sarcoma in the general population.[4]
- Spunt et al found that 4 of their 6 secondary ESFT developed in the bone, most commonly the rib.[2]
- Risk factors for subsequent bone sarcomas include younger age at time of cancer diagnosis (<4 years), radiation therapy, and exposure to both anthracyclines and alkylating agents.[4,5]
  - Both patients were older at time of diagnosis and did not receive radiation therapy.
  - Patient 2 received >300 mg/m2 cumulative anthracycline dosage.
- Moke et al found a significantly increased risk of secondary malignancy among patients who were obese both at the time of diagnosis and at the end of treatment.[6]
  - Patient 1 was at the 92nd percentile for BMI whereas patient 2 was at the 93rd percentile.
- Both patients resided in Northeast Pennsylvania with abundant hydraulic fracturing (or "fracking") wells that have been linked to the release of carcinogens.[7]
  - Others have reported locally increased incidence of rare EWS.[8]

Conclusion

- This case series emphasizes the importance of continued surveillance and regular cancer screening for childhood cancer survivors.
- Further investigation is warranted to evaluate environmental factors that may increase the risk of EWS.

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