A 10-Year-Old Girl with Fever and Labored Breathing

Luis Seguias, MD; Adrienne McMillan, MD; and Melissa Cossey, MD

A 10-year-old previously healthy white female with a history of subjective fever and labored breathing for the previous 24 hours was referred to our hospital by her primary care provider. The patient reported she had experienced chest discomfort and general malaise for the previous 2 days; her parents had noticed decreased activity and perceived easy fatigability during this period. Her mother also stated that the patient had been sleeping sitting up to relieve symptoms. Review of systems was negative for nasal congestion, cough, or decreased appetite. Her parents denied any past medical history of asthma, heart disease, or recurrent respiratory infections. There were no sick contacts at home and her immunizations were up-to-date.

Physical examination upon admission revealed a well-developed and well-nourished adolescent girl in mild respiratory distress. Her initial vital signs showed fever (temperature: 103.4°F); tachypnea (respiratory rate: 36/minute); tachycardia (pulse: 152/min); normal oxygen saturation (pulse oximetry: 97%); and a widened pulse pressure (blood pressure: 126/55). HEENT examinations were normal. Cardiac auscultation was unremarkable. A chest inspection exhibited mild intercostals retractions. A lung examination was notable for diminished breath sounds/poor aeration over the entire left lung field without wheezing or rales. An abdominal exam showed no organomegaly or masses on palpation. The patient was alert and active with no neurological deficits.

On the day of the admission, a chest X-ray was performed. A large left pleural effusion was noted with shift of the mediastinum to the left (Figure 1, see page 53). A chest ultrasound was obtained to better delineate the effusion. It showed extensive left parenchymal microcystic changes that suggested necrotic lung tissue and early abscess formation. A mild to moderate pleural effusion was again reported. She was admitted with the presumptive diagnosis of infectious necrotizing pneumonia and subsequent-
ly started on dual antimicrobial coverage with ceftriaxone plus clindamycin to cover suspected pathogens, including *Streptococcus pneumoniae* and *Staphylococcus aureus*.

The patient was discharged home after a 5-day course of intravenous antibiotics. Upon discharge, she had been afebrile for 48 hours and no longer had any respiratory distress. Her parents agreed to continue with a 4-week oral antibiotic regimen of high-dose amoxicillin/clavulanate with follow-up chest imaging to be performed and reviewed by her pediatrician.

**LUNG MASS IN AN OLDER CHILD**

Two weeks later, the patient was readmitted for further diagnostic evaluation based on persistent chest X-ray findings, despite the resolution of her presenting symptoms.

A follow-up magnetic resonance imaging (MRI) study with contrast showed a large cystic mass in the left hemithorax, suggestive of extra osseous cystic sarcoma (Figure 2). A lung biopsy microscopic description reported small rounded cells with a high nuclear-cytoplasmic ratio. Concurrently, a positive immunohistochemical surface stain for glycoprotein p30/32MIC2 (CD99) suggested an extra-skeletal Ewing’s sarcoma. Conversely, reverse transcriptase polymerase chain reaction (RT-PCR) did not confirm the usual translocation involving Ewing’s sarcoma breakpoint region (*ESWR1*) gene and Friend leukemia integration 1 transcription factor (*FLI1*) gene. Alternative gene fusion FUS/ERG specific assay for Ewing’s sarcoma family tumors (ESFT) was not performed. An additional metastatic workup was negative.

![Figure 1. Chest X-rays of a 10-year-old girl with a large left pleural effusion and shift of the mediastinum to the left. Source: Seguias L, et al. Reprinted with permission.](image1)

![Figure 2. MRI with contrast showing a large cystic mass in the left hemithorax that is suggestive of extra osseous cystic sarcoma. Source: Seguias L, et al. Reprinted with permission.](image2)
Case Challenge

DISCUSSION

The patient was started on a novel combination protocol of chemotherapy for localized Ewing’s sarcoma (National Cancer Institute/Clinical Trials (AEWS1031): Phase III Randomized Study of Adding Vincristine, Topotecan, and Cyclophosphamide (VTC) to Standard alternated vincristine, doxorubicin, cyclophosphamide (VDC) plus ifosfamide and etoposide (IE) [VDC-IE] Chemotherapy in patients with Non-Metastatic Extracranial Ewing’s Sarcoma).

Ewing’s sarcoma (ES) of the bone and primitive neuroectodermal tumors (PNET) constitute (ESFT). ES of the bone, although rare, is still the second most prevalent primary malignant bone tumor after osteosarcoma. PNET has been described at other anatomical sites, such as the lung, kidney, uterus, ovaries, pancreas, and colon.1

To date, fewer than 11 cases of primary ES of the lung have been reported in the literature. There is a slight epidemiological male predominance, with a mean age close to the third decade of life. ES mostly affects whites.

In ESFT, regional pain is the most common clinical manifestation initially. A palpable mass can be present. Constitutional symptoms such as fever, general malaise, and weight loss may be experienced in late stages of the disease. Unfortunately, one-quarter of these patients have evidence of metastatic involvement at the time of the diagnosis.2

Histology of classic ES is characterized by conglomerate, small primitive rounded cells. The malignant cells have scanty cytoplasm and round nuclei with homogenous granular chromatin on hematoxylin and eosin stain. In 95% to 100% of ES cases, a distinctive cell-surface glycoprotein p30/32MIC2 (CD99) expression can be demonstrated by immunohistochemistry using monoclonal antibodies to this antigen.3

ESFTs are classically defined by the presence of nonrandom translocations leading to the fusion of the EWSR1 gene to an EWSR1-related gene, the most common of which are FLI1 at 11q24 and ERG at 21q22.345 The EWSR1/FLI1 reciprocal chromosomal translocation (11:22)(q24;q12) is detected in 85% of the ESFT cases.3

Currently, treatment for ESFT comprises systemic chemotherapy and surgery with or without radiotherapy. Until the introduction of combination chemotherapy, the 3- to 5-year survival rate for patients with ES was less than 10%. Current overall 5-year survival rate is about 60% among cases of ESFT.6

Results from several clinical trials have shown improved survival for patients without metastases who received a chemotherapy combination called VDC-IE, in which the administration of VDC is alternated with the administration of IE, and by reducing the interval between cycles of VDC-IE.5

The most important prognostic factor for patients is whether the disease is localized or metastatic.

FOLLOW-UP

There have been no major developments. The child is still receiving chemotherapy.

REFERENCES


Diagnosis:
Localized Ewing’s Sarcoma

Ewing’s sarcoma is the second most prevalent primary malignant bone tumor after osteosarcoma.