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Primary extraosseous Ewing sarcoma of the lung: Case report and literature review

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Ewing sarcoma is the second most common primary osseous malignancy in children and young adults. However, infrequently, it can arise outside the skeletal system; rarer still, it can originate within the lung parenchyma. In this case report, we describe such a case in a 23-year-old male. We also review the literature to summarize imaging findings for this rare malignancy.

Introduction

Ewing sarcoma, first described in 1921 (1), represents the second most common primary osseous malignancy in children and young adults, surpassed in incidence only by osteogenic sarcoma (2). Common locations include the axial skeleton, as well as the diaphyseal portion of long bones, most commonly those of the lower extremities (3). However, extraskeletal Ewing's sarcoma, first described in 1969 (4), represents a less frequent but histologically similar entity that can originate within a wide array of extraosseous/soft-tissue locations, including the retroperitoneum, chest wall, or paravertebral space (5). Primary pulmonary involvement is rare; to our knowledge, only about twelve cases have been described in the literature.

Case report

A 23-year-old male presented at an outside institution with cough. A radiograph was recommended but not obtained due to lack of insurance. Two months later, the patient developed hemoptysis with interval worsening of his cough, as well as worsening dyspnea on exertion. Five months later, significant weight loss of 9 pounds over a 2-month period was also noted. During this time, he received several courses of antibiotics, with no significant improvement in clinical symptoms.

A chest radiograph was eventually obtained (Fig 1A). Partial opacification of the right hemithorax was noted, spanning the pleural and mediastinal surfaces. A noncontrast CT of the chest was subsequently performed (Fig. 1B). A large soft-tissue mass was noted within the right hemithorax, centered within the lung parenchyma and demonstrating diffuse, speckled internal calcifications. The mass insinuated within the mediastinum, with significant mass effect upon the right mainstem bronchus; it also extended to the pleural surface and chest wall, however without definite evidence for invasion.

CT-guided biopsy yielded an undifferentiated malignancy. Metastatic workup, including MRI of the brain, CT of the abdomen and pelvis, and a nuclear medicine bone scan demonstrated no evidence for distant metastases. The patient was then transferred to our facility for continued metastatic workup and management. PET/CT confirmed a metabolically active mass (SUV = 14.7) in the right hemithorax within the lung parenchyma, with no additional foci of increased radiotracer activity to suggest metastatic disease (Fig. 1C).

Review of the final pathology of the original biopsy specimen at our institution demonstrated densely packed neoplastic cells in a background of fibromyxoid stroma with patchy hemorrhage, fibrosis, and geographic necrosis (Fig. 2). The neoplastic cells showed strong membranous CD99 (O-13) immunoreactivity, characteristic of Ewing's sarcoma/primitive neuroectodermal tumor (PNET). The EWSR1 gene rearrangement was demonstrated by fluorescence in-situ hybridization studies. The patient was initially started on chemotherapy as per Ewing sarcoma BAT pro-

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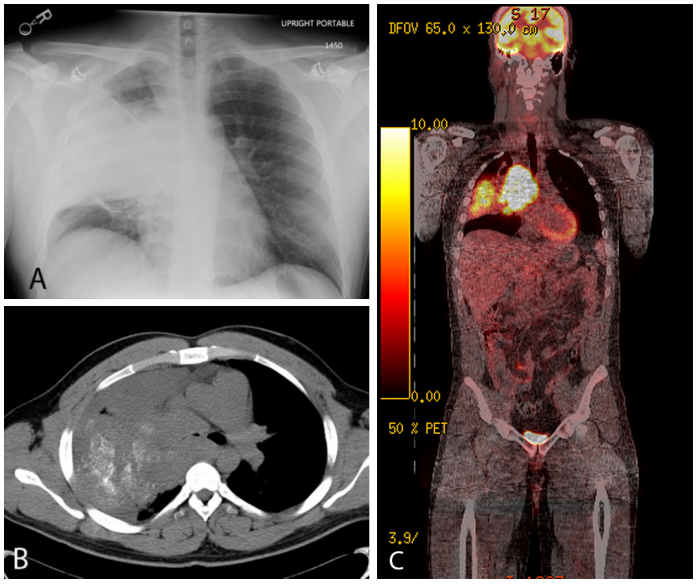

Figure 1. 23-year-old male with extraosseous pulmonary Ewing sarcoma. Initial presentation. (A) Chest x-ray demonstrates partial opacification of the right hemithorax; a triangular, dense opacity in the mid-lung extends from the right hilum to the chest wall. (B) A noncontrast chest CT at the level of the right mainstem bronchus demonstrates a large, slightly hypodense soft-tissue mass in the right upper lung with internal foci of hyperattenuation representing calcifications. The mass abuts, but does not invade, the pleural space and chest wall. Note the absence of adjacent osseous destruction. However, the mass does insinuate within the mediastinum, with significant mass effect on the right mainstem bronchus, which is nearly completely occluded. Small ipsilateral effusion was also present, though not demonstrated in this image. (C) PET/CT confirms the presence of an FDG-avid mass in the right mid-lung invading the right upper mediastinum, with no additional foci of radiotracer uptake to suggest metastatic disease.

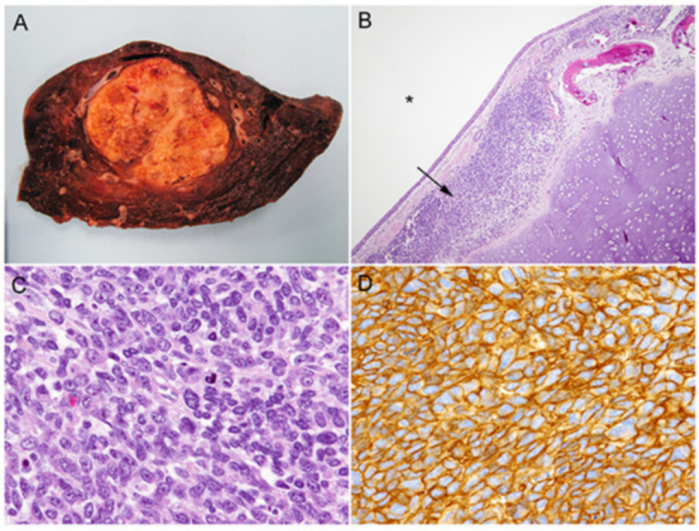

Figure 2. 23-year-old male with extraosseous pulmonary Ewing sarcoma. Pathology of the tumor. A. A nodular, focally necrotic, and calcified tumor wtihin the right upper lobe. B. Nests of tumor cells infiltrate the subepithelial space of a bronchus (H&E, X10). C. Higher manigification shows primitive small-to-medium cells with focally increased mitotic figures (X400). D. Characteristic CD99 immunoreactivity of the cell membranes (X400).

tocol. After six cycles of chemotherapy, there was significant decrease in size of the mass (Fig. 3A), and the patient underwent right upper lobectomy, right mainstem bronchus resection, right sixth rib resection, and mediastinal tumor resection. Chemotherapy was resumed, along with radiation. It has now been six months since initial diagnosis, and followup CT imaging demonstrates post-surgical changes with no evidence of disease recurrence (Fig. 3B).

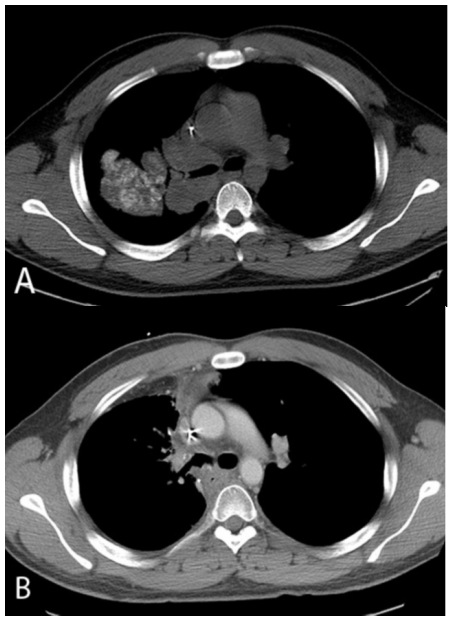

Figure 3. 23-year-old male with extraosseous pulmonary Ewing sarcoma. Post-therapy. (A) During pre-operative chemotherapy, contrast-enhanced chest CT was obtained. Image at the level of the carina demonstrates significant interval reduction in size of the mass. The right mainstem bronchus is no longer occluded, though it remains narrowed. Subsequently, surgical resection was performed, and followup contrast-enhanced CT was performed 3 months postoperatively. (B) Contrast-enhanced CT after surgery demonstrates no evidence of residual disease. Mild irregularity along the posterior wall of the right mainstem bronchus suggests granulation tissue at the surgical site; the right mainstem bronchus is otherwise widely patent.

Discussion

The Ewing sarcoma family of tumors (ESFT), characterized histologically by primitive small round cells of neuroectodermal origin, includes classic osseous Ewing sarcoma, PNET, Askin tumor (Ewing sarcoma of the chest wall) and extraosseous (soft-tissue) Ewing sarcoma (6). Extraskeletal Ewing sarcoma represents a small subset of the ESFT, though the exact incidence has not yet been ascertained (7). While more frequent sites of ESFT include the retroperitoneum, paravertebral space, and chest wall (5), specific organs of involvement described in the literature also include the kidneys, pancreas, colon, uterus, and ovaries (6). The prognosis for treated patients has been reported to be similar to that for Ewing sarcoma patients (8). The lung represents a rare organ of primary

Article	Presence of solitary mass	Age	Sex	Mass size (cm)	CT appearance	Calcifications	Pleural effusion
Catalan et al (14)	Yes	29	M	16 x 15 x 13	Heterogeneous	Yes	Yes
Tsuji et al (15)	Yes (2 cases)	25 15	F M	3.6 x 2.7 7.0 x 8.0	Case 1: Noncontrast CT: heterogeneous Case 2 : Not described and cannot be seen on image presented in lung window	No in both cases	Case 1, yes Case 2, no
Imamura et al (16)	Yes (2 cases)	41 30	M F	5cm 4.2 x 5.0 cm	Case 1: Homogeneous and hypoenhancing on contrast-enhanced CT Case 2: Heterogeneous and hypoenhancing on contrast-enhanced CT	No in both cases	No in both cases
Mikami (17)	Yes	17	F	5.5 x 5	Described as homogeneous; only window CT image provided	No	No
Paik (18)	Yes	28	F	9.2 x 8.4 x 6.3	Heterogeneous and hypoenhancing on contrast-enhanced CT	Yes	Yes
Takahashi (6)	Yes	8	M	N/A	Heterogeneous and hypoenhancing on contrast-enhanced CT	No	Yes
Lee (19)	Yes	67	M	4	Heterogeneous and partially enhancing on contrast-enhanced CT	No	Yes
Hancorn et al (10)	Yes	44	M	8.4 x 8.4 x 10.1	Homogeneous and hypoenhancing on contrast-enhanced CT	No	Yes
Suarez et al (5)	Yes	22	F	5 x 4	Heterogeneous and hypoenhancing on contrast-enhanced CT	No	Yes
Ichiki (20)	Yes	42	M	3.0 x 2.6	Homogeneous and hypoenhancing on contrast-enhanced CT	No	Yes

involvement, to our knowledge being described about twelve times in the literature. Initially reported in 1989 (9), it occurs in a wide age distribution spanning the pediatric and adult age range, with the mean age of onset around 20 years as compared to 15 years for osseous Ewing (5), and occurring more commonly in males than in females (6, 10).

Imaging characteristics of extraskeletal ESFT have been described in the literature, although characterization of pulmonary Ewing sarcoma has been limited.

In an attempt to identify common radiological features of pulmonary Ewing sarcoma, we reviewed the CT imaging findings described in prior case reports, or present on the images provided, and summarized the results in the table.

In all cases, a solitary mass was predominantly circumscribed or well-defined in nature. In the majority of cases (7 out of the 11 cases in which CT findings were described or could be evaluated), the lesion demonstrated a heterogeneous appearance, with regions of low density suggesting necrosis. For the majority of patients, a contrast-enhanced

CT was performed, with the mass usually showing a hypoenhancing pattern. Amorphous calcifications (as seen in our case) were also described in two previous cases. Ipsilateral pleural effusion was noted in three cases, while adjacent invasion (either mediastinal or chest wall involvement) was seen in two cases. In summary, primary pulmonary Ewing sarcoma most commonly presents as a circumscribed solitary mass with heterogeneous CT appearance both on noncontrast as well as contrast-enhanced CT. Occasionally, intralesional calcifications or an ipsilateral pleural effusion may be seen. Infrequently, a mass may demonstrate evidence of invasion of adjacent structures.

As for the differential diagnosis of solitary lung lesions, primary pulmonary neoplasms in children are rare; secondary malignancy, from primary tumors such as Wilms tumor, osteosarcoma, or rhabdomyosarcoma, are far more common (11)—however, these usually present with multiple lesions. Primary pulmonary neoplasms in children are more frequently malignant than benign (12). Carcinoid represents the most common primary pulmonary malignancy in children. Bronchogenic carcinoma and pulmonary blastoma represent the second and third most frequent pediatric primary pulmonary cancers, respectively. Sarcomas represent an even rarer subset of primary pulmonary malignancy in children. In all age ranges, the most frequently encountered thoracic sarcomas include angiosarcoma, rhabdomyosarcoma, sarcomatoid mesothelioma, and leiomyosarcoma, but those known to affect the pediatric population include rhabdomyosarcoma, Ewing sarcoma, PNET, and endobronchial fibrosarcoma (13).

While the diagnosis of extraosseous pulmonary Ewing sarcoma relies on pathologic features, awareness of this clinical entity can help the radiologist broaden the differential diagnosis of primary lung masses, leading toward early diagnosis, comprehensive staging, and prompt treatment.

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