Radionuclide Detection of Primary Pulmonary Osteogenic Sarcoma: A Case Report and Review of The Literature

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A healthy elderly white man was admitted for right inguinal herniorrhaphy. Preoperative chest x-ray revealed a large mass in the lower lobe of the left lung. CT-directed needle biopsy was nondiagnostic. Technetium-99m methylene diphosphonate (^{99m}Tc-MDP) bone scan revealed intense soft-tissue activity in the lower left hemithorax with no evidence of abnormal activity in the osseous skeleton. Because of the degree of uptake in the lesion, a presumptive diagnosis of extraosseous osteogenic sarcoma was made. The patient had a left lower lobectomy and the lesion was diagnosed as an osteosarcoma of primary pulmonary origin.

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Extraosseous osteogenic sarcoma is very rare and primary pulmonary osteogenic sarcoma exceedingly rare. There have been only seven cases described to date, none of which has been demonstrated scintigraphically (*1–5*). Here we present a case which was presumptively diagnosed by its unique appearance on bone scan and confirmed histologically.

CASE REPORT

A 70-yr-old man was admitted to Stanford University Medical Center in January 1989 for elective repair of a right inguinal hernia. He was asymptomatic. Admission chest radiograph (Fig. 1) revealed a large pleural based soft-tissue mass in the superior segment of the left lower lobe, which was not present on chest roentgenogram in August 1986. A computed tomograpy (CT) scan of the thorax (Fig. 2) confirmed the presence of this left lung mass but no hilar or mediastinal lymphadenopathy. CT-guided transthoracic needle biopsy showed a mixed cellular stroma with atypical cells suggestive of carcinoma. A magnetic resonance imaging (MRI) scan of the brain was normal as were complete blood count and screening chemistries.

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Technetium-99m-methylene diphosphonate (^{99m}Tc-MDP) bone scan showed a markedly intense focus of activity in the lower left hemithorax on whole-body images (Figs. 3 and 4). Apart from some minor changes in joints which were thought to be degenerative in origin, the bone scan was normal. Because of the intense radiopharmaceutical uptake in the chest lesion, suggesting marked osteoblastic activity, a diagnosis of osteogenic sarcoma was postulated. Fiberoptic bronchoscopy was negative. At operation on 2/13/89 a 6-cm tumour was found in the superior segment of the left lower lobe. The tumor was adherent to the parietal pleura. A left lower lobectomy was performed and the tumor was excised from the chest wall with a wide margin of pleura.

PATHOLOGIC FINDINGS

Macroscopically, the tumor appeared as a firm, well circumscribed tan mass measuring 5×3.5×6cm. Sections revealed a bulging-cut surface of bony and cartilaginous consistency with a focal cyst measuring 1.5 cm at the periphery. The tumor did not communicate with the bronchus but there was focal extension through overlying pleura. Multiple histologic sections (Fig. 5) revealed an osteosarcoma characterized by an anaplas-

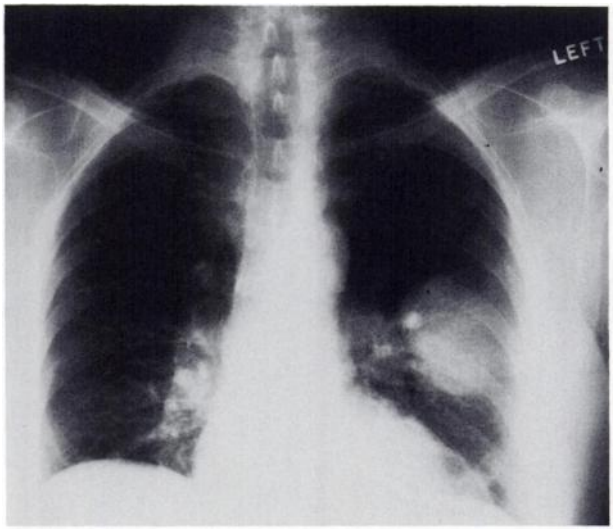

FIGURE 1
Chest radiograph demonstrating left lower lobe lung mass.

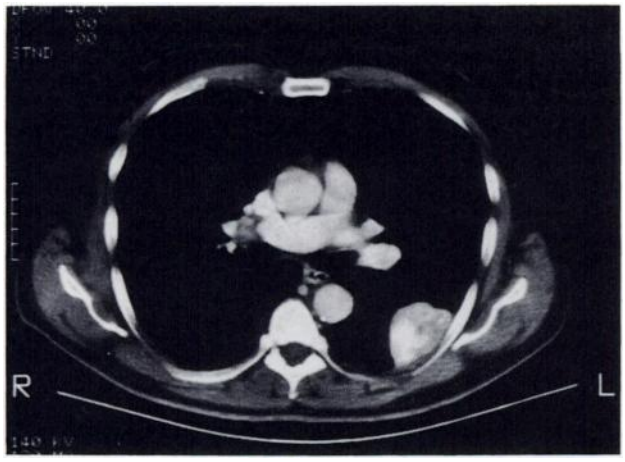

FIGURE 2
CT image of the thorax demonstrating pleural-based left lower lobe mass.

tic mesenchymal parenchyma with the formation of osteoid and bone by the tumor cells. Numerous atypical mitotic figures were present. Osteoclastic giant cells were scattered throughout and cartilaginous foci also were evident. The tumor focally extended through the visceral pleura and in some areas the inked surgical margin was characterized by the presence of skeletal muscle and adipose tissue with adjacent tumor, thus representing probable extension to the parietal pleura and onto the chest wall. Sections of uninvolved lung

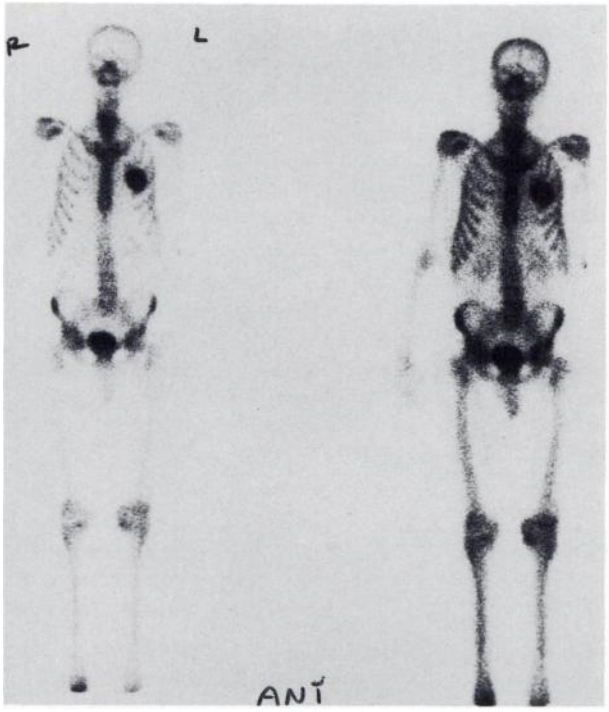

FIGURE 3
Anterior whole-body ^{99m}Tc-MDP scintigram demonstrating intense uptake in the left hemithorax and no significant osseous lesions.

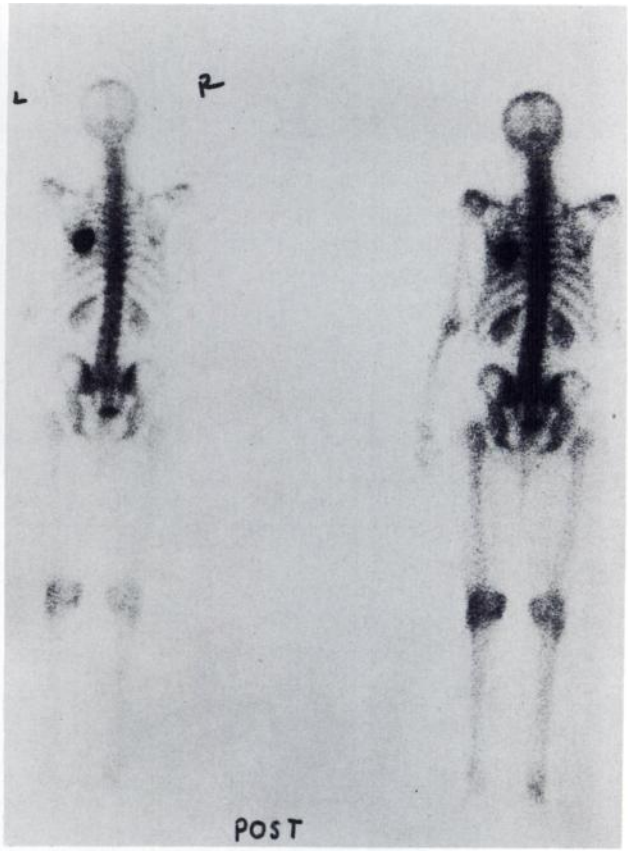

FIGURE 4
Posterior whole-body ^{99m}Tc-MDP scintigram demonstrating intense uptake in the left hemithorax and no significant osseous lesions.

were negative as were lymph nodes from the region of the inferior pulmonary artery and vein and hilum.

The patient had an uncomplicated postoperative course. He received a total dose of 6000 cGy of external beam radiation therapy to the left chest wall via isocentric tangental fields using 200 cGy fractions over 42 days. Six months after surgery, he was asymptomatic,

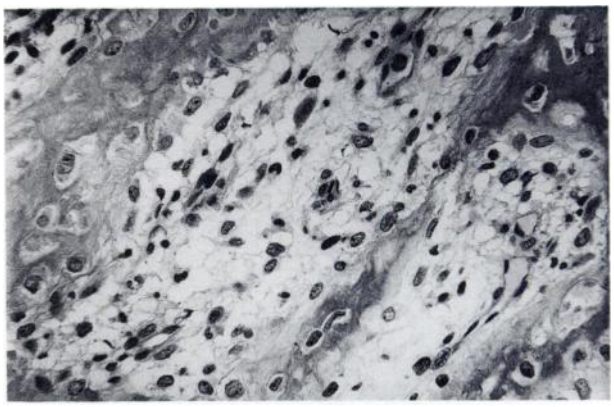

FIGURE 5
Histologic section (× 40) of tumor showing atypical mitotic figures with formation of osteoid and bone (H&E)

and chest radiograph showed only postsurgical changes. The patient refused to have chemotherapy.

DISCUSSION

Extraosseous osteogenic sarcoma is a rare malignant neoplasm constituting 1.2% of all soft-tissue sarcomas and 4.6% of all osteogenic sarcomas (*6*). There have been ~120 cases described in the world literature and the majority of these occur in the soft-tissues of the lower extremities (*7*). Primary pulmonary osteogenic sarcoma is even rarer and only seven cases have been previously reported (Table 1).

Unlike osseous osteogenic sarcoma, extraosseous osteogenic sarcoma arises in an older age group. The mean age has been reported at 53 yr (*7*). In the eight cases of primary pulmonary osteogenic sarcoma described, all cases but one have arisen in patients in the 6th to 8th decade. They are also distributed equally between the sexes. Three cases have involved the right lung and five the left lung. Three patients were asymptomatic, the remaining five all developed severe respi-

TABLE 1
Reported Cases of Primary Pulmonary Osteogenic Sarcoma

Author*	Age	Sex	Symptoms	Clinical findings	Histology	Comment
Greenspan	35	F	Fever, chills, and bloody pleural effusion	(Autopsy) 7-cm mass in L main bronchus involving hilar lymph nodes, diaphragm, heart and left pul. artery	Osteosarcoma, chondrosarcoma, and fibrosarcoma	Died in 6 mo. No osseous primary found.
Reingold and Amronin	62	M	Asthma 20 yr with new onset pneumonia	(Autopsy) 6 × 6 × 4 cm mass in right middle lobe.	Fibrosarcoma osteosarcoma, poorly differentiated mesenchymal cells, and anaplastic chondrocytes	Died 7 mo later from severe recurrent respiratory infections. No osseous primary found.
	56	F	Chills, fever, and L chest pain	L pneumonectomy 7 × 5 cm tumor.	Fibrosarcoma, poorly diff. mesenchymal cells, osteoid, immature cartilage and bone	Skeletal radiographic survey was negative twice despite mets in R lung later.
Nosanchuk	66	M	4 mo weakness dyspnea, chest pain, and hemoptysis	Left pleural effusion with hilum displaced to Left. (Autopsy) LUL filled with necrotic tumor 1 cm distal to L main stem bronchus	Fibrosarcoma, chondrosarcoma, and osteosarcoma	Died in 1 mo from staphylococcous respiratory infection.
Yamashita	74	F	Progressive asthmatic symptoms	(Autopsy) large mass replacing L lung with mets in R lung.	Cartilaginous features with scattered foci of osteogenic sarcoma	Death 6 mo after onset of symptoms. No skeletal primary found.
Nascimento, Unni, and Bernatz	77	F	Asymptomatic	R middle lobe lobectomy, 4-cm tumor	Osteosarcoma	Died within months of unrelated cardiac cause.
	72	M	Asymptomatic	R upper lobe lobectomy, 5.5-cm tumor	Osteosarcoma	Died within months of unrelated cardiac cause.

* See References 1–5.

ratory symptoms of whom in four cases death was due to a related cause in less than one year following diagnosis. In two cases, death was due to an unrelated cause. The patient described above remains alive 6 mo after diagnosis and the outcome of the remaining patient is unknown.

In establishing the diagnosis of extraosseous pulmonary osteogenic sarcoma, it is important to demonstrate first that the tumors are histologically characteristic of this neoplasm with increased cellularity, cellular pleomorphism, mitoses, osteogenesis, and atypical osteoid formation (*8*). It also is important to distinguish pseudomalignant from true osteogenic sarcoma. In pseudomalignant tumors, the osteoid, although very cellular, has neither the anaplastic appearance nor the frequency of mitoses found in truly malignant tumors (*9*).

Secondly, it is important to rule out a skeletal primary sarcoma anywhere in the body but particularly in the overlying chest wall and adjacent ribs. In four of the cases described above the primary origin of the tumor was confirmed at autopsy (*1–4*). In only two cases were radiographic skeletal surveys performed (*2*). Here is presented the only case where the diagnosis was made scintigraphically on bone scan prior to surgery.

Soft-tissue uptake of bone-seeking agents in the thorax is not an uncommon finding. Breast uptake is occasionally seen, particularly after local surgery and accumulation of bone agents has been reported in cases of breast adenocarcinoma (*10*). Uptake has also been reported in pleural effusions, more frequently in malignant than bacterial, and almost exclusively in the noncellular compartment of the fluid (*11,12*). The uptake is usually diffuse but can be well circumscribed in loculated effusions. Less commonly, uptake is seen following radiation therapy to the chest (*13*) or due to radiation pneumonitis (*14*). Pulmonary accumulation, thought to be due to metastatic calcification, has been reported in a hypercalcemic patient (*15*). Pulmonary activity has been noted in squamous cell carcinomas of the lung (*16*) and metastatic disease in the thorax from a variety of tumors, colonic adenocarcinoma (*17*), bladder carcinosarcoma (*18*), extragenital seminoma (*19*), and, finally, osteogenic sarcoma (*20–23*). Interestingly, the scintigraphic sensitivity for pulmonary metastases of osteogenic sarcoma has been reported at only 21% (*22*). However, McKillop et al. in their series demonstrated increased uptake of radiopharmaceutical in only 4 of the 28 patients who had developed lung metastases (*23*). Primary osteogenic sarcoma has also been described in the mediastinum (*24*), the pleura (*25*), and the chest wall (*26*).

In the case described here, there was a known lung mass without evidence of pleural effusion on chest x ray or CT. However the intensity of the radiopharmaceutical uptake was of such a degree to make a bone-forming tumor the most likely diagnosis. Additionally, the bone scan confirmed absence of a skeletal primary. Fine calcification was just detectable on the chest x-ray. Unfortunately, calcification of the tumor on the CT scan could not be demonstrated as the scan had not been recorded on tape and, therefore, could not be redisplayed on bone windows.

The association of elevated alkaline phosphatase in the absence of liver disease has been reported in advanced stages of soft-tissue osteogenic sarcoma (*26*). It is thought that this may be a measure of increasing osteoblastic activity when large amounts of tumor are present.

Due to the rarity of this disease, no effective treatment program has been established. Only the patient presented here received radiation therapy. Sordillo et al. followed the course of 45 patients with extraosseous osteogenic sarcoma (unfortunately none of whom had the primary pulmonary variety). Survival in those patients treated with wide excision followed by radiation therapy was improved with a median survival time of 60+ mo compared to 26 mo for radiation therapy alone and 28 mo for resection alone. Median survival time after development of metastases was only 9 mo (*7*). The role of chemotherapy has not been assessed, however, it has been suggested that adjuvant chemotherapy may have a role in the multimodality approach to treatment of these patients. In Sordillo's series, four of the seven patients who survived after local recurrence or metastases had received adjuvant chemotherapy (*7*).

Prognosis is poor. The size of the tumor is probably the most important prognostic factor, particularly in those 5 cm or larger (*5*). Inadequate excision and local recurrence also are prognostically bad.

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