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Pulmonary Pleomorphic Carcinoma Metastasis to the Midfoot

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ABSTRACT

Metastases to the bones in the foot are extremely uncommon, occurring in approximately 0.01% of all metastatic bone disease. We describe a case of an 82-year-old female with a metastatic pulmonary sarcomatoid carcinoma lesion to the midfoot. This rare and aggressive pulmonary malignancy has a poor prognosis. The purpose of the present case report was to highlight the key roles that medical history and biopsy, combined with a multispecialty approach, play in accurately diagnosing and appropriately treating a patient with metastatic bone disease.

Bone is a common site for metastasis in cancer and occurs in roughly 30% of all malignancy cases (1–3). The incidence of acrometastasis (defined as metastasis to the hand or foot) is quite rare, accounting for approximately 0.1% of all metastatic bone disease (3,4). Acrometastasis specifically to the bones of the foot, however, is a more infrequent occurrence. Typically indicating widespread dissemination, acrometastatic lesions can indicate a poor prognosis.

In cases of metastatic lesions to the bones in the foot, the lung has been the most common primary organ site (5). Carcinomas of the lung are classified according to their morphologic appearance, and various subtypes exist. Pulmonary sarcomatoid carcinoma represents a heterogeneous type of non–small-cell lung cancer that has 5 different histologic variants (6). Pleomorphic carcinoma (PC) is a variant that consists of combined non–small-cell carcinoma and either giant or spindle cells (7). PC is a rare pulmonary malignancy, constituting less than 1% of all lung cancers (7). Current published data has provided evidence of PC metastasizing to the bowel; however, to our knowledge, no cases of a PC metastatic lesion to the foot have been published.

Case Report

An 82-year-old female presented with a 1-month history of swelling, redness, and bruising to her right midfoot. She had previously been seen for this condition by her primary care physician and a differential diagnosis of acute gout had been given. A joint aspirate was performed that was negative for crystals. The low serum uric acid level and a lack of improved symptoms from a prednisone course made the diagnosis of acute gout unlikely. She denied any history of trauma or fever.

Her medical history was most significant for stage IIA lung cancer 1 month after right upper pulmonary lobectomy and mediastinal lymph node dissection. Lymphovascular invasion was present; however, the margins and all 9 lymph nodes were negative. Additional medical history included a neurogenic bladder, anxiety, a longstanding history of tobacco use, chronic airway obstruction, lumbar disc disease, benign neoplasm of the large bowel, cervical carcinoma in situ, a history of squamous cell carcinoma in situ in left jaw, right postauricular basal cell carcinoma, basal cell carcinoma of the left jaw line, actinic keratosis, and osteoarthritis.

The physical examination was remarkable for edema, erythema, and ecchymosis of the navicular tarsal region, with no signs of proximal tracking. She was neurovascularly intact. Radiographs revealed marked soft tissue swelling and lytic disruption of the medial and intermediate cuneiform and bases of the first and second metatarsals, with no adjacent bone involvement. The radiographs obtained at that visit were compared with the radiographs taken 2 months earlier by her primary care physician, which showed no signs of cortical disruption or osteolytic changes (Figs. 1 to 3).

With a high index of suspicion for metastatic cancer, an open osteotomy excisional biopsy of the midtarsal region of the right foot was performed. The intraoperative findings included a large hematoma of the midfoot with bony fragments. Abnormal tissue with red and gray discoloration was noted and sent for pathologic

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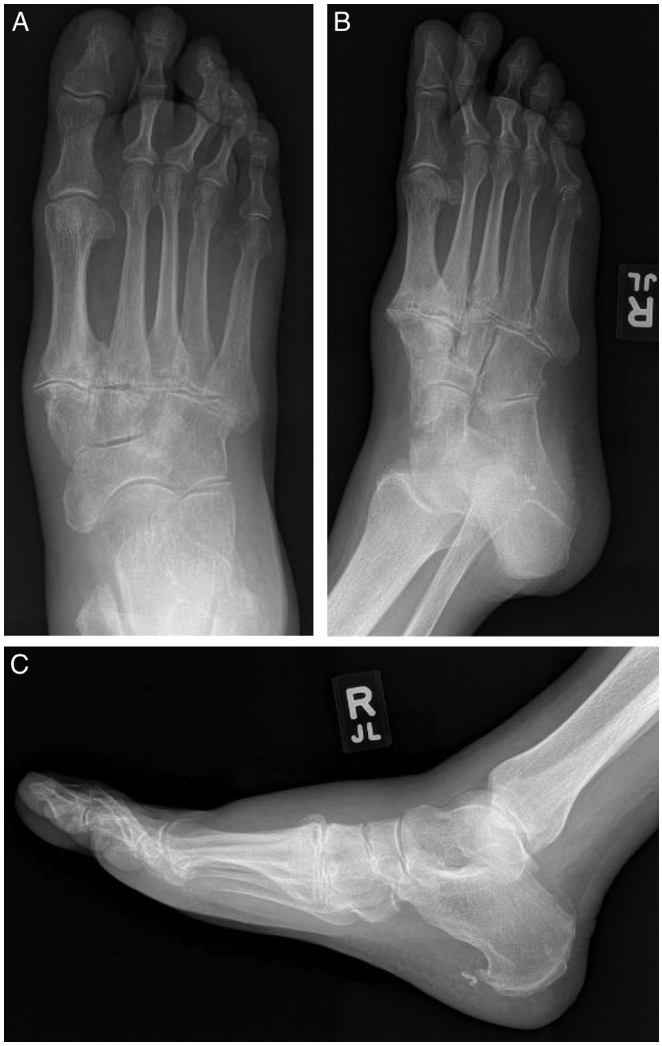

Fig. 1. Plain film radiographs taken by primary care physician 2 months before the initial podiatric evaluation showing no cortical disruption or osteolytic changes to the midfoot. (*A*) Anteroposterior view. (*B*) Medial oblique view. (*C*) Lateral view.

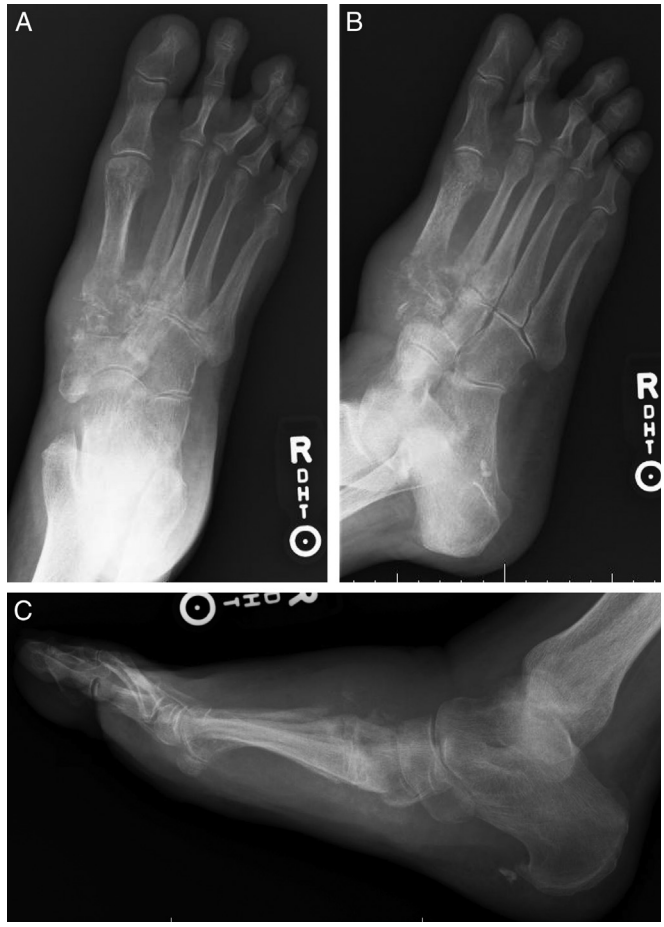

Fig. 2. Plain film radiographs taken at initial podiatric visit showing marked osteolysis to the middle and intermediate cuneiforms and to the base of the first and second metatarsals. (*A*) Anteroposterior view. (*B*) Medial oblique view. (*C*) Lateral view.

examination. Histologic sections were prepared from 10% formalin-fixed, paraffin-embedded tissue cut at 3 to 4 μm. Sections for light microscopy were stained with hematoxylin and eosin. Immunostains were performed using the following antibodies: AE1/AE3 (AE1 & AE3, Leica Biosystems, St. Louis, MO), CAM5.2 (BD Biosciences, Franklin Lakes, NJ), CK7 (clone RN7, Leica Biosystems), epithelial membrane antigen (GP1.4, Leica Biosystems), napsin A (rabbit polyclonal, Cell Marque, Rocklin, CA), PAX-8 (rabbit polyclonal, Cell Marque), S-100 (rabbit polyclonal, Leica Biosystems), and thyroid transcription factor 1 (SPT240, Leica Biosystems). The sections were stained for immunohistochemistry using an automated immunostainer (Leica Bone III, Leica Biosystems) using the biotin-avidin technique with diaminobenzidine as the chromogen. The histologic sections showed poorly differentiated non–small-cell carcinoma infiltrating bone (Fig. 3*A*). The tumor predominantly consisted of discohesive multinucleated and mononucleated giant cells with eosinophilic cytoplasm (Fig. 3*A*). Large areas of necrosis and frequent mitosis were present. The tumor did not have specific patterns of adenocarcinoma, squamous cell carcinoma, or large cell carcinoma. Immunohistochemical studies demonstrated the neoplastic cells to be positive for epithelial markers such as CAM5.2 (Fig. 3*B*) and mixed keratin AE1/AE3 (Fig. 3*C*), confirming the diagnosis of metastatic carcinoma. They showed diffuse cytoplasmic staining with napsin A (Fig. 3*D*) and focal weak nuclear staining with thyroid transcription factor 1 (Fig. 3*E*) and were negative for the remainder of the markers tested. Given the history of sarcomatoid carcinoma of the lung (giant cell type) with similar morphologic (Fig. 4) and immunophenotypic features, the overall findings were consistent with a primary pulmonary origin. Given these findings, the patient was diagnosed with stage IV metastatic lung cancer with an estimated prognosis of 2 to 6 months. Because of the patient's advanced age, frailty, and poor performance status, the risk of chemotherapy outweighed the benefits; therefore, palliative radiotherapy was recommended by the oncologist, followed by hospice care thereafter. At 1 week postoperatively, she was re-evaluated and reported a new onset of bilateral hip and buttock pain, a loss of appetite, and continued weight loss. She also reported having severe pain and uncontrolled bleeding to her right midfoot after suffering a contusion to her foot that day. The patient did not survive through her expected prognosis and died 1 month later.

Discussion

Metastases to bones in the foot are extremely rare, occurring in approximately 0.01% of all metastatic bone disease (8,9). Much of the published data regarding metastatic lesions to the bones of the foot consist of case reports and small cohorts, providing limited data on

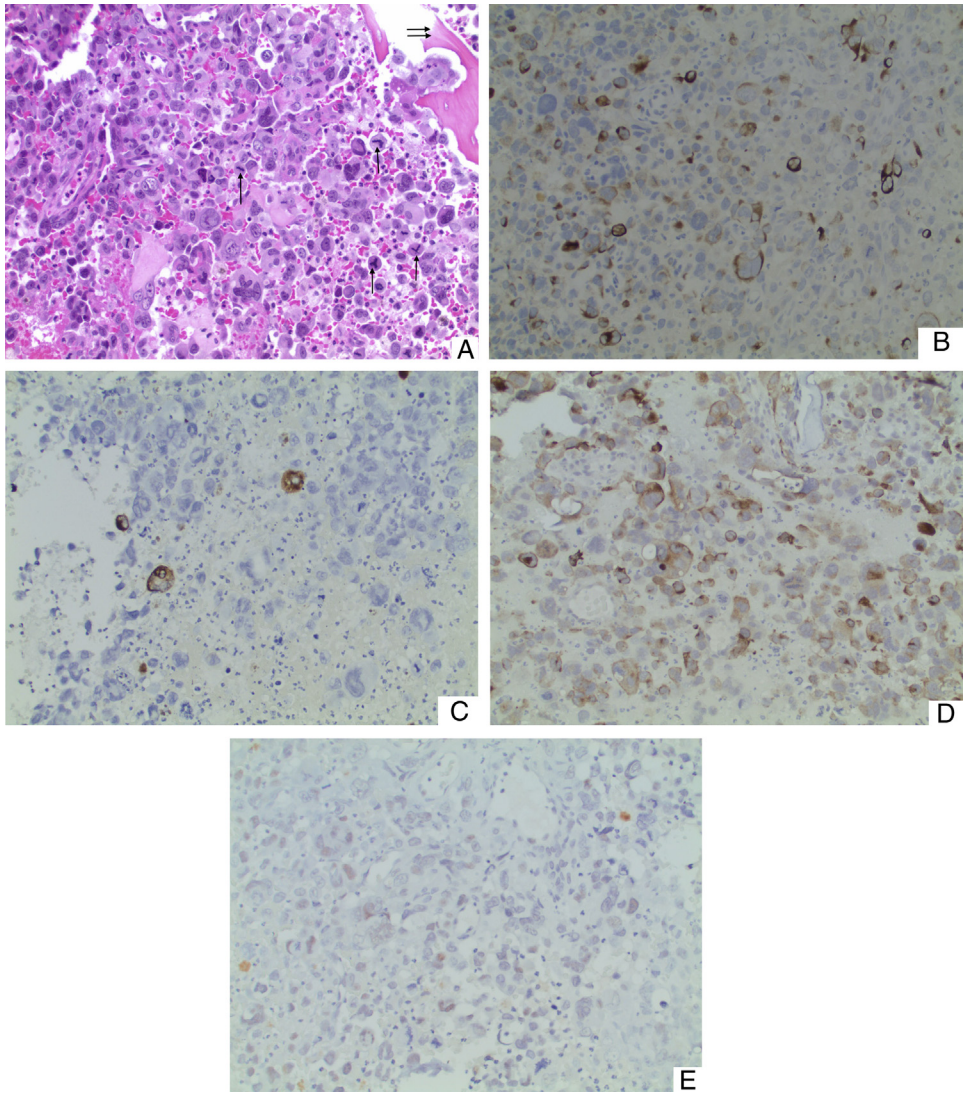

Fig. 3. Light micrograph of right midfoot specimen stained with hematoxylin and eosin. (*A*) Histologic section showing poorly differentiated non–small-cell carcinoma infiltrating the bone. Immunohistochemical studies demonstrating neoplastic cells positive for (*B*) epithelial marker, CAM5.2, and (*C*) mixed keratin AE1/AE3. (*D*) Diffuse cytoplasmic staining with napsin A. (*E*) Focal weak nuclear staining with thyroid transcription factor 1.

this subject. In a recent literature review of 264 metastatic lesions to the foot, Maheshwari et al (10) concluded that the lung was the most common primary organ site. Another recent case series not included in the cited review supported these findings (11). Of the 26 bones that constitute the foot, the calcaneus is the most common bone affected by metastatic lesions, followed by the talus (10). Overall, the hindfoot tends to have a greater prevalence of metastatic lesions than the midfoot or forefoot (10).

The patient in the present case report was diagnosed with an extremely rare lung malignancy known as pulmonary sarcomatoid carcinoma, a form of non–small-cell lung cancer that contains a component of sarcoma or sarcoma-like elements (12). Of the 5 subgroups under the term *pulmonary sarcomatoid carcinoma*, this patient was found to have PC. PC is a poorly differentiated non–small-cell lung cancer that contains at least 10% spindle cells and/or giant cells and is the most common variant (6,7). PC constitutes 0.1% to 0.3% of all lung cancers (7) and is more common in males than in females, with the ratio ranging from 2.7:1 to 9.7:1 (7,13–15). This rare and aggressive cancer has had a 5-year relative survival rate of 11.8% to 33%, depending on the study (6,14,16,17).

Metastatic bone disease involving the foot can affect the quality of life of a patient, particularly if they are ambulating. The manner in which our patient presented, with complaints of pain and swelling, is rather common for those with metastatic bone lesions (5,9,18,19). Bone metastasis is the most common cause of cancer-related pain (1,20). A delay in treatment can lead to subsequent problems such as pathologic fractures, which have been reported to occur in up to 30% of metastatic lesions (20).

In conclusion, this is the first documented case of PC of the lung metastasizing to the foot. PC is a rare lung neoplasm that has a poorer prognosis than other non–small-cell lung cancers. Given the aggressive clinical nature of PC, an accurate and prompt diagnosis can be beneficial, especially in instances of distant metastasis. Although it was an equivocal clinical presentation, a thorough patient history, prompt biopsy, and a multispecialty approach led to accurate cancer staging and a more appropriate treatment plan.

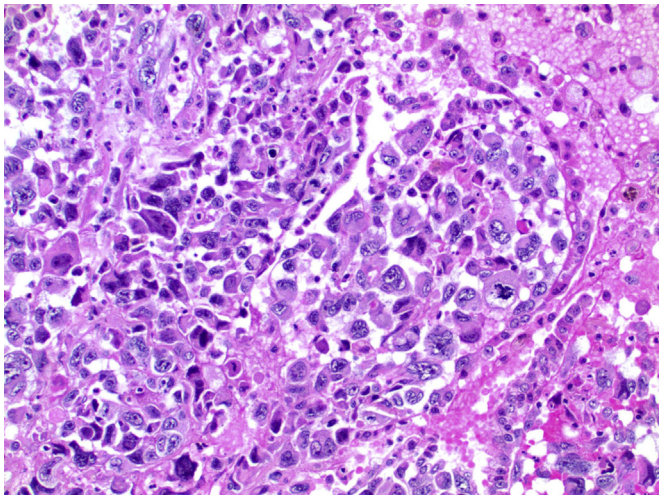

Fig. 4. Light micrograph of pulmonary specimen stained with hematoxylin and eosin demonstrating similar morphologic features to those of the midfoot specimen.

References

1. Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res 12:6243s–6249s, 2006.
2. Roodman GD. Mechanisms of bone metastasis. N Engl J Med 350:1655–1664, 2004.
3. Healey JH, Turnbull AD, Miedema B, Lame JM. Acrometastases: a study of twenty-nine patients with osseous involvement of the hands and feet. J Bone Joint Surg Am 68:743–746, 1986.
4. Mavrogenis AF, Mimidis G, Kokkalis ZT, Karampela I, Papagelopoulos PJ, Armaganidis A. Acrometastases. Eur J Orthop Surg Traumatol 24:279–283, 2014.
5. Zindrick MR, Young MP, Daley RJ, Light TR. Metastatic tumors of the foot: case report and literature review. Clin Orthop Relat Res 170:219–225, 1982.
6. Pelosi G, Sonzogni A, De Pas T, Galetta D, Veronesi G, Spaggiari L, Manzotti M, Fumagalli C, Bresaola E, Nappi O, Viale G, Rosai J. Review article: pulmonary sarcomatoid carcinomas: a practical overview. Int J Surg Pathol 18:103–120, 2010.
7. Koh H, Chiyotani A, Tokuda T, Suzumura H, Kamiishi N, Takahashi H, Hirose S. Pleomorphic carcinoma showing rapid growth, multiple metastases, and intestinal perforation. Ann Thorac Cardiovasc Surg, 2014.
8. Wu KK, Guise ER. Metastatic tumors of the foot. South Med J 71:807–808, 1978.
9. Hattrup SJ, Amadio PC, Sim FH, Lombardi RM. Metastatic tumors of the foot and ankle. Foot Ankle 8:243–247, 1988.
10. Maheshwari AV, Chiappetta G, Kugler CD, Pitcher JD, Temple HT. Metastatic skeletal disease of the foot: case reports and literature review. Foot Ankle Int 29:699–710, 2008.
11. El Ghazaly SA, DeGroot H III. Metastases to bones of the foot: a case series, review of the literature, and a systematic approach to diagnosis. Foot Ankle Spec 1:338–343, 2008.
12. Beasley MB, Brambilla E, Travis WD. The 2004 World Health Organization classification of lung tumors. Semin Roentgenol 40:90–97, 2005.
13. Terada T. Pleomorphic carcinoma of the lung: a case report with immunohistochemical studies. Respir Med CME 3:252–256, 2010.
14. Fishback NF, Travis WD, Moran CA, Guinee DG Jr, McCarthy WF, Koss MN. Pleomorphic (spindle/giant cell) carcinoma of the lung: a clinicopathologic correlation of 78 cases. Cancer 73:2936–2945, 1994.
15. Rossi G, Cavazza A, Sturm N, Migaldi M, Facciolongo N, Longo L, Maiorana A, Brambilla E. Pulmonary carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements: a clinicopathologic and immunohistochemical study of 75 cases. Am J Surg Pathol 27:311–324, 2003.
16. Huang S-Y, Shen S-J, Li X-Y. Pulmonary sarcomatoid carcinoma: a clinicopathologic study and prognostic analysis of 51 cases. World J Surg Oncol 11:252, 2013.
17. Wick MR, Ritter JH, Humphrey PA. Sarcomatoid carcinomas of the lung: a clinicopathologic review. Am J Clin Pathol 108:40–53, 1997.
18. Bricout PB. Acrometastases. J Natl Med Assoc 73:325–329, 1981.
19. Mundy GR. Metastasis: metastasis to bone: causes, consequences and therapeutic opportunities. Nat Rev Cancer 2:584–593, 2002.
20. Mercadante S. Malignant bone pain: pathophysiology and treatment. Pain 69:1–18, 1997.