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Case Reports and Series

Rare Pedal Manifestation of Diffuse Multiple Myeloma Lesions

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ABSTRACT

Multiple myeloma is a malignancy of plasma cell proliferation leading to production of monoclonal immunoglobins. Among the classic features of multiple myeloma are bone lesions, which typically manifest in the axial skeleton, vertebrae, pelvis, skull, ribs, and proximal extremities. The several types of multiple myeloma include symptomatic multiple myeloma, monoclonal gammopathy of undetermined significance, smoldering/indolent myeloma, and solitary plasmacytoma of bone. Although rare, plasmacytomas of the foot and ankle have been described in published studies. We present, to the best of our knowledge, the first description of classic diffuse myelomatosis lesions associated with symptomatic myeloma in the foot of a patient with advanced disease who was treated in the podiatric surgery clinic for pathologic fracture.

Multiple myeloma (MM) is a malignancy of plasma cell uncontrolled proliferation leading to excessive production of monoclonal immunoglobulins. Plasma cell production occurs in bone marrow, and aberrant proliferation subsequently results in numerous skeletal changes that portend the characteristic features of the disease. These features include painful, lytic lesions of bones, hypercalcemia, increased total serum protein, renal failure, and unexplained anemia (1).

MM accounts for 1% of all cancers in the United States (2). Similar incidence rates have been reported between Europe and the United States, at roughly 4 to 5 cases per 100,000 (3). The average age at diagnosis is 65 years, with only 3% of patients <40 years old (4).

Radiographic studies, including plain film radiograph skeletal surveys, magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (CT) are frequently used to diagnose and track disease progression. The presence of numerous, similar-size osteolytic lesions are known as diffuse myelomatosis and are one of the characteristic features of the disease. Diffuse myelomatous lesions are classically noted in the spine; however, their presence is frequently noted in many other bones, including the pelvis, skull, ribs, and proximal aspects of extremities. An alternative bone lesion presentation is solitary and is referred to as a plasmacytoma. Although solitary plasmacytomas have infrequently been described in the foot, to the best of our knowledge, we present the first reported case of diffuse myelomatosis lesions located in the metatarsal and phalanx.

Case Report

In February 2009, a 56-year-old white male began experiencing low back pain that became exacerbated in October 2009 when he was pulling up carpet. An MRI scan in November 2009 showed a solitary lesion at L3 with loss of vertebral height. CT-guided biopsy confirmed a diagnosis of plasmacytoma. The lesion was removed surgically in December 2009 with adjunctive fusion of L2–L4 with use of an autologous iliac crest bone graft. The perioperative period was complicated by the development of bilateral pulmonary embolism. Radiation therapy was initiated to a total dose of 45 Gy. MRI of the thoracic and lumbar spine in January 2011 showed no recurrence. Elevation of kappa free light chains were noted in November 2011; however, the bone marrow biopsy examination was negative for myeloma, and the positron emission tomography/CT scan showed no changes. In December 2011, new lytic lesions were noted in the left femur, proximal tibia, and right distal tibia, with an increase in kappa light chains, which necessitated several cycles of biologic therapy with bortezomib, a proteasome inhibitor (1.3 mg/m^2 on days 1, 4, 8, and 11), and dexamethasone (40 mg orally on days 1 to 4, 9 to 12, and 17 to 20). These were performed in 28-day cycles for 4 iterations. An autologous stem cell transplant was performed in May 2012, followed by maintenance therapy with

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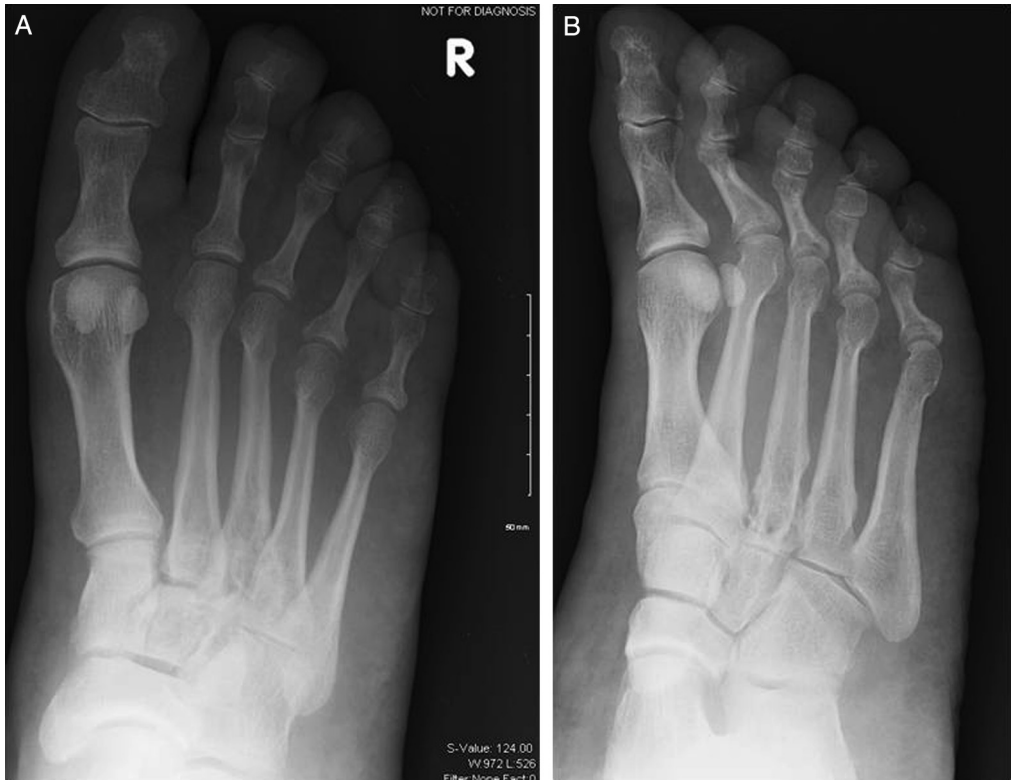

Fig. 1. Plain film radiographs of the right foot, July 2014. (*A*) Anteroposterior projection. (*B*) Lateral oblique projection showing early changes at the base of the third metatarsal.

lenalidomide, an immune modulator (10 mg daily for 21 days consecutively, in three 28-day cycles), and prednisone (5 mg daily). Skeletal survey plain film radiographs with 24 views showed no further lytic lesions in December 2012. No characteristic lesions were ever identified in the patient's skull.

Throughout 2013, the patient received several rounds of bisphosphonate (zoledronic acid, 4 mg intravenously monthly) with only an abnormal finding of slightly elevated kappa free light chains (3.17 mg/dL; reference range, 0.33 to 1.94 mg/dL) and lambda light chains in June 2013 seen using serum protein electrophoresis and immunofixation electrophoresis. Additionally, no proteins were noted in the urine. In July 2014, the patient presented to the emergency department because of right foot swelling. A deep vein thrombosis was ruled out; however, radiographs were obtained, which showed some early lytic changes to the third metatarsal (Fig. 1). In October 2014, the patient experienced pain in his left hand, leading to an MRI scan, which showed marrow replacement of the third metacarpal shaft. In November 2014, he presented with jaw pain, which prompted imaging studies. Head, chest, and abdomen CT scans in November 2014 showed a frontal sinus mass, a left first and second rib anterior mass, and a liver lesion, respectively. The sinus mass was excised in the operating room. Pathologic examination showed an atypical plasmacytoma positive for kappa light chains and negative for CD79a and CD68. The rib mass was diagnosed as an extramedullary plasmacytoma by its appearance on the CT scan. The liver lesions were biopsied by interventional radiology and diagnosed as plasmacytoma (Fig. 2). The mandibular lesion that initially measured $2.3 \times 3.1 \times 3$ cm was treated with 4000 cGy of radiation in 20 fractions until January 2015.

In March 2015, the patient was referred to the podiatry clinic because of right midfoot pain after removing his compression stockings. The patient denied any other trauma. The foot was edematous without any erythema or ecchymosis. Plain film radiographs were obtained (Fig. 3), which showed lytic, erosive changes in the third metatarsal and a smaller, similar lesion at the head of the proximal phalanx of the second digit proximal phalanx. Pathologic fractures were noted in both of these bones. The patient was placed in controlled ankle motion boot for immobilization. Despite knowledge of the lesions, the patient refused radiation therapy for his right foot, because he was just beginning therapy for his right jaw lesion. The patient, however, did experience total symptomatic relief of the right foot pain with immobilization. The free kappa light chain level was 302 mg/dL at that time. In May 2015, the patient developed a nondisplaced fracture of his ulna when moving a couch. He was also noted to have continued enlargement of the liver lesions for which he was undergoing bortezomib and dexamethasone cycles as before, with the addition of cyclophosphamide (500 mg/m^2/day orally on days 1, 8, and 15) and thalidomide (50 mg/day orally) prescribed by his hematology and oncology physician. At that time, he also had a pericardial effusion and urine kappa free light chains of $\sim$9 g/day, indicating substantial overproduction. Late in May 2015, the patient was admitted for bacteremia in the setting of pancytopenia, and he continued to have high free kappa light chain myeloma. In June 2015, the patient was experiencing an increase in falls and numbness. A head CT scan showed a myelomatous lesion in the right frontal parietal region of the calvarium, which could have been causing the mass effect changes resulting in his symptoms. Follow-up orbital MRI showed continued progression of myelomatous lesions, which include several cervical and thoracic vertebrae but not affecting the spinal cord. The free kappa light chain level at that time was 677 mg/dL. At the last follow-up examination, no additional chemotherapy or radiation therapy had been initiated, with the patient receiving occasional blood transfusions for disease-related anemia. The patient was then placed in hospice care and succumbed to his disease within 1 month.