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CASE REPORT

Solitary osseous sarcoidosis: a rare reason for pathologic fracture

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Abstract Sarcoidosis with osseous involvement as the initial manifestation is rare. Due to lack of other organ involvements, the diagnosis is somehow difficult to establish. We report a case with osseous sarcoidosis as the initial and major manifestation that developed spontaneous bone fracture. Our case emphasizes the importance of histological evidence and exclusion of other diseases i.e. rheumatoid arthritis, before making the diagnosis of osseous sarcoidosis.

Keywords Osseous sarcoidosis · Pathologic fracture

Sarcoidosis is a chronic non-caseating granulomatous disease of unknown etiology, and the most commonly affected organ is the lung, followed by lymph nodes, eyes and skin. The diagnosis of sarcoidosis is made by a combination of clinical, radiological and histological findings. Clinical symptoms vary from weight loss, fatigue, fever, night sweats to coughing and shortness of breath. Chest X-ray findings include lymphadenopathy and/or extensive parenchymal destruction. Osseous involvement is relatively uncommon in sarcoidosis and associated with chronic multiorgan involvements [1], with frequency ranging from 1 to 13% [2]. Osseous involvement, although sometimes painful, is usually asymptomatic [3]. Pathologic fracture caused by osseous sarcoidosis is extremely rare, and to the best of our knowledge, only 13 cases have been reported in literature [4]. Here, we report a case of which osseous sarcoidosis was the initial and major manifestation that eventually led to pathologic bone fracture.

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Case report

A 52-year-old woman was admitted because of pain and swelling of bilateral proximal interphalangeal (PIP) joints and spontaneous bone fracture for 4 years. In June 2004, she developed persistent swelling, tenderness of bilateral PIP. She had no fever, rash, chest pain and cough at that time. Her hand X-ray revealed punched-out lesion in her left fourth phalanx (Fig. 1a). She was treated with non-steroid anti-inflammatory drugs. In December 2004, she developed bone fracture of that phalanx and received excision surgery. After that, she was treated with Chinese traditional medicine, though her joint pain and swelling were never alleviated. In April 2006, she had another fracture of her left third phalanx and received excision again. A skin biopsy revealed an epithelioid giant cell granuloma with no organisms or caseous necrosis (Fig. 2). Because she had a history of tuberculosis 20 years ago, she was empirically treated with anti-phthisic drugs in local hospital for 1 year, though her symptom was aggravating and she developed swelling of her toes.

At this stage, she was referred to the Department of Rheumatology, Peking Union Medical College Hospital for further investigation. Physical examination revealed swelling and tenderness of bilateral PIPs of both hand and feet,

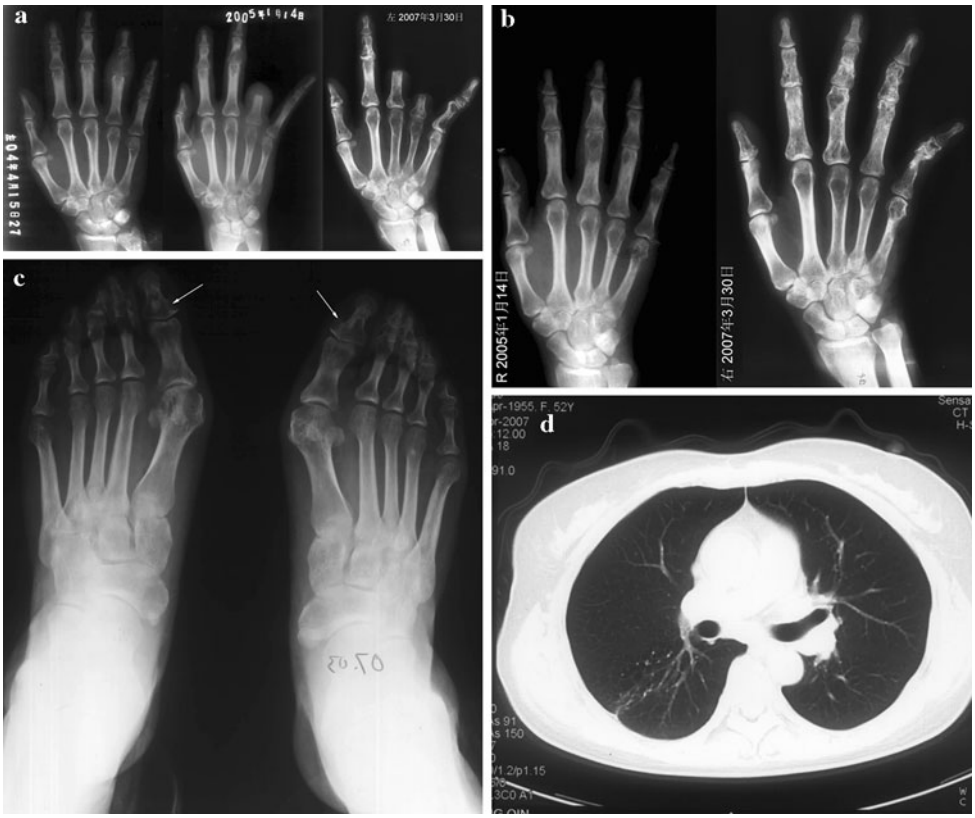

Fig. 1 **a** The development of left hand X-ray from April 2004 to March 2007. In April 2004, radiography of fourth finger on left hand showing extensive cortical bone destruction. Extensive soft-tissue swelling is also present. In January 2005, after operation showing loss of cortical bone in the third finger, absence of fourth finger. In March 2007, after second operation a year later showing loss of cortical bone in the second and fifth finger of the left hand, absence of midpiece of middle and ring finger of the left hand. Extensive soft-tissue swelling persists. **b** The development of right hand X-ray from January 2005 to March 2007. In 2005, X-ray showing loss of cortical bone in the midpiece of third and fourth finger of the right hand, which become worse in 2007. Fracture of fifth finger also was seen in 2007. **c** Feet X-ray in March 2007, patching and low density shadow was found at pediphalanx of the feet on the X-ray. **d** Chest CT shows multiple lung lesions and bilateral hilar lymph adenopathy

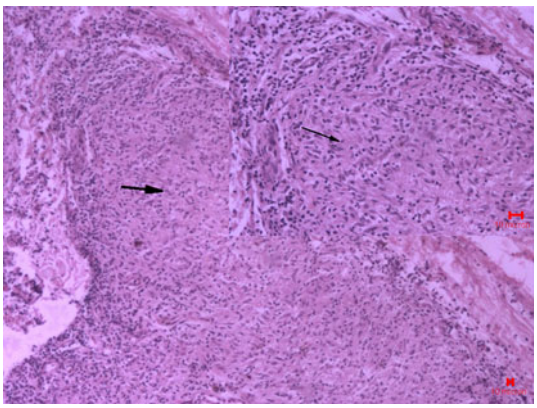

Fig. 2 Histopathologic findings in the biopsy specimen of the skin. Non-caseating epithelioid cell granuloma were found (HE, bar 10 μm)

as well as her metacarpal phalangeal joints (MCP). The mid-pieces of her left middle and ring finger were missing. She had no skin rash, and there was no symptom or sign about her eyes, respiratory, cardiovascular, digestive, nervous and urinary system. Her erythrocyte sedimentation rate was 17 mm/h and C-reactive protein level was normal. Other laboratory findings including blood cell counts, liver and renal functions, uric acid, serum calcium and phosphate as well as serum parathyroid hormone were also within normal ranges, and tests for rheumatoid factor, antinuclear antibodies, and anti-double-strand DNA antibodies were negative. Her PPD test and microbiological studies for tuberculin were negative, and serum angiotensin converting enzyme (ACE) level was 84.8 u/L (10–68 u/L). Here, hand X-ray showed that the distal digits of her left middle and ring finger were missing, and lacey reticulations were found in the middle digits of her right third to fifth fingers and her left second and fifth fingers. Extensive soft-tissue swelling was also present (Fig. 1a, b). Patching and low density shadow was found at her phalanges of toes on feet X-ray (Fig. 1c). The CT scan showed bilateral hilar lymphadenopathy with multiple small patching shadow at right lower lobe (Fig. 1d), and ^{99M}Tc-HMDP bone scan revealed intense tracer uptake at multiple areas in both hands and

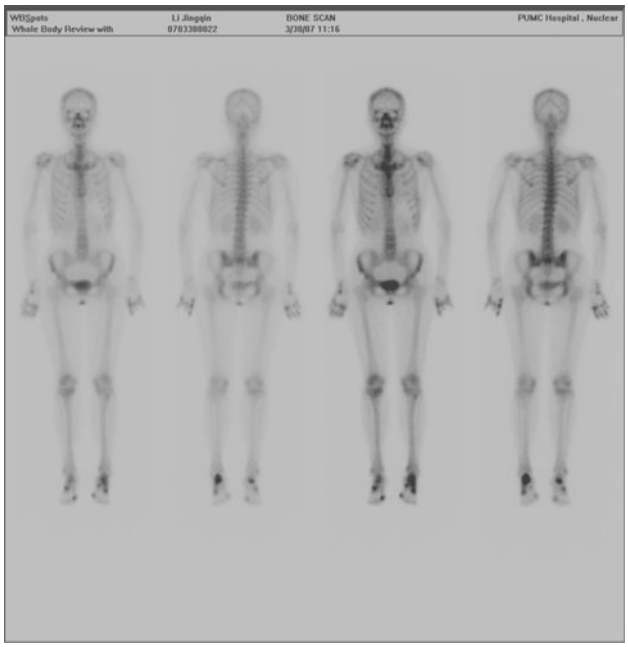

Fig. 3 ^{99M}Tc-HDP bone scintigraphy showing multiple focal areas of abnormal radiotracer accumulation mainly in both hands and feet

feet (Fig. 3). Other tests, such as X-ray of her nasal bones, skull and pelvis appeared normal, as well as ultrasound scan of her abdomen and pelvis, and parathyroid ECT. Her clinical, radiological and histological findings were consistent with sarcoidosis. She was started on oral prednisone 40 mg/day, and the dose was gradually tapered. After 4 months of treatment, her symptoms completely disappeared, and her serum ACE was normal. Repeated chest CT showed improvement of the lesion, whereas her hand X-ray showed no change.

Discussion

Sarcoidosis is a chronic systemic inflammatory disease of unknown cause, characterized by the presence of non-caseous granuloma. It has protean manifestations and can affect virtually any organ [5]. Rheumatologic symptoms can be present in around 4–38% of patients with sarcoidosis [6]. The first case of osseous sarcoidosis was described in 1898 by Benisnier [7]. It remains unclear how extrapulmonary lesion of sarcoidosis occurs. One possible explanation is the migration of activated T cells to other tissues through the blood and lymphatic vessels causing the formation of granulomas [8]. Based on the histological finding of non-caseating granuloma, punched-out lesions in hand X-ray, bilateral hilar lymphadenopathy in CT scan as well as elevated level of serum ACE, the patient was diagnosed as having lung and bone sarcoidosis.

Osseous involvement in sarcoidosis is usually asymptomatic, but could be painful and tender. Soft-tissue swelling and skin lesions can also occur in conjunction with osseous sarcoid lesions [9]. Sarcoidosis causes cystic, reticular, or destructive lesions involving mainly the hands and feet, particularly the middle and distal phalanges. Our patient complained of pain and swelling of her bilateral PIP, which mimicked rheumatoid arthritis. However, in osseous sarcoidosis, the periosteum and articular cartilage are usually spared, and adjacent soft tissues may be minimally disrupted [10], which is helpful in the differential diagnosis.

Osseous sarcoidosis is more common in black and in women, often associated with long-standing disease with multiorgan involvements, especially skin disease. Therefore, the occurence of osseous sarcoidosis usually indicates a chronic, persistent, and irreversible systemic disease [6]. Bone fracture caused by osseous sarcoidosis is rare. Among 13 cases with bone fractures published in literature, 6 were black, and there was no report of Chinese patient. Bone fractures most commonly affected the phalanges, followed by the ulna, femur, metacarpus, and the rib. Patients with fracturing osseous sarcoidosis as the initial and major involvement are extremely rare. Spontaneous healing has been reported to be characteristic of osseous sarcoidosis [11]. In our case, however, osseous sarcoidosis was persistently progressive and led to pathologic fracture.

X-ray film is most often used to identify osseous lesions. Abnormal findings include minute osteolysis (83%), manifesting as small punched-out lesions, with diameters less than 5 mm; permeative or reticular changes in cortical bone (33%); or destructive process with larger osteolytic lesions, causing permanent destruction of the normal bone structure (10%) [12]. Most of these abnormalities are non-specific. Differential diagnosis of lytic lesions include neoplasms, gout, hyperthyroidism, Wegener's granulomatosis, and infectious diseases including tuberculosis, bone infarction, and Paget's disease [13]. In our case, X-ray showed small punched-out lesions and the above-mentioned conditions were all excluded. Radionuclide scan is a more sensitive test than plain radiographs for detecting bone sarcoidosis [14]. In our case, an additional osseous lesion was also found in one pediphalanx by bone scan, which was clinically silent and missed by plain radiographs, suggesting that both bone scintigraphy and radiographs should be applied to detect osseous sarcoidosis [15].

Treatment of bone sarcoidosis remains controversial. Pain, bone destruction, and hypercalcaemia usually require treatment [16]. Corticosteroids may alleviate symptom and inflammation, though it may not affect the course of osseous sarcoidosis. It is believed that the patient's prognosis is significantly worse when osseous involvement occurs. Some previous reports suggested careful excision of the

affected lesion followed by reconstruction with bone grafts seemed to improve patients prognosis, whereas similar to our case, Adelaar also reported a case of osseous sarcoidosis with progressive phalangeal bone fracture despite lesion excision and placement of a bone graft [17]. In our case, patient was at risk of pathological fracture again due to destruction of trabeculae, therefore systemic treatment with corticosteroids was started, and her symptoms were rapidly alleviated.

In conclusion, we report a case with osseous sarcoidosis as the initial and main manifestation that developed spontaneous fracture. This situation is extremely rare and somehow difficult to diagnose due to its resemblance to other diseases, including metastatic malignancy.

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