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CASE REPORT

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Osteomyelitis and pyomyositis due to *Staphylococcus aureus* in an osteomalacic adult with multiple fractures

Masumi Ogawa[a], Takatoshi Kitazawa[b], Yusuke Yoshino[b], Koji Morita[b], Toshio Ishikawa[b] and Yasuo Ota[b,c]

[a]Department of Internal Medicine, Self-defense Forces Central Hospital, Tokyo, Japan; [b]Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan; [c]National Hospital Organization Higashisaitama Hospital, Hasuda, Japan

ABSTRACT

Multifocal osteomyelitis and pyomyositis usually arise from hematogenous dissemination, especially in patients with immunodeficiency, trauma, or injection drug abuse. We report the case of a 75-year-old man with multifocal pyomyositis and osteomyelitis, which were due to *Staphylococcus aureus* and were presumably related to multiple fractures. The patient had no risk factors for these hematogenous infections. He was treated with antibiotic therapy for about 80 days and drainage of the abscesses. Regarding the cause of his multipe fractures, he was found to have hypophosphatemia and eventually diagnosed as osteomalacia. To our best knowledge, this case was the first report on multifocal osteomyelitis and pyomyositis around the fracture sites in an osteomalacic adult. Osteomalacia should be considered as one of the differential diagnoses when osteoarticular infection with multifocal fractures is detected.

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1. Introduction

Adult hematogenous osteomyelitis accounts for approximately 20% of osteomyelitis cases; it most commonly involves the vertebral bones and less frequently involves the long bones of the skeleton [1,2]. Pyomyositis is a purulent skeletal muscle infection that arises from hematogenous dissemination and is usually accompanied by abscess formation [3]. *Staphylococcus aureus* is the most frequent pathogen of hematogenous osteomyelitis and muscular abscesses [1,4]. Herein, we report a case of multiple fractures accompanied by multifocal pyomyositis and osteomyelitis due to *S. aureus*. He had hypophosphatemia on admission and was finally diagnosed as osteomalacia.

2. Case

A 75-year-old Japanese man was referred to our hospital due to prolonged fever, malaise, leukocytosis (16,000/μL), and high serum C-reactive protein (CRP) level (39.3 mg/dL). He had hypertension and hyperuricemia; femoral neck replacement surgery for a right femur fracture at age 70 years; open reduction and internal fixation of left femoral trochanteric fracture at age 71 years; but no history of trauma or intravenous drug abuse. The patient did not have any family history of metabolic bone diseases.

On admission, he was conscious and had a body temperature of 37.7°C, a blood pressure of 123/90 mmHg, an irregular heart rate of 126/minute, a respiratory rate of 30/minute, and an oxygen saturation of 97% on room air. There were no abnormalities in the head and neck regions. His chest examination showed coarse crackles on both lung fields, but no cardiac murmur was heard. No abnormality was found in the abdomen, but there was mild tenderness on the left costal area and left lower back. There were no rashes or wounds. His neurologic findings were grossly normal.

His laboratory results were as follows: white blood cell count 17,500/μL with 87% neutrophils, serum alkaline phosphatase 526 U/L (normal range: 106–322 U/L), creatine kinase 1,223 U/L (normal range: 59–248 U/L), creatinine 1.44 mg/dL, calcium 9.3 mg/dL, and phosphorus 1.3 mg/dL. His anti-human immunodeficiency virus (HIV) antibody was negative. Plain computed tomography (CT) demonstrated left pleural effusion and multiple rib fractures. Two sets of blood cultures were collected. On the 2nd day, he developed septic shock caused by gram-positive cocci that were detected from the 2 sets of blood cultures; therefore, intravenous teicoplanin 600 mg twice daily was initiated (Figure 1). The bacteria were later identified as methicillin-susceptible *Staphylococcus aureus*; therefore, teicoplanin was changed to intravenous cefazolin 2 g three

CONTACT Takatoshi Kitazawa tkitazaw@med.teikyo-u.ac.jp Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan

All authors meet the ICMJE authorship criteria.

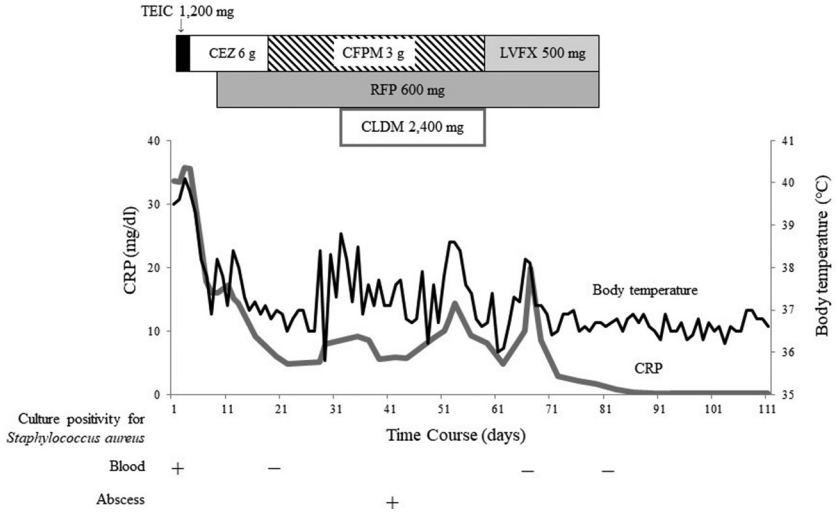

Figure 1. Clinical course for the patient. Bars in the upper area show the administered antibiotics and their daily doses. The graph shows body temperature and CRP during the hospitalization. Symbols at the bottom show culture positivity for *Staphylococcus aureus*. TEIC; teicoplanin, CEZ; cefazolin, CFPM; cefepime, CLDM; clindamycin, LVFX; levofloxacin, CRP; C-reactive protein.

times daily. Because his condition did not improve, oral rifampicin 600 mg daily was added to the treatment on the 7th day. On contrast-enhanced CT, multiple abscesses were observed adjacent to the fracture sites and inside the right iliopsoas, right piriformis, right spinae, and left obturator muscles (Figure 2 (a,Figure 2b)). No fluid accumulation was observed in the right artificial femoral head. On the 17th day, cefazolin was changed to intravenous cefepime 1 g three times daily since the involvement of central nervous system was not completely denied due to mild confusion, and intravenous clindamycin 600 mg four times daily was also initiated. On transesophageal echocardiography, neither valvular

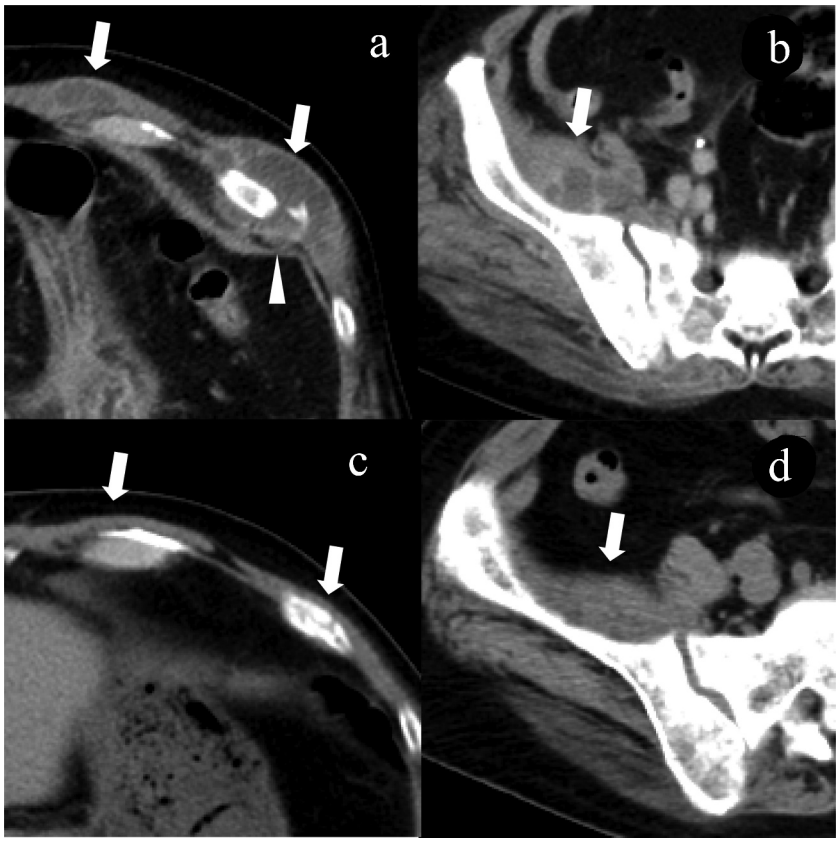

Figure 2. Chest and pelvic computed tomography scans in our patient. Before treatment, there is a left rib fracture (A, arrowhead), and the adjacent muscles (A, arrow) and right iliac muscle (B, arrow) are swollen, with fluid retention. There is resolution of these muscle abscesses after treatment (C and D, arrow).

vegetation nor regurgitation was detected. According to the modified Dukes criteria, only two minor criteria were met for the diagnosis of infective endocarditis. Therefore, he was diagnosed as pyomyositis and purulent osteomyelitis caused by *S. aureus* at the fracture sites.

All the blood culture tests, except the ones taken on admission, were negative during treatment. On the 43rd day, the abscess fluid from the left obturator muscle was drained and grew *S. aureus* on culture. Its antibiotic susceptibility testing results were identical to those from blood cultures. On the 59th day, cefepime and clindamycin were switched to oral levofloxacin 500 mg daily. On the 79th day, levofloxacin was discontinued, because CT showed resolution of the abscesses (Figure 2(c,Figure 2d)) and the serum CRP level decreased to 1.7 mg/dL. After discontinuation of antibiotic therapy, there was no evidence of recurrence.

In searching for the cause of the multiple fractures, we focused on his hypophosphatemia. Additional examinations revealed low maximal tubular reabsorption of phosphate to glomerular filtration rate (TmP/GFR) of 0.67 mg/dL; elevated alkaline phosphatase; 1α, 25-dihydroxyvitamin D level of 40.8 pg/mL; high normal intact parathyroid hormone level of 63 pg/mL, which was consistent with 25-hydroxyvitamin D deficiency (7 ng/mL); and elevated intact fibroblast growth factor 23 (FGF23) of 155 pg/mL. Therefore, he was diagnosed as FGF23-related hypophosphatemic osteomalacia. No tumor was detected on CT, and the patient refused additional studies. After treatment with sodium dihydrogenphosphate and alfacalcidol, the serum phosphate normalized.

3. Discussion

Multifocal osteomyelitis is usually caused by hematogenous dissemination of the pathogen from a main infection source, which is not necessarily close to the osteomyelitis lesions [1]. Likewise, pyomyositis is caused by hematogenous dissemination rather than by local extension of a contiguous infection [5]. The common predisposing factors for hematogenous osteomyelitis and pyomyositis are immunodeficiency, trauma, and intravenous drug abuse [5–7]. Our patient had no such risk factors before the onset of infection. In hematogenous osteomyelitis in adults, the common sites of infection are the vertebrae and the sternoclavicular and pelvic bones, and the long bones are rarely involved [2]. In our case, the sites of osteomyelitis were the ribs, and the sites of muscle abscess were adjacent to the fracture sites.

Normal bone is highly resistant to infection, which can only occur as a result of very large inocula, trauma, or the presence of foreign bodies [8]. *S. aureus* binds to fibronectin via the fibronectin-binding protein on its surface [9,10]. In animal models of rib fracture, fibronectin expression transiently increased in the fracture callus during fracture healing [11]. In other animal studies, rabbits with fractures and *S. aureus* bacteremia developed hematogenous osteomyelitis in the metaphysis of the bone with closed fracture [12,13]. Acute hematogenous osteomyelitis occurring at the site of closed fractures is rare [14]. In this present case, we speculated that during the fracture healing process, *S. aureus* was disseminated from a distant infection focus to the fractured bone and surrounding damaged muscle and eventually caused the formation of multifocal hematogenous osteomyelitis and muscle abscesses.

In this patient, the cause of his multiple fractures was believed to be FGF23-related hypophosphatemic osteomalacia. Moreover, his bone strength was probably impaired by secondary hyperparathyroidism, which was presumably due to 25-hydroxyvitamin D deficiency, renal dysfunction, and FGF23-induced inhibition of 1α, 25-dihydroxyvitamin D synthesis. FGF23 measurement had been reported to be useful for the differential diagnosis of hypophosphatemic diseases, such as tumor-induced osteomalacia [15]. One of the common clinical manifestation in osteomalacic patients is fracture, which is observed in 76% [16]. Curiously, for some reason, our patient had mild tenderness on some fracture sites, despite his normal sensory function. We speculated that the external force on the ribs might not have been strong.

Tumor-induced osteomalacia (TIO) can be cured by complete resection of the responsible tumor. However, the tumor may be difficult to identify, because it is usually small and can arise anywhere in the body [17]. In TIO localization, a stepwise approach with functional imaging modality and anatomical imaging study had been advocated. Functional imaging includes gallium-68-DOTATATE positron emission tomography (PET), indium-111-pentetreotide single photon-emission computed tomography (SPECT) and fluorine-18-fluorodeoxyglucose PET, whereas anatomic imaging studies include CT and magnetic resonance imaging. Neither these imaging examinations nor pathological examinations were available in our case because the patient refused further examinations.

To the best of our knowledge, this was the first report on multifocal osteomyelitis and pyomyositis around the fracture sites in an osteomalacic adult. Fractures with osteomalacia can be induced by weak external force and are, therefore, usually closed. Compared with open fractures, closed fractures have a lower rate of infection [2], although acute hematogenous osteomyelitis can occur, even in patients with closed fractures [18]. In a study on 372 patients with

vertebral compression fractures, 6 patients had vertebral osteomyelitis [18]. We should recognize the possibility that closed fractures in osteomalacic adults can cause acute hematogenous osteomyelitis.

Prolonged antibiotic administration is required to treat osteomyelitis and pyomyositis due to *S. aureus*; our case needed antibiotic treatment for more than 2 months. The Infectious Diseases Society of America Clinical Practice Guidelines recommend a total duration of 6 weeks of antimicrobial therapy for most patients with bacterial vertebral osteomyelitis [19]. In a study on hematogenous vertebral osteomyelitis, the risk factors for recurrence were methicillin-resistant *S. aureus* infection, undrained paravertebral/psoas abscesses, and end-stage renal disease. In patients with these risk factors, prolonged antibiotic therapy for over 8 weeks resulted in a relatively low recurrence rate [20].

In conclusion, we experienced a case of multifocal osteomyelitis and pyomyositis around the fracture sites in an osteomalacic adult. There had been no previous report on acute hematogenous osteomyelitis in an osteomalacic case with fractures. In a case of osteoarticular infection with multifocal fractures, osteomalacia may be suspected.

Disclosure statement

No potential conflict of interest was reported by the authors.

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