Diabetes With Osteomyelitis in Rare Sites With Sepsis as the First Diagnosis: Three Case Reports and Literature Review

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Research article

Keywords: type 2 diabetes mellitus, osteomyelitis, diagnosis, treatment

Posted Date: July 24th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-44918/v1

Abstract

Background: Osteomyelitis is an infectious bone disease. Common clinical symptoms are fever, local limb pain and redness. Anti-infective treatment is commonly used, but the efficacy varies in different patients. Sometimes surgery is needed to relieve patients' symptoms. Diabetic patients have a high risk of osteomyelitis due to long-term hyperglycemia, activated inflammatory response and immune deficiency.

Patient Concerns: In our study, the three patients were men who were admitted to the hospital due to fever and pain. Two patients had upper limb pain, and the third had lumbar spine pain. All of them had blood cultures that suggested bacterial infections and increased levels of C-reactive protein.

Diagnosis: Two patients in our study had osteomyelitis that was verified by magnetic resonance imaging; osteomyelitis was confirmed by postoperative histopathological examination in the third patient.

Interventions: All patients received intravenous infusion of antibiotics to treat osteomyelitis. The third patient underwent debridement of the lumbar spine.

Outcomes: Among the three patients, two recovered after adjustment of the antibiotic therapy, and one recovered after a surgical operation.

Conclusion: Our study reports three patients with diabetes with osteomyelitis in rare sites. We should be aware that diabetes is one of the risk factors for osteomyelitis. When diabetic patients present with fever and pain, healthcare professionals should be alert to the possibility of osteomyelitis. Blood tests are helpful for clarifying the degree of inflammation, and imaging tests are helpful for locating the infection site. However, for some atypical cases, we cannot rely too much on auxiliary examinations, and we need to pay attention to the clinical symptoms and signs. Glycemic control and anti-infective therapy are common methods for the treatment of osteomyelitis, and surgical intervention should be considered if necessary to relieve local symptoms.

Background

Osteomyelitis is a type of infectious bone disease. The location of the infection is affected by the source of the infection. Diabetic patients have compromised immune systems and are more susceptible to infections as a result of disordered glucose and lipid metabolism. Therefore, the early diagnosis and treatment of osteomyelitis is very important in patients with diabetes.

Due to lower extremity arteritis, peripheral neuropathy, nutritional deficiencies, and poor glycemic control [1–2], the bones of the lower limbs and feet are the most common sites of osteomyelitis in diabetic patients [3–5]. With the continuous development of modern society, the average life expectancy has increased, and the incidence rates of lumbar spondylosis and periarthritis have also increased significantly. Lumbar spondylosis and periarthritis are mainly characterized by local bone pain, which is

similar to the main clinical symptom of osteomyelitis. Therefore, pain in the waist and shoulder in diabetic patients is often misdiagnosed as lumbar spondylosis or periarthritis rather than a bone marrow infection.

Our study included 3 diabetes patients with osteomyelitis who were first diagnosed with sepsis and had lesions on the humerus, shoulder and lumbar spine. The principles of early detection, diagnosis and treatment of osteomyelitis are reviewed in our study to explain the importance of diagnosing and treating osteomyelitis in rare sites in diabetic patients.

Case Report

All three patients were admitted to our hospital's endocrinology department in 2014, 2017, and 2018 due to poor glycemic control combined with physical pain. After obtaining the patients' informed consent, we retrospectively analyzed the clinical diagnosis and treatment of three patients with type 2 diabetes mellitus (T2DM) and osteomyelitis in rare sites that was first diagnosed as sepsis.

Case 1

A 50-year-old man presented with high fever (peak body temperature 38°C) and left shoulder bone pain; he received insulin treatment daily and had poor glycemic control. One month prior to presentation, he suffered a trauma to his left shoulder and then felt pain in his left shoulder accompanied by general weakness and a high fever. During the medical examination, mild edema in the lower limbs and swelling of the left shoulder were noted. After admission, his examination suggested leukocytosis (15.93×10^9/L), with a differential count of 91.1% neutrophils and a high level of C-reactive protein (CRP) (107.5 mg/L; reference range <10 mg/L). The results of the blood culture suggested infection with *Staphylococcus aureus*. Magnetic resonance imaging (MRI) showed bone marrow edema and cystic lesions in the proximal humerus, which were consistent with changes due to osteomyelitis (Fig. 1). During hospitalization, the swollen part of his left shoulder was lanced, and the wound was flushed, draining 300 ml of purulent fluid. The purulent fluid culture suggested infection with *S. aureus*. He received treatment with insulin, antibiotics and human albumin. After a 30-day course of antibiotics (Fig. 2), his fever subsided, and his symptoms gradually improved.

Case 2

A 62-year-old man with diabetes who was treated with insulin and metformin daily and had good glycemic control presented with a high fever (peak body temperature 39°C) and right shoulder bone pain. He took diclofenac sodium before coming to the hospital, but his symptoms did not improve. Laboratory testing revealed a white blood cell count (WBC) of 5.98×10^9/L with a differential count of 77.4% neutrophils, erythrocyte sedimentation rate (ESR) of 120 mm/h (reference range≤ 43 mm/h) and CRP of 83.4 mg/L. His blood culture results suggested *S. aureus* infection. MRI showed bone marrow edema near the right humerus, indicating a bone infection (Fig. 3). Single-photon emission computed tomography (SPECT-CT) suggested active bone formation on the right humeral head, which led to the

diagnosis of osteomyelitis. Despite treatment with antibiotics and an initial decline in body temperature, his fever rose again (peak body temperature 38.5°C) (Fig. 4), and he developed a cough. CT showed inflammation in the left lower lung lobe. Pharyngeal swabs were positive for fungi. The patient recovered well after treatment with fluconazole.

Case 3

The third patient was a 60-year-old man with diabetes who was treated with mitiglinide and metformin daily and had good glycemic control. One month before coming to our hospital, he experienced chills and a high fever (peak body temperature 40°C). He received treatment at another hospital. Laboratory testing revealed a procalcitonin (PT) level of 17.2 ng/ml (reference range 0.021~0.500 ng/ml) and a CRP level of 109 mg/L, the blood culture was positive for *Escherichia coli*, and the chest CT revealed limited local inflammation. The patient was treated with intravenous fluids for half a month, and his fever subsided. He underwent chest CT again, which showed that the inflammation had improved. During hospitalization, the patient presented with lumbar pain that radiated to the lower extremities. X-ray imaging showed degeneration of the lumbar spine. The pain was improved after 10 days of bed rest but was aggravated on the fourth day after discharge and was accompanied by a high fever (peak body temperature 39.5°C). He returned to the same hospital. Laboratory testing showed a WBC count of 10.9×10^9/L with a differential count of 91.1% neutrophils, CRP level of 101 mg/L, PT level of 6.87 ng/ml and blood culture that was positive for *E. coli*. He was treated with intravenous meropenem for two days, but his symptoms persisted.

He was admitted to our hospital because of intolerably severe lumbar pain that made it impossible for him to get out of bed. Blood culture was positive for *E. coli* for the third time. MRI showed changes that suggested the diagnosis of lumbar degenerative disc disease (Fig. 5). The patient's symptoms persisted after treatment with intravenous biapenem therapy for 14 days in our hospital. We upgraded the antibiotic to imipenem and sulfamethoxazole based on the results of the drug sensitivity test. His WBC, CRP level, and PT level gradually returned to the normal reference ranges, his fever subsided (Fig. 6), and the blood culture was negative for bacteria. However, his lumbar pain was not alleviated. On physical examination, both of his lower limb straight leg elevation tests were suspected to be positive. Based on the extremely severe pain and the result of the physical examination, orthopedists thought that the diagnosis of lumbar osteomyelitis should be considered. The patient underwent debridement of the lumbar spine near the lumbar intervertebral foramen on the 29^{th} day after admission. Histopathological examination of the intraoperative findings suggested pyogenic vertebral osteomyelitis. The patient received levofloxacin and piperacillin/tazobactam treatment after surgery and recovered well.

Discussion

The symptoms of osteomyelitis are often nonspecific. They usually include a low fever, local pain, and swelling of the limbs or erythema.

Markers of inflammation in the blood may be helpful for diagnosing osteomyelitis. In a recent study, Stucken et al. [6] reported that when the WBC, ESR and CRP level were increased simultaneously, the predicted probability of an infection reached 100%. However, even when the above three indicators are in the normal reference ranges, approximately 20% of patients still have an infection. In the acute phase of the osteomyelitis, the sensitivity of X-ray for the detection of the disease is low (43% -75%), while the specificity is slightly higher (75% -83%). The results of X-rays can be normal within 14 days after the emergence of symptoms, and osteomyelitis becomes apparent on X-rays when at least 50% of the bone is damaged. In the early stage, X-ray can be used to distinguish osteomyelitis from other related diseases, including fractures and bone tumors. Ultrasound scans are usually negative (46% -74% sensitivity, 63% -100% specificity), which limits its use [7]. CT, which is suitable for patients with contraindications to MRI [8], is useful for finding necrotic bones, which assists in the diagnosis of chronic osteomyelitis. MRI has a high sensitivity (82% -100%) and specificity (75% -99%) and is helpful for reaching a diagnosis of osteomyelitis [9]. MRI helps locate lesions, define the extent of the destruction, track the development of the disease and plan surgical interventions. An isotope scan can help distinguish between inflammation in the bone and soft tissue.

The treatment of diabetic patients with osteomyelitis mainly includes controlling blood sugar levels, eliminating the infection, and clearing the lesions. A duration of antibiotic therapy of 4 to 6 weeks is recommended [10], but the duration ultimately depends on the systemic and local infection statuses, surgical strategy and immune status of the patient.

The following are antibiotics that can be selected for parenteral administration. β-lactam antibiotics (penicillin, cephalosporin and carbapenem) penetrate the bone tissue at a serum concentration of approximately 5–20%, which exceeds the minimum inhibitory concentration of osteomyelitis pathogens. *S. aureus* is the most common microorganism that causes osteomyelitis [11], and vancomycin is the drug of choice for the treatment of *S. aureus* infections [12]. Daptomycin is a new type of antibiotic with a success rate of treating osteomyelitis due to *S. aureus* of 82.7% [13]. The following are antibiotics that can be selected for oral administration. Fluoroquinolones [14], linezolid [15], and trimethoprim [16] can reach adequate concentrations in the bone that are 50% of the serum concentrations. Community-associated methicillin-resistant *S. aureus* is sensitive to doxycycline and clindamycin [17]. An alternative oral antibiotic used to treat anaerobic osteomyelitis is metronidazole [18]. Although rifampicin cannot be used alone to treat osteomyelitis, it can improve the cure rate when added to various other antibiotics [19]. In addition, fusidic acid [20] and fosfomycin [21] are suitable adjuvant drugs for combination therapy.

The surgical removal of necrotic and infected bone, combined with antibiotic treatment, can increase the cure rate of osteomyelitis. The main treatment for acute osteomyelitis is the local drainage of the pus. The purpose is to alleviate the symptoms of toxemia and prevent the transition to chronic osteomyelitis. Surgery is recommended when the symptoms remain uncontrolled 48–72 hours after the initiation of antibiotic treatment. The purpose of surgery in patients with chronic osteomyelitis is to completely

remove the lesions, remove necrotic bone, remove hypertrophic scars and granulation tissue, eliminate dead spaces, and improve the local blood circulation to promote healing.

In conclusion, shoulder, humerus and lumbar osteomyelitis are rare in diabetic patients. Due to similar clinical symptoms, they are often misdiagnosed as periarthritis and lumbar spondylosis, leading to the missed diagnosis of osteomyelitis and the consequent exacerbation and prolongation of the condition. We cannot rely on auxiliary examinations when the imaging is not clear in some osteomyelitis cases. We should pay attention to the patient's medical history, clinical symptoms, and physical examination and closely monitor changes in the patient's condition. Due to poor immunity in diabetic patients and the long duration of anti-infective treatment for osteomyelitis, we should be alert to the occurrence of co-infections and strengthen supportive treatment if necessary.

Abbreviations

T2DM
type 2 diabetes mellitus
CRP
C-reactive protein
MRI
Magnetic resonance imaging
WBC
white blood cell count
ESR
erythrocyte sedimentation rate
SPECT-CT
Single-photon emission computed tomography
PT
procalcitonin.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication

Written informed consents were obtained from the patients for publication of the case reports and the accompanying images. The copy of the written consents is available for review by the Editor-in-Chief of this journal.

Availability of data and materials: Not applicable

Competing interests

The authors declare that they have no competing interests.

Funding

The funding is from the local government. Item liable person is Xiaohong Jiang (chief physician). Item Number is CJ20140061.

Authors' contributions

Jiayan Zhou is responsible for writing manuscript and literature review. Xiaohong Jiang is responsible for advising on design and reviewing manuscript. The final manuscript are approved by all the authors.

Acknowledgements: Not applicable

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Figures

Figure 1

Left shoulder MRI of the patient in case 1.

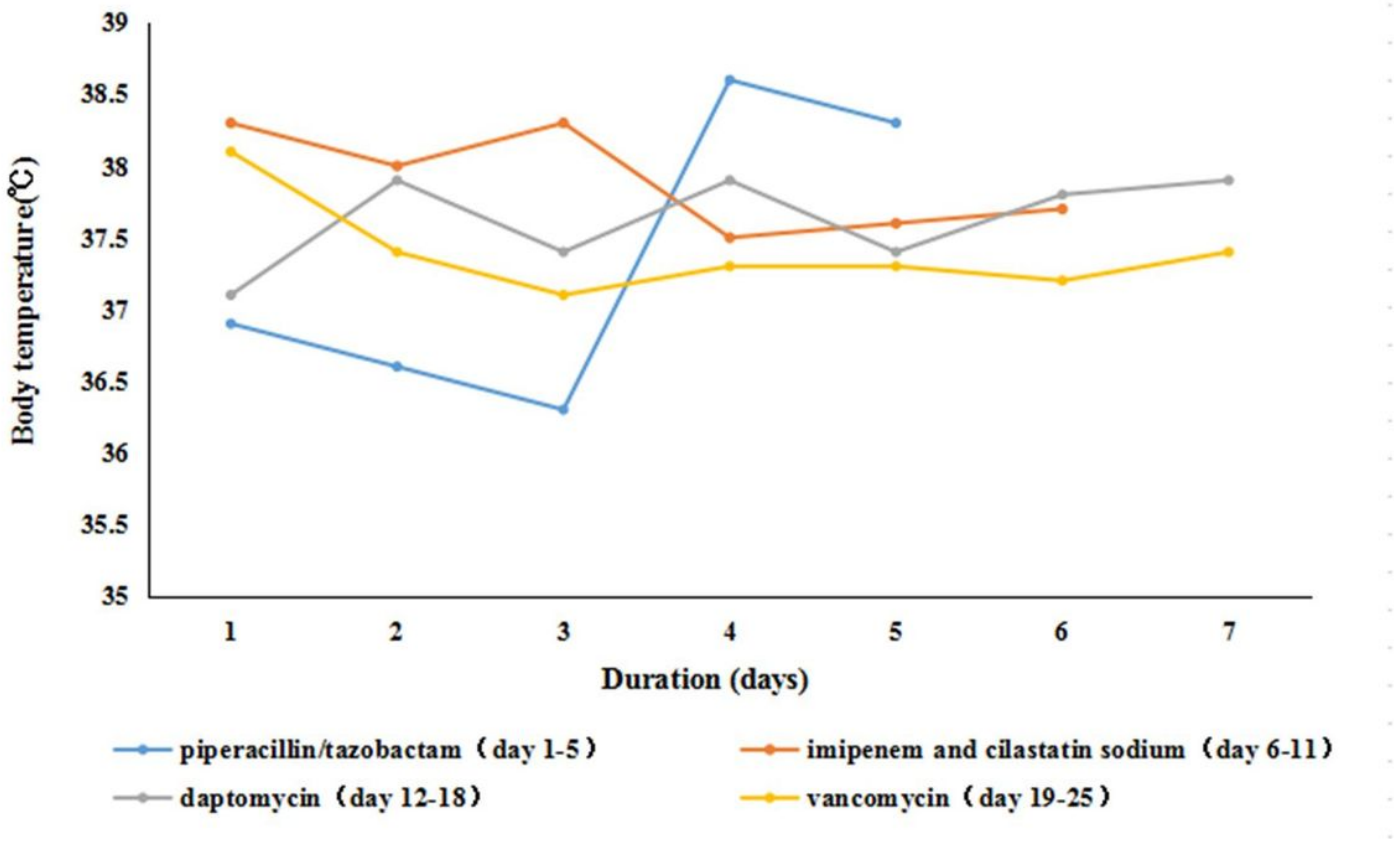

Figure 2

The body temperature of the patient in case 1.

Figure 3

Right humerus MRI of the patient in case 2.

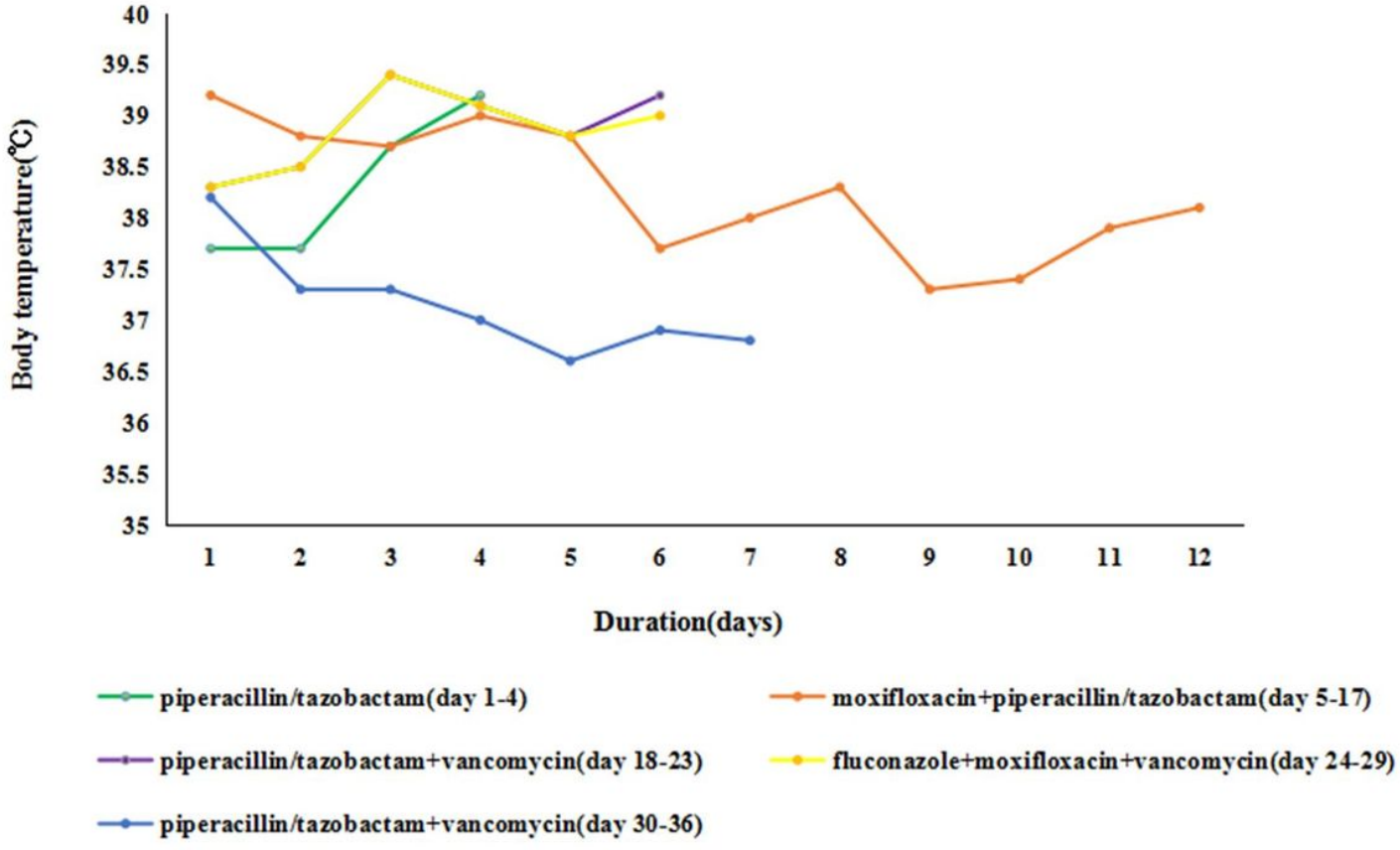

Figure 4

The body temperature of the patient in case 2.

Figure 5

Lumbar spine MRI of the patient in case 3.

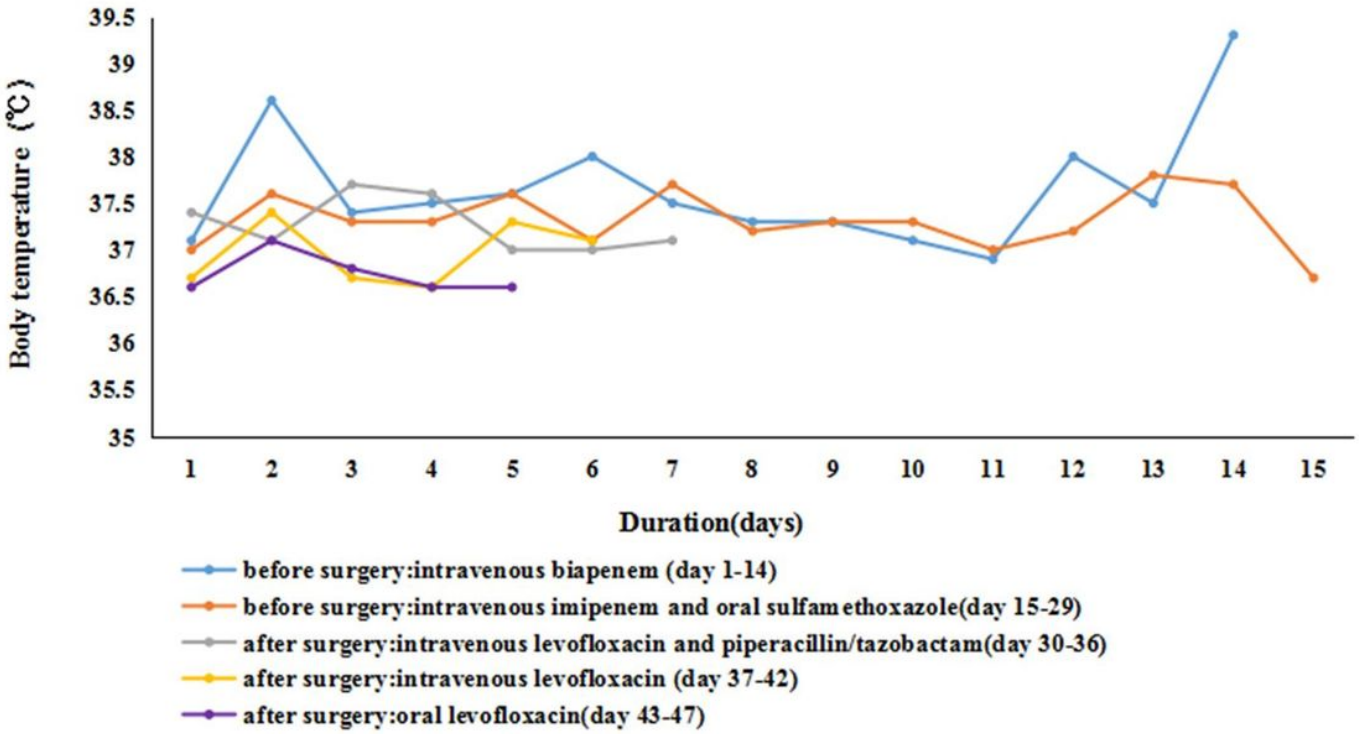

Figure 6

The body temperature of the patient in case 3.