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Case Report

What *Corynebacterium amycolatum* has to do with Bones?

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Abstract

Orthopaedic infections are associated with a substantial risk of recurrence due to the difficult penetration of antibiotics in bone tissue. Though most often the causative agent is Gram positive bacteria, in some cases, unusual pathogens can cause bone infections due to underlying clinical conditions.

A 56-year-old woman affected by an autoimmune hepatitis treated with mycophenolic acid (1g per day) and steroids (prednisone 12.5 mg per day) since 2004, was evaluated because of a haematoma in the right-side gluteus secondary to a fall. A CT scan of the pelvis showed an abscess of the right gluteus (41 x 68 mm x 7.5 cm) and an exophytic part of the bone close to a minor bleeding arteriole. The biopsy showed emphysematous chronic osteomyelitis; the microbiological examination of the bone and the drainage performed before antibiotic treatment were positive for *Corynebacterium amycolatum*, in absence of other pathogens. *C. amycolatum* infections are usually described in immune-compromised individuals. Most commonly it was reported in paediatric patients who underwent peritoneal dialysis and developed peritonitis, other reported the pathogen in corneal ulcers or even endocarditis. Usually, *C. amycolatum* is isolated as part of a mixed flora.

This is the first single-pathogen bone infection due to *C. amycolatum*; the isolation of this bacteria indicates that even alone, it could cause invasive infections alone in immunocompromised patients.

Keywords: *Corynebacterium amycolatum; Osteomyelitis; Immunosuppressed*

Introduction

Orthopaedic infections, such as arthritis of native joint, peri-prosthetic joint infections, and osteomyelitis are usually chronic infections difficult to diagnose and treat [1]. Acute osteomyelitis presents typically with a duration of symptoms ranged from few days to few weeks. Chronic osteomyelitis is a long-standing infection, over months of year and sequestra (necrotic bone that separate from the viable one) are usually present; they form because of necrosis or ischemia of the bone and can be usually seen radiographically [2].

Pathogens responsible for osteomyelitis vary depending on the pathogenesis of the infection; haematogenous infections are commonly caused by *Staphylococcus aureus,* but any pathogen capable of inducing a bacteraemia can potentially cause osteomyelitis [3,4]. Furthermore, infections can develop also by contiguous sites and are due to skin commensal (such as coagulase-negative *staphylococci*, *Cutibacterium spp*, or *Corynebacterium spp*). In these cases, the growth of the same bacteria on multiple bone samples (at least two) is mandatory to determine if the specific bacterium is the real pathogen or a commensal.

Case Report

A 56-year-old woman went to her general practitioner because of a haematoma in the right-side gluteus secondary to a fall on the ground occurred while collecting wood in a forest in the South of Switzerland. She had in anamnesis an autoimmune hepatitis treated with mycophenolic (1g per day) acid and steroids (prednisone 12.5 mg per day) since 2004, and a previous diagnosis of chronic osteomyelitis by *Citrobacter koseri* and *Proteus vulgaris* that was treated with a complex surgery to clear the infection that then required plastic surgery to rebuild the epidermidis on both legs and pelvis. She also received antibiotic treatment (cefepime 2g/8h as empiric treatment at the beginning, then oral amoxicillin/clavulanic acid 1g/8h) for six weeks with a complete resolution of the infection. No surgical wound infection occurred during the post-surgery follow-up.

For the management of haematoma, the patient underwent to three evacuations, before being referred to the hospital for short-term recurrences. She never had fever or other systemic symptoms. Blood tests showed a mild increase of C reactive protein (7 mg/l), leucocytes (13.3x10^9/l), and of liver enzymes, due to the anamnestic auto-immune hepatitis.

A CT scan of the pelvis showed an abscess of the right gluteus (41 x 68 mm in the axial plane, with cranio-caudal extension of 7.5 cm) and an exophytic part of the bone close to a minor bleeding arteriole. The haematoma was surgical evacuated, and a drainage was placed in order to drain the abscess; a biopsy of the exophytic mass was also performed and sent for histopathology examination showing emphysematous chronic osteomyelitis. Both the microbiological examination of the bone and the drainage showed the growth of *C. amycolatum* (Figure 1), in absence of other pathogens. Patient was treated empirically with 2 days of vancomycin (1g/12h) and piperacillin/tazobactam (4.5g/8h). After identification of *C. amycolatum,* the antibiotic was modified according to the antibiogram and oral clindamycin (600mg/8h) was started and continued for a total of 6 weeks. No clinical or laboratory recurrences were observed after six months of follow-up.

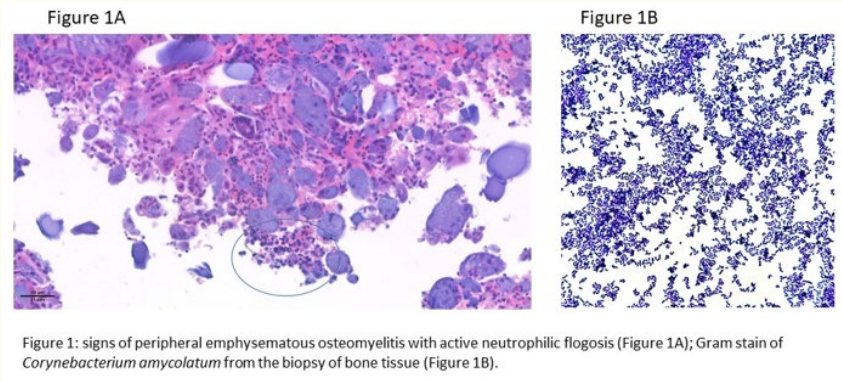

Figure 1: signs of peripheral emphysematous osteomyelitis with active neutrophilic flogosis (Figure 1A); Gram stain of *Corynebacterium amycolatum* from the biopsy of bone tissue (Figure 1B).

Review of Literature

Corynebacterium amycolatum is a gram positive, aerobic or facultative anaerobic *bacillus* that only rarely causes clinical infections. *C. amycolatum* is a common component of human skin flora and mucous membranes; therefore, it is often considered a contaminant of blood-cultures or microbiological samples. *C. amycolatum* infections are usually described in immune-compromised individuals, in uncontrolled diabetes or in patients in dialysis treatment due to end-stage renal disease, or in paediatric premature infants. We ran research on Pubmed and Scopus using the key word *C. amycolatum* and infection. We found 17 available papers.

Few cases were reported of peritonitis due to *C. amycolatum*, of which two were paediatric patients [5] and 5 were adults undergoing peritoneal dialysis for more than 2 years. Among immunocompromised children, a Brazilian group reported 7 cases of central venous

catheter infection due to *C. amycolatum*. It is to notice that together with *C amycolatum*, coagulase-negative staphylococci were isolated, that could be more likely the actual cause of the infection [6].

Another peculiar presentation of *C. amycolatum* was a corneal ulcer in a 72-years-old patient in India. This patient underwent a cataract surgery 10 years before and had an open globe injury due to a fall; despite surgical repair was performed, endophthalmitis occurred. Four months after the infection, an epithelial defect was noted in the eye cornea with a profuse discharge and conjunctival and circum-corneal ciliary congestion. Corneal scraping was sent for further analysis, and it turned out to be positive for *C.* amycolatum [7].

Some authors reported *C. amycolatum* related endocarditis [8-10]; Dalal., *et al*. [8] reported a case of an 84-year-old female resident in a long-term care facility, known for end-stage renal disease, dependent on dialysis that presented with hypotension, fever, and a loud cardiac murmur in the mitral area. Blood-cultures were positive for gram-positive rods, identified as *C. amycolatum*. Transoesophageal echocardiography revealed a vegetation on the mitral valve. Da Rocha and Knox [9,10] reported cases of nosocomial *C. amycolatum* endocarditis; these cases were related either to prosthetic cardiac valve or to indwelling intravascular devices.

In 2020, Fernandez., *et al*. [11] reported a *C. amycolatum* mastitis in a healthy, non-pregnant woman that was treated with antibiotics with a positive outcome. Another mastitis occurred in India, in a 43-years-old female otherwise healthy [12].

Sengupta., *et al*. [13] described a case series of 12 patients with purulent discharge from the ear.

Few *C. amycolatum*- bone infections were described to date; Clarke., *et al*. [14] reported a case of septic arthritis in a naïve hip joint of a 63-year-old man. The patient underwent a right femoral popliteal bypass graft secondary to occlusion of the right superficial femoral artery and atheromatous change of the common iliac vessel one year before the infection of the naïve left hip. In Switzerland, 22 cases of prosthetic joint infections related to *C. amycolatum* were reported between 1992 and 1997 [15]. This bacterium was the most frequently isolated, even if often in mixed infections. More recently, Kalt reviewed cases of *Corynebacterium spp* orthopaedic infections; among those, 17/97 (17.5%) patients were positive for *C. amycolatum*, with 11 (15.7%) who had positive orthopaedic isolates and blood cultures [1]. However, only one of them had a documented monomicrobial infection, the others had polymicrobial infections and therefore, the role of *C. amycolatum* was uncertain.

A recent case report [16] described an immunosuppressed patient with subcutaneous abscesses on the trunk and extremities. Histopathology results were positive for *C. amycolatum.*

Like our patient, Sharma., *et al.* [17] reported a multifocal emphysematous osteomyelitis of the spine in a female patient in India. Samples collected from the left pelvis and gluteal region were positive for *Escherichia coli* and *C. amycolatum.* After the drainage, she started the antibiotic treatment according to the germs' susceptibility. However, due to the mixed infection the specific role of *C. amycolatum* in this case in unlikely.

Conclusion

To our knowledge, this is the first report of a confirmed, mono-pathogen emphysematous osteomyelitis due to *C. amycolatum*. Other reports published up to now, describe a mixed flora, in which other microorganisms were present together with *C. amycolatum*, leading to a less probable diagnosis. The isolation of *C. amycolatum* in multiple microbiological samples indicates that this bacterium could be considered the cause of emphysematous osteomyelitis in our patient. Our patient has a long history of immune-depression due to the autoimmune hepatitis and, therefore, is more prone to develop unusual infections. Our report suggests that in immunocompromised patients, also rare bacteria should be considered as differential diagnosis and should be included in clinical reasoning.

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