

Short Research Communication

A Rare Case of Osteomyelitis Caused by *Haemophilus Parainfluenzae*

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Abstract

Haemophilus parainfluenzae is a rare cause of bone and joint infections. We report a case of calcaneal osteomyelitis due to this microorganism with a review of all published. A 23-year-old woman presented with a 1-month history of pain and inflammation in the calcaneus area. Osteomyelitis was suspected at this location based on computed tomography images. Culture of six bone biopsies and surrounding tissue resulted in the isolation of *H. parainfluenzae*. Surgical drainage and debridement was performed, and antibiotic treatment was prescribed, resolving the infection.

Key words: osteomyelitis, *Haemophilus parainfluenzae*, pain, drainage.

Introduction

Osteomyelitis is an inflammatory disease caused by microorganisms and accompanied by local bone destruction [1]. Its etiology can be hematogenous, contiguous (due to local spread), secondary to vascular insufficiency or the result of direct trauma-induced bacterial inoculation [2]. *Staphylococcus aureus* is the pathogen most commonly associated with this infection, but many other microorganisms can be implicated depending on epidemiological factors and clinical conditions [2]. Postsurgical or posttraumatic osteomyelitis, as well as chronic evolution or nosocomial infections is generally produced by Gram-negative pathogens *Enterobacteriaceae* and *Pseudomonas aeruginosa*, and other Gram-negative rods have also been implicated in bone and joint infections, such as *Haemophilus parainfluenzae*. This microorganism is a common inhabitant of the oral cavity and respiratory tract and a frequent etiological agent of respiratory tract infections. We recently encountered a rare case of

osteomyelitis due to this bacterium in a patient with underlying risk factors for this clinical entity.

Case Report

A 23-year-old woman with a 1-month history of pain and inflammation due to a chronic trauma-induced calcaneal chronic ulcer because of a preceding traumatism came to our Emergency Department after some days with increased pain and exudate. She was under treatment with non-steroidal anti-inflammatories. She had been treated with ventriculoperitoneal shunt for meningocele and spine bifida in her childhood. Physical examination revealed a fever (38.5° C), inflammatory signs and exudate in the calcaneus ulcer. Complete blood count, chemical profile and urinalysis were normal except for a C-reactive protein (CRP) of 121 mg/L. Computed tomography imaging revealed: cortical destruction of the calcaneus, a periosteal reaction, and soft-tissue involvement due to an abscess draining to

the skin surface, suggesting osteomyelitis.

Surgery was performed with local debridement of the lesion and drainage of the abscess, obtaining six intraoperative samples from the bone and surrounding tissue.

Each sample (1 cm²) was placed in 3 ml of sterile saline solution and vortexed for 30 seconds. Then, the sample was inoculated in aerobic and anaerobic blood agar (BD Columbia Agar 5% Sheepblood®, Becton Dickinson), chocolate agar (BD Choco Agar, Becton Dickinson) and thioglycolate broth (BD™ Fluid Thioglycollate Medium, Becton Dickinson), all incubated at 37° C.

After 18 h. of incubation, pathogen growth was observed for all samples but in chocolate agar medium alone. The bacterium was identified as *H. parainfluenzae* by mass spectrometry (score 2.203) (Bruker Biotyper, Billerica, MA, USA), and susceptibility to this strain was then tested by the E-test method in *Haemophilus* test medium (BD *Haemophilus* Test Medium Agar). The isolate was susceptible to amoxicillin/clavulanic acid (0.25 µg/mL), ampicillin (0.38 µg/mL), cefotaxime (0.016 µg/mL), and levofloxacin (0.047 µg/mL) and was resistant to azithromycin (6 µg/mL) and trimethoprim/sulfamethoxazole (>4/76 µg/mL) according to CLSI criteria [3]. After two weeks of treatment with ceftriaxone (2 g/12 h), she was discharged home with a prescription of amoxicillin (500 mg/8 h) for a further six weeks. At the latest follow-up (3 months post-discharge), the patient was clinically improved, with normal laboratory findings.

Discussion

Osteomyelitis is a common and severe bone tissue infection [1]. Staphylococci, above all *S. aureus*, are the main microorganisms that cause this infection [1].

H. parainfluenzae is a Gram-negative rod in the HACEK group and is frequently observed in the human oral cavity and respiratory, urogenital and gastrointestinal tracts. It can be responsible for a broad spectrum of serious infections such as endocarditis, bacteremia, and pneumonia [4]. However, osteomyelitis due to *H. parainfluenzae* is an extremely rare entity, with only five cases reported in the medical literature [5-8] (table 1). This opportunistic pathogen usually produces infection in immunocompromised individuals or those with other risk factors. Diseases known to increase the likelihood of osteomyelitis and/or *Haemophilus* infection have been recorded in five out of the six cases now reported to date, and only one patient had no risk factors. The presence of this pathogen should therefore be suspected in patients with symptoms of osteomyelitis and the presence of chronic systemic disease or undergoing diagnostic or therapeutic procedures involving oral and/or nasopharyngeal sites, including dental treatments. In patients with no risk factor for contiguous infection, it is likely that osteomyelitis develops *via* hematogenous spread facilitated by mucosal destruction [9]. A contiguous soft tissue infection appears to be the cause in the present patient, given her chronic trauma-induced ulcer.

Table 1. Main findings in 6 patients with osteomyelitis caused by *Haemophilus parainfluenzae*.

| Patient (reference/year of publication) Author | Age (years)/ sex | Localization of infection | Risk factors * | Time until diagnosis (days) | Clinical manifestations | Laboratory findings | Microbiological diagnosis | Treatment | Outcome/ follow-up (months) |
|--|------------------|---------------------------|--|-----------------------------|-------------------------------------|---------------------|--|--|-----------------------------|
| 1(5/1987) Olk DG | 49/M | Vertebral | Nasal septoplasty 3 months before | 22 | Back pain | ESR 39 mm/h | Percutaneous aspiration biopsy Blood cultures (-) | Ceftriaxone Percutaneous aspiration | Cure/12 |
| 2(6/1991) Auten GM | 74/M | Vertebral | Tooth abscess 2 weeks before | NR | Neck pain | NR | Abscess culture Blood cultures (-) | Vancomycin + tobramycin + aztreonam TMP/SMZ + tobramycin Ciprofloxacin Abscess drainage | Cure/4 |
| 3(7/1992) Beauvais C | 70/F | Vertebral | Colon cancer 15 years before Colonoscopy and gastroscopy 1 month before | 6 | Back pain, fever, chills | ESR 84 mm/h | Percutaneous aspiration biopsy Blood cultures (-) | Cefotaxime + gentamicin Cefixime + pefloxacin Percutaneous aspiration | Cure/3 |
| 4(8/2007) Khor BS | 79/M | Vertebral | Gastroscopy | 12 | Back pain, tenderness | NR | Intraoperative sample tissue Blood cultures (-) | Cefazolin + gentamicin Ampicillin Surgical debridement | Cure/12 |
| 5(8/2007) Khor BS | 36/M | Iliac bone and sacrum | NR | NR | Fever, pain | NR | Blood cultures (+) | Oxacillin + gentamicin Ampicillin | Cure/6 |
| 6(PR/2016) Cobo F | 23/F | Calcaneus | Skin ulceration due to a preceding traumatism Ventriculo-peritoneal shunt | 15 | Pain, inflammation, fever, drainage | CRP 121 mg/l | Intraoperative bone biopsy | Ciprofloxacin Amoxicillin + Clavulanic acid Surgical debridement | Cure//3 |

* Risk factors for both osteomyelitis and *H. parainfluenzae* infection.

M: male; F: female; NR: not reported; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TMP-SMZ: trimethoprim/ sulfamethoxazole; PR: present report.

Pain, fever, tenderness, and inflammatory signs are observed in the majority of patients with suspicion of osteomyelitis. In the reviewed cases of osteomyelitis due to *H. parainfluenzae*, these symptoms had generally been experienced for three weeks (mean of two weeks) before medical treatment was sought. Symptoms are the same as those for osteomyelitis caused by other microorganisms. The most frequent localization of this infection in the reviewed cases was the spine.

A rapid and accurate diagnosis is vital, because inappropriate or delayed treatment may lead to irreversible bone destruction. Culture of biopsy from the involved bone is the main diagnostic technique for ruling out osteomyelitis [10, 11], and blood cultures are generally only essential in hematogenous osteomyelitis. Some authors have proposed the gathering of at least three bone samples to increase the positivity rate [12]. In the published cases of osteomyelitis by *H. parainfluenzae*, diagnosis was by blood culture in only one case, being based on aspiration biopsy or intraoperative tissue/bone sample in others. Finally, one case was diagnosed by culture of abscess drainage, although the results should be interpreted with caution because samples might have included non-pathogenic microorganisms. Erythrocyte sedimentation rate (ESR) and/or CRP levels were reported in three patients and were elevated in these cases. As in other infections, normal CRP and ESR values are useful to rule out infection (including osteomyelitis), but abnormal levels are non-specific for this infection.

Due to its rarity as cause of osteomyelitis, empirical antimicrobial treatment of osteomyelitis may be inadequate for *H. parainfluenzae* and should be changed after identification of this pathogen. Before susceptibility results are obtained, the recommended empirical antibiotic treatment of high-risk Gram-negative pathogens is with quinolones or third-generation cephalosporins [2]. However, empiric antibiotic therapy in stable patients should be avoided until appropriate tissue specimens are collected. Usually, 4-6 weeks of treatment are sufficient to obtain a positive outcome in osteomyelitis cases. A wide variety of treatment regimens were applied in the six reviewed cases, mainly cephalosporins and/or aminoglycosides, and a complete cure was always achieved (table 1).

Surgery is necessary in almost all cases, especially when an abscess is present [12]. Drainage and debridement are performed after confirmation of the diagnosis and are the keys to successful treatment. Surgery was performed in five out of the six cases in this review.

In summary, osteomyelitis due to *H. parainfluenzae* is a rare entity that should be differentiated from other causes of acute osteomyelitis as soon as possible to allow appropriate therapy to be initiated. This infection should be included in the differential diagnosis of patients with symptoms compatible with osteomyelitis and with risk factors such as a chronic systemic disease or recent dental procedure. Microbiological analysis, including susceptibility testing, should be performed in these cases to establish a correct diagnosis and treatment.

Informed consent

The patient described in this case report gave her informed consent for the inclusion in this publication.

Competing Interests

The authors declare no competing interest.

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