ORIGINAL ARTICLE

Clinical features and outcome of bone and joint infections with streptococcal involvement: 5-year experience of interregional reference centres in the south of France

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Abstract

Streptococcal bone and joint infections are less common than staphylococcal cases. Few studies have reported the cases with well-identified *Streptococcus* species. Their clinical features and prognosis are not clearly known to date. Moreover, no treatment regimen has yet been clarified. We reviewed the streptococcal bone and joint infection cases managed in our centres from January 2009 to December 2013. We described the epidemiology, clinical and microbiologic characteristics, treatment approach and outcome. Among the 93 cases, 83% of patients were men with a median age of 60 years, and 90% of patients had comorbidities or risk factors. Bacteraemia occurred in 14% of cases. Serious complications occurred in six patients, including severe sepsis (two cases) and infective endocarditis (two cases). Orthopaedic device infections were observed in 35% of cases, including 17 patients with internal osteosynthesis device infection, 14 with prosthetic joint infection and three with vertebral osteosynthesis device infection. The median time between orthopaedic device implantation and onset of infection was 447 days. Fourteen species of *Streptococcus* were identified, including 97 isolates using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and three isolates using molecular identification. The five most represented species included *S. agalactiae* (37%), *S. dysgalactiae* (12%), *S. anginosus* (11%), *S. constellatus* (10%) and *S. pneumoniae* (9%). Streptococci isolates were susceptible to amoxicillin, with the exception of one *S. mitis* isolate. Remission 1 year after the end of treatment was recorded in 83%. One patient died of infection; eight patients had infections that failed to respond to treatment; and seven patients experienced relapse. Twenty patients (22%) had an unfavourable functional outcome, including 19 amputations and one arthrodesis. Five significant prognostic factors associated with an unfavourable clinical outcome were identified, including peripheral neuropathy (p 0.009), peripheral arterial disease (p 0.019), diabetes mellitus (p 0.031), location in the femur (p 0.0036), location in the foot (p 0.0475), osteitis without an orthopaedic device (p 0.041) and infection caused by *S. dysgalactiae* (p 0.020). The rate of poor outcomes remains high despite the low number of *Streptococcus* isolates resistant to antibiotics. Some prognostic factors, such as the presence of *S. dysgalactiae,* are associated with an unfavourable clinical outcome. Antibiotic regimens of streptococcal bone and joint infections are not standardized and need to be further investigated.

Keywords: Arthritis, bacterial infection, bone and joint infection, human, MALDI-TOF MS, osteitis, osteomyelitis, prosthetic joint infection, streptococci, *Streptococcus*

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Introduction

Although streptococcal bone and joint infections such as arthritis and osteomyelitis are less common than infections due to staphylococci, their role as causative agents of bone and joint

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infection remains significant [1–5]. Previous studies of streptococcal bone and joint infection have reviewed the clinical characteristics and the outcome of streptococcal arthritis or joint prosthesis infection by streptococcal groups classified by Lancefield and Sherman [3–10]. Only a few studies of streptococcal bone and joint infection with well-identified species have been reported [11–15].

Identification of *Streptococcus* species is difficult and constantly evolving. The current method used for identification relies on phenotypic conventional techniques (Gram stain, evaluation of hemolysis, Lancefield antigen) that appear to be less sensitive [16]. In addition, new methods have been developed to identify the *Streptococcus* genus, including PCR amplification of the 16S rRNA gene, which has led to a change in the taxonomy of streptococci [17,18]. Specific nucleic acid probes for *S. pneumoniae* and *S. agalactiae* identification have been developed [19]. Recently *rpo*B, *Gro*EL, *soda* and *tuf* gene sequence–based identification has been used to identify the species of *Streptococcus anginosus* groups [16,19–21].

Matrix-assisted desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) identification has been successfully implemented in routine bacterial identification in clinical laboratories [22]. More recently, MALDI-TOF MS has been used as a reliable routine identification tool for *Streptococcus* species compared to phenotypic and molecular identification [23–25].

The objective of this study was to review the clinical characteristics and outcomes of well-defined monomicrobial and polymicrobial bone and joint infections caused by *Streptococcus* species managed at our referral centre for the treatment of bone and joint infections.

Materials and Methods

Study population

This study was approved by the institutional research ethics board, and written informed consent was provided by each patient. We retrospectively reviewed 93 cases of streptococcal bone and joint infection in 3931 patients (inpatients and outpatients aged >18 years) managed in our referral centre for the treatment of bone or joint infections from January 2009 to December 2013. All cases were managed at four university hospitals with 4000 beds in Marseille, France, including four orthopaedic surgery units, two plastic surgery units and two infectious disease units.

Streptococcal bone and joint infections were diagnosed on the basis of medical history with clinical evidence of infection using biological and/or radiologic compliant data, with at least one positive culture from two or more deep samples based on surgical procedures that excluded the contaminated bacteria, as previously described [26]. Prosthetic joint infection was defined when patients had Infectious Diseases Society of America or Musculoskeletal Infection Society criteria meeting the definition for prosthetic joint infection [27,28]. Infections involving a prosthetic joint were classified according to the time of onset after implantation: early infection (within 1 month) or chronic infection (after 1 month) [29].

We recorded the patients' medical history including demographic characteristics, comorbidities and risk factors associated with bone and joint infection, clinical presentation, and type and site of infection. We then recorded the medical and/or surgical treatment approach and the duration of relapse-free time after treatment. We evaluated treatment success as the remission rate at 3, 6 and 12 months after the end of antibiotic treatment.

An unfavourable clinical outcome was defined as failure to treat, relapse or death caused by infection. Failure to treat was defined by pain and swelling of the bone or joint, wound drainage, implant site erythema, induration or edema, joint pain, joint effusion, fever, purulent discharge from the wound, sinus tract drainage and persistent positive culture from deep samples based on surgical procedures during the treatment period.

Relapse was defined by pain and swelling of the bone or joint, wound drainage, implant site erythema, induration or edema, joint pain, joint effusion, fever, purulent discharge from the wound, sinus tract drainage and persistent positive culture from deep samples based on surgical procedures after the end of treatment and during follow-up examinations at the clinic. An unfavourable functional outcome was defined as amputation, arthrodesis or severe functional deterioration.

Specimen collection and microbiologic analysis

For all patients, deep samples were obtained by surgical procedures, i.e. joint fluid, crushed tissue or bone biopsy samples inoculated on 5% sheep's blood, chocolate, Mueller-Hinton, trypticase soy and MacConkey agar plates (bioMérieux, Marcy l'Etoile, France) and incubated at 37°C in a 5% CO_2 atmosphere and in an anaerobic atmosphere for 10 days. Pure bacterial cultures, obtained by picking isolated colonies, were identified with MALDI-TOF MS and molecular methods, as previously described [22,30]. The antibiotic susceptibilities of *Streptococcus* sp. isolates were determined and interpreted according to the recommendations of the French Society for Microbiology and the European Committee on Antimicrobial Susceptibility Testing (CA-SFM/EUCAST, available at http://www.sfm-microbiologie.org/UserFiles/files/casfm/CASFM_EUCAST_V1_0_2014.pdf).

Statistical analysis

Data analyses were performed by SPSS 20.0 (IBM SPSS, Chicago, IL, USA). We conducted a descriptive analysis of our