# Streptococcal vertebral osteomyelitis: multiple faces of the same disease

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## Abstract

The role of *Streptococcus* species as an aetiological microorganism of vertebral osteomyelitis (VO) is considered to be of little relevance. We aimed to describe a large number of cases of streptococcal vertebral osteomyelitis (SVO), to analyze the clinical features associated with different *Streptococcus* species, and to compare them with a cohort of patients with VO caused by *Staphylococcus aureus*. An incidence study and a retrospective, multicenter, observational clinical study of cases of SVO (1991–2011) were performed. Statistical comparison of SVO by different species and between them and staphylococcal VO was carried out. Over the whole period there was an increasing incidence in the number of VOs and SVOs per year ($p < 0.05$). Among 58 cases of SVO, those caused by non-*viridans streptococcus* (*Streptococcus pneumoniae*, *Streptococcus agalactiae* and *Streptococcus pyogenes*; $n = 26$) mimicked VO by *S. aureus,* and presented with more fever, neurological symptoms and paravertebral abscesses in comparison with those caused by the *viridans* group (remaining species). In contrast, the latter have a sub-acute clinical picture and were associated with the presence of endocarditis ($p < 0.05$). Among non-*viridans* SVOs, concomitant infection was specifically related to *S. pneumoniae* ($p < 0.05$). In conclusion, SVO presents a wide range of clinical patterns. The relationship between VO and diagnosis of endocarditis was established with SVO caused by the *viridans* group. Whereas non-*viridans* SVO mimics acute characteristics of VO caused by *S. aureus*, cases of *viridans* SVO are significantly more likely to have a sub-acute clinical presentation. The increased incidence of SVO during the last decades could support a new epidemiological scenario.

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## Introduction

Vertebral osteomyelitis (VO) has increased its incidence in recent years [1–3]. While *Staphylococcus aureus* is most frequently responsible for VO, the role of *Streptococcus* species has so far been considered to be of little relevance [2,4].

The classifications developed by Lancefield and by Sherman grouped the wide variety of *Streptococcus* species into *viridans* and non-*viridans* streptococci, depending on their microbiological characteristics and potential ability to cause different kinds of infection [5,6]. While there are well-recognized infections caused by streptococci [7–12], streptococcal vertebral osteomyelitis (SVO) is less widely reported and, to our knowledge, its particular features have yet to be described and analysed in detail [2,4,13–15].

Recently, certain epidemiological changes have been pointed out in relation to VO, including a higher incidence of cases caused by low-virulence bacteria and those with no microbiological diagnosis [3,16–18]. These cases are characterized by the slow appearance of signs and symptoms of vertebral osteomyelitis, mainly in older people with debilitating diseases. Thus, we hypothesized that low-virulence SVO could be related to the increased incidence of vertebral osteomyelitis without microbiological diagnosis.

The aim of the present study was therefore to analyse epidemiological changes in SVO over time and to describe the characteristics of a large number of cases of SVO. We also sought to analyse the particular clinical features associated with different *Streptococcus* species, especially the *viridans* and non-*viridans* groups, and to compare them with a cohort of patients with VO caused by *S. aureus*.

## Patients and Methods

### Setting

This study was performed in the Osteoarticular Infection Units of three tertiary-care Spanish teaching hospitals (in Barcelona, Malaga and Seville). The research groups involved have published several works in the field of vertebral osteomyelitis [3,19–22].

### Basic management protocol

*Definitions.* Vertebral osteomyelitis was diagnosed by the presence of a compatible clinical picture and characteristic imaging findings (computed tomography or magnetic resonance imaging) [1,2]. Diagnosis was considered *definitive* (VO microbiologically confirmed) if a pyogenic microorganism was isolated in blood cultures or spinal biopsy specimens, and *probable* (vertebral osteomyelitis with no microbiological diagnosis, VO-NM) if no organism was isolated [1,2]. Concomitant infection was defined as any infection (cause or consequence of the VO) diagnosed at the time of VO.

In line with the Lancefield and Sherman classifications, *Streptococcus* species were divided into two groups: non-*viridans* species (*Streptococcus pyogenes*, *Streptococcus agalactiae* and *Streptococcus pneumoniae*) and *viridans* streptococci (*Streptococcus bovis* and *Streptococcus milleri*, along with the remaining species). Endocarditis was diagnosed using Duke criteria [23]. When streptococcal bacteraemia was identified, echocardiography was performed if deemed appropriate by clinicians, but it was not routinely carried out.

### Study design

*Incidence study.* We registered all episodes diagnosed or treated in the three hospitals from 1991 to 2011. Cases from hospitals were all identified after double checking both the general patient records of each hospital and the files from the infectious diseases and rheumatology wards. Incidence data were calculated after adjusting for the population of our health area per year.

*Clinical study.* All patients with a diagnosis of VO who were admitted and prospectively treated in the three hospitals were included. Cases of facet joint infection with no involvement of intervertebral disk or vertebral soma, cases caused by *Mycobacterium tuberculosis*, *Brucella* sp. or fungus, and postsurgical cases were all excluded. The clinical study period differed between hospitals: from January 1991 to December 2011 in Malaga and Seville, and from January 2003 to December 2011 in Barcelona. All cases were retrospectively reviewed and SVO was identified and analysed. Statistical comparison of cases coming from different hospitals was performed to ensure that no differences existed. For further comparisons between SVO and other VOs, cases of VO caused by *S. aureus* were recorded in patients admitted to hospital in Barcelona during the established study period.

*Data collection.* Data collected on an itemized form included the following: (i) underlying medical condition, (ii) vertebral level involved, (iii) clinical presentation, (iv) microbiological diagnosis, (v) concomitant infection, (vi) laboratory tests, (vii) diagnostic imaging data and (viii) treatment procedures.

*Follow-up and outcome.* Clinical follow-up was performed by one of the authors during treatment and up till 12 months thereafter.

Treatment failure was considered if (i) the patient died due to causes related to the infection, (ii) there was persistence of infection (isolation of the same microorganism in new samples or persistently clinical signs and symptoms or high acute-phase reactants in the absence of other inflammatory causes) or (iii) the patient relapsed (same criteria as for persistence but following a period of clinical improvement).

### Statistical analysis

Data were analysed using SPSS software (version 15.0). Simple linear regressions were conducted to assess changes in the incidence of vertebral osteomyelitis. To analyse cases of PVO, either the $\chi^2$ test or Fisher's exact test was used to compare categorical variables, while the *t*-test or the Mann–Whitney *U*-test was used to compare continuous variables. A p value $<0.05$ was considered statistically significant.

## Results

### Incidence study (1991–2011)

The total numbers of episodes of VO and SVO are presented in Table 1. There were 76 cases of SVO (46 *viridans* and 30 non-*viridans Streptococcus*). The prevalence of SVO (1991–2011) was 14% with respect to the total cases of VO, or 17% when considering only cases of VO that were microbiologically confirmed. The proportion of SVO among all cases of VO during the first (1991–2000) and second decade (2001–2011) was maintained (14%), whereas the proportion of SVO with respect to cases of microbiologically confirmed VO increased