Reumatol Clin. 2019;15(5):e62–e65

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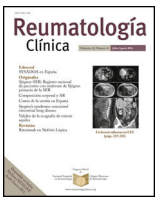

Images in Clinical Rheumatology

Osteoarticular Infections Caused by *Streptococcus pneumoniae* Since Authorization of Conjugate Vaccines☆

Afectación osteoarticular por *Streptococcus pneumoniae* tras la autorización de las vacunas conjugadas

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ARTICLE INFO

Article history:
Received 29 March 2017
Accepted 8 May 2017
Available online 17 October 2018

Introduction

Streptococcus pneumoniae is a bacteria associated with the development of upper and lower respiratory tract infections, pneumonias and bacteremias, and less frequently with other infections such as meningitis or peritonitis. Osteoarticular involvement is much less common; the incidence of septic arthritis is approximately 3%,[1] and it is less frequently involved in individuals over the age of 50 years.[2]

However, in one of the largest series in the literature—4 hospitals in the United States, the authors reported 13 cases, stressing that joint involvement by *S. pneumoniae* is the third cause of septic arthritis.[3]

In Spain, in a study on arthritis due to pneumococcal bacteremia, the authors described 4 cases, pointing out the rareness of the condition.[4]

In 2010, the 13-valent pneumococcal conjugate vaccine (PCV-13) was authorized by the Food and Drug Administration of the United States for the prevention of invasive pneumococcal disease. This vaccine contains the polysaccharides of serotypes 1, 3, 5, 6A, 7F and 19A, which were added to the 7 serotypes contained in the 7-valent conjugate vaccine.

In 2002, the Spanish Association of Pediatrics recommended the use of the 7-valent conjugate vaccine and, in June 2010, authorized the use in children of PVC-13. Nevertheless, on the Spanish island of Mallorca, as in other Spanish provinces, these vaccines were not financed by the national health care system. The use is recommended but is funded privately, and it is not incorporated into the universal vaccine coverage.

The 23-valent polysaccharide vaccine was included in the Spanish vaccination schedule for adults in 2003, for patients with comorbidities and those over 60 years of age. However, PCV-13 was recommended in 2012 for immunocompromised adults and patients with comorbidities, but is not financed in the last group.

According to data provided by the Health Department in the regional parliament of the Balearic Islands, which includes Mallorca, based on reports from public and private pediatricians, the rates of childhood vaccination are around 24%–26%. In terms of the data provided by Pfizer, the rates are about 50% (according to the number of vaccines sold).

In adults, these rates are lower; individuals over the age of 65 years have a coverage of 2.6% (all with the 23-valent polysaccharide vaccine).[5]

Given the scarcity of data on osteoarticular involvement due to *S. pneumoniae* over the past decade, our objective was to describe the epidemiological and clinical characteristics of the patients with osteoarticular involvement produced by pneumococci treated in our setting.

☆ Please cite this article as: Arrizabalaga M, Borjas Y, Peñaranda M, Garau M, Ruíz de Gopegui E, Payeras A. Afectación osteoarticular por *Streptococcus pneumoniae* tras la autorización de las vacunas conjugadas. Reumatol Clin. 2019;15:e62–e65.

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Methods

The cases were recorded from January 2006 until January 2016 among the patients attended to in 2 hospitals in Mallorca, Spain: teaching hospital Son Espases and hospital Son Llàtzer. The two centers attend a population sector of 500,000 inhabitants.

We retrospectively reviewed the medical records of patients with blood cultures that were positive for pneumococci and the results of the cultures and antigens of pneumococci in joint fluid, according to the microbiological registry of both centers.

Pneumococcal osteoarticular involvement was considered to be any septic arthritis or osteomyelitis.

The study was approved by the research commissions of both centers.

Results

During the study period, we registered 10 individuals with osteoarticular involvement (9 cases of arthritis and 1 of vertebral osteomyelitis), respectively, 1.8% of the septic arthritis and 0.8% of the cases of spondylodiscitis diagnosed in the two centers. Of a total of 523 pneumococcal bacteremias, only 10 had osteoarticular involvement (1.9%).

The demographic, clinical and microbiological characteristics of the 10 patients are summarized in Table 1. All but 2 patients had at least 1 comorbidity, with a mean Charlson Comorbidity index of 3.55 (standard deviation [SD] 2.46).

Only 1 of the patients was of pediatric age (2 years) and the mean age for the 9 adult patients was 62 years (range: 32–79). Osteoarticular involvement was much more frequent among women: 8 cases (80%). Previous presence of a condition involving the upper airway was encountered in 1 patient, and another 3 had pneumonic infiltrates.

In 3 patients (30%), the arthritis was over a prosthesis (2 knees and a shoulder). None of our study group had had a previous injury in the affected joint and there was no history of arthropathy.

Among the laboratory findings, we observed leukocytosis in all of the patients, with a mean of 16.7×10^9 cells/L (SD 5.37×10^9 cell/L).

Arthrocentesis was performed in the 9 cases of arthritis and the culture was positive in 8.

Only 5 patients had fluid samples that could be processed by biochemical means; in the other 3 cases, the analysis was not carried out because the fluid was very purulent. Table 2 shows the biochemical characteristics of the fluid.

Among the viable strains of *S. pneumoniae* (8/10), all were sensitive to penicillin and to cephalosporins.

In 4 patients, we obtained the following serotypes (11D, 19A, 23F and 24F). Only 2 patients had been vaccinated against pneumococcus; 1 had received PCV-13 and was infected by a nonvaccine serotype (24F), and the other who had been vaccinated with the 7-valent conjugate vaccine, was infected by a strain of 19A.

Table 1
Demographic, Clinical and Microbiological Characteristics of the Patients.

Case	Sex/age (years)	Comorbidity	Site	Blood cultures	Other positive microbiological tests
1	F/60	Heart disease	Knee	Negative	Synovial fluid culture
2	M/58	Alcoholism Previous surgery	Elbow	NP	Synovial fluid culture
3	M/75	Diabetes Heart disease Neoplasm Renal insufficiency	Knee	Negative	Synovial fluid culture
4	F/79	Smoking	Knee (prosthesis)	Negative	Sputum Pleural fluid Gram stain Synovial fluid Gram stain Antigens in synovial fluid
5	F/62	Heart transplantation Tacrolimus and everolimus therapy	Shoulder (prosthesis)	Positive	Synovial fluid culture BA Antigens in urine
6	F/32	HIV infection	Spondylodiscitis	Positive	NP
7	F/72	Smoking	Knee	Negative	Synovial fluid culture
8	F/2	No comorbidity	Hip	Negative	Synovial fluid culture
9	F/60	Lymphoma Neoplasm Splenectomy	Wrist	Positive	NP
10	F/77	No comorbidity	Knee (prosthesis)	Positive	Synovial fluid culture

BA, bronchial aspirate; F, female; HIV, human immunodeficiency virus; M, male; NP, not performed.

Table 2
Surgical Approach, Duration of Antibiotic Therapy and Outcome.

Case	Surgical approach	Duration of antibiotic therapy (days)	Outcome
1	Drainage by arthroscopy	14 iv, 30 oral	Slight functional limitation
2	Intraoperative lavage	3 iv, 7 oral	Complete recovery
3	No	8 iv	Death
4	Synovectomy, change of polyethylene and intraoperative lavage	13 iv, 60 oral	Minimal limitation
5	Debridement, intraoperative lavage and removal of osteosynthesis material	18 iv, 23 oral	Moderate limitation
6	No	42 iv, 60 oral	Complete recovery
7	Intraoperative lavage	28 iv	Complete recovery
8	Intraoperative lavage	15 iv, 15 oral	Complete recovery
9	Intraoperative lavage	28 iv	Complete recovery
10	Intraoperative lavage	30 iv	Death

iv: intravenous.

Of the 10 patients, 8 survived and 2 died from complications associated with the infection: one had pneumonia and the other developed endocarditis.

The survivors received intravenous antibiotic therapy for an average of 19.3 days (SD 12.1 days), followed by oral antibiotic therapy during an average of 32.1 days (SD 22.83 days).

Table 2 shows the types of surgical approach, the duration of treatment and the outcome.

Discussion

In our setting, osteoarticular infection caused by pneumococcus is not very common, taking into account that the rate of bacteremia was only 1.9%, data that are similar to others reported previously. In a review of invasive pneumococcal disease, only 1.3% of the episodes of pneumococcal bacteremia resulted in septic arthritis.[6] Moreover, in a series by Frankel et al.[7] involving 147 patients with pneumococcal bacteremia, there were only 2 cases of arthritis (1%).[8] In a number of Spanish series on septic arthritis in different locations, the rarity of this condition is also stressed,[9,10] with arthritis caused by pneumococcus representing less than 5% of the cases of septic arthritis.[8]

In our series, we observed a clear predominance of involvement among women, a finding that varied depending on the authors of the different reports.[3,11] We should point out the fact that the majority of our patients were adults with an age of 60 years or more and that there was only one child. This contrasts with the article by Ross et al. who, in a review of the literature, compiled 190 cases of pneumococcal septic arthritis in which 43% of the patients were of pediatric age.[3] The data from that study correspond to a period prior to the introduction of conjugate vaccines. The reduction in the number of pediatric patients is probably influenced by the massive vaccination of the pediatric population that began in 2002, which prevented invasive pneumococcal infections.

Half of the patients reviewed had some comorbidity, with a high Charlson Comorbidity Index, and another 3 patients had conditions closely related to invasive pneumococcal disease, immunosuppressive therapy, splenectomy or were smokers.[11]

It is not uncommon that another extraarticular infection precedes or coexists in patients with osteoarticular infection produced by *S. pneumoniae*; in fact, it seems to occur more frequently than septic arthritis caused by other microorganisms.[6]

In our series, pneumonia was observed to be the most common extraarticular focus.

As was expected, the joint most frequently affected was the knee, since it is the structure that is related in up to 50% of cases of bacterial septic arthritis.[1,2] In our series, we include a case of pneumococcal vertebral osteomyelitis, considered a rarity.[12] The lumbar site and absence of side effects after appropriate antibiotic therapy are common factors in this type of involvement.[13]

It has been reported that *S. pneumoniae* most frequently causes polyarticular involvement in comparison with other microorganisms related to septic arthritis, attributed to high rates of bacteremia in those patients with pneumococcal septic arthritis.[3] We encountered no cases of polyarticular involvement in our registry.

Given that this was a retrospective study, the data on the vaccination status of our patients cannot be corroborated. However, it is striking that the 2 patients vaccinated with a known serotype did not get infected with a vaccine strain, although one of them did get infected due to a related serotype (19A).

The standard management of septic arthritis consists of adequate draining of the affected joint, together with appropriate antibiotic therapy, in a reduced period of time, to favor functional recovery.[14] The majority of the patients received a combination of intravenous antibiotic therapy, followed by oral treatment and surgical drainage of the joint.

The outcome of this infection is usually good, although it is determined by the severity of the underlying diseases.[4] The mortality rate in septic arthritis varies depending on the different studies, but is normally around 11% in those cases of monoarticular septic arthritis[14]; this percentage is similar in cases of pneumococcal arthritis, although it ranges depending on the series from 11% to 32%.[1,6] In the population we studied, the mortality was 20%, 2 patients out of 10, both of whom were over 65 years of age and had significant comorbidities. One of them did not even receive surgical treatment; due to the comorbidity and the seriousness of the case, palliative measures were implemented.

The limitations of this study are the retrospective nature, as well as the small sample size. However, it is the largest series reported in the last decade. Although only 4 patients had positive blood cultures, we can assume that all of them presented bacteremia at some time during the course of the disease, given that hematogenous spread is key in these cases.

Conclusions

As was the case before the use of conjugate vaccines, pneumococcal osteoarticular involvement in our setting is very uncommon. It is observed above all in women and elderly patients with associated comorbidities, predominantly in the form of monoarticular septic arthritis affecting the knee. The course is usually favorable and deaths were related to the presence of other synchronic foci, such as pneumonia or endocarditis. We cannot conclude that vaccination in adults is effective in the prevention of osteoarticular complications, given the low prevalence; however, massive vaccination of the pediatric population seems to have an impact on the prevention of this infection.

Ethical Disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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