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Original

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Bacterial osteomyelitis: microbiological, clinical, therapeutic, and evolutive characteristics of 344 episodes

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ABSTRACT

Introduction. Osteomyelitis is a difficult-to-cure infection, with high relapse rate despite adequate therapy. Large published osteomyelitis series in adults are rare.

Material and methods. A total of 344 adult osteomyelitis patients were studied and followed > 12 months after hospital discharge. Demographic, microbiological, clinical, therapeutic and outcome data were analyzed.

Results. Mean age was 52.5 ± 18.3 years and 233 (67.7%) were male. Main osteomyelitis types were post-surgical (31.1%), post-traumatic (26.2%) and hematogenous (23%). Tibia (24.1%) and femur (21.8%), and methicillin-susceptible *S. aureus* (29.6%) were the most commonly involved bone and bacteria, respectively. Median follow-up was 12.0 (IQR 0-48) months. Inflammatory markers were increased in 73.6%. Overall, patients were treated by IV and oral routes with one (IV: 44.5%, oral: 26.7%), two (IV: 30.1%, oral: 21.8%) or ≥ 2 (IV: 15.2%, oral: 6.1%) antibiotics. Median duration on IV/oral antimicrobials was 28.0 (IQR 24-28) and 19.5 (IQR 4-56) days, respectively. Anti-staphylococcal β-lactams cloxacillin/cefazolin (19.2%) and ciprofloxacin (5.5%) were the most frequently used IV and orally, respectively. Overall 234 (68.0%) underwent surgery, 113 (32.8%) debridement, 97 (27.4%) debridement + muscle flap and 24 (7%) amputation. At the end of follow-up 208 patients (60.6%) did not have relapsed. Operated patients had significantly less relapses (p<0.0001). A total of 23 (6.7%) died, 11 (3.2%) by infectious complications and 48 (14%) were lost in the follow-up.

Conclusions. Osteomyelitis is due to different causes complicating its therapy. Risk factors or causal microorganism could influence its treatment and outcome. Aggressive surgery along with adequate antimicrobial therapy are mandatory for cure.

Keywords: osteomyelitis, relapse, severity factors, debridement, muscular flap, antibiotics

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Osteomielitis bacteriana: aspectos microbiológicos, clínicos, terapéuticos y evolutivos de 344 episodios

RESUMEN

Introducción. La osteomielitis es una infección difícil de curar, de etiología múltiple y con una alta tasa de recidivas a pesar del empleo de tratamientos combinados médicos y quirúrgicos. Hay muy pocas series amplias de aspectos generales de la osteomielitis publicadas hasta ahora.

Material y métodos. Se siguieron 344 pacientes adultos diagnosticados de osteomielitis durante > 1 año tras el alta médica. Se recogieron y analizaron sus características demográficas, microbiológicas, clínicas, terapéuticas y evolutivas.

Resultados. La edad media fue de 52,5 ± 18.3 años y 233 (67,7%) eran hombres. Los principales tipos de osteomielitis fueron post-quirúrgica (31,1%), post-traumática (26,2%) y hematógena (23%). Tibia (24,1%) y fémur (21,8%) y *Staphylococcus aureus* sensible a meticilina (29,6%) fueron los huesos y bacteria implicados con mayor frecuencia, respectivamente. El tiempo medio de seguimiento fue de 12 (RIQ 0-48) meses. Los reactantes de fase aguda estaban elevados en 73,6%. Los pacientes fueron tratados con uno (44,5% y 26,7%), dos (30,1% y 21,8%) o más de dos antibióticos (15,2% y 6,1%) por vía IV y oral, respectivamente. La duración media de la terapia antimicrobiana IV/oral fue de 28,0 (RIQ 24-28) y 19,5 (RIQ 4-56) días, respectivamente. Los β-lactámicos antiestafilocócicos cloxacilina/cefazolina (19,2%) y ciprofloxacino

(5,5%) fueron los antimicrobianos más frecuentemente usados por vía IV y oral, respectivamente. Un total de 234 pacientes (68%) fueron sometidos a cirugía, de ellos 113 (32,8%) a desbridamiento, 97 (27,4%) a desbridamiento + colgajo muscular y 24 (7%) a amputación. Un total de 208 pacientes (60,6%) no recidivaron. Los pacientes operados presentaron menos recidivas (p<0,0001). Un total de 23 (6,7%) pacientes fallecieron, 11 (3,2%) por complicaciones infecciosas y 48 (14%) se perdieron durante el seguimiento.

Conclusiones. La osteomielitis se debe a causas diversas que complican su abordaje terapéutico. Los factores de riesgo o microorganismos causales podrían influir en los resultados del tratamiento y en la remisión de la enfermedad. Una cirugía agresiva junto con un tratamiento antimicrobiano adecuado son imprescindibles para obtener la curación

Palabras clave: osteomielitis, recidiva, factores de gravedad, desbridamiento, colgajo muscular, antibióticos

INTRODUCTION

Osteomyelitis is a bone marrow inflammation, usually caused by an infectious agent. It has a heterogeneous pathophysiology, and is one of the most difficult infections to cure. The source of the infection may be haematogenous, acquired from a contiguous infectious focus or by direct inoculation into the bone. Osteomyelitis can be classified into acute, subacute or chronic, according to the time of evolution. Acute osteomyelitis has usually a good response to antimicrobials and, if necessary, to surgery. On the opposite, chronic osteomyelitis represents a great therapeutic challenge, becoming surgery essential to obtain the best results [1–4]. Several classifications of osteomyelitis have been reported so far, being that established by Cierny-Mader-Pennick and Waldvogel the most frequently used [5,6]. Waldvogel classification is based on the time course and etiopathology of the bone infection [5]. According to the time course, osteomyelitis could be acute or chronic; by its etiology, haematogenous or secondary to a contiguous focus of infection. Waldvogel classification includes also the presence or absence of vascular disease, giving a key role to tissue perfusion in the evolution of the bone infection. Cierny-Mader-Pennick classification includes pathologic and immunological approaches [6]. By the pathological approach osteomyelitis can be divided in four types (figure 1): I-Medullary, II-superficial, III-localized and IV-diffuse. It also classifies osteomyelitis patients in type A host, that has no comorbidities; type B host, that has one or two general diseases; and type C host, in which the risk of surgical treatment exceeds the cure benefits due to the carriage of several comorbidities [1,4,7].

The signs and symptoms of bone infection are non-specific very often. Low grade fever or local pain are usually present, but others as limb swelling or erythema are occasional. Drainage, fistula or abscess can be more frequently observed in osteomyelitis caused by a contiguous focus. The main abnormalities found in blood tests are increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Although non-specific, these lab findings are very useful in the follow-up of treated bone infections. Imaging studies are essential. X-ray images can show a lytic area with a periosteal reaction, but usually other studies as CT or MRI are needed to demonstrate the necrotic bone. Isotopic scans, like bone scintigraphy with Technetium^{99}, Gallium^{67} or, more specifically, Indium^{111}, can help to differentiate bone from soft tissue infection or inflammation. PET-CT is one of the best nuclear studies for osteomyelitis diagnosis, but is not available in many hospitals. Bone cultures, especially from surgical biopsies, are essential in the diagnosis. *Staphylococcus aureus* is the pathogen most frequently found, although more than one pathogen can be isolated from the cultures [1,4,8].

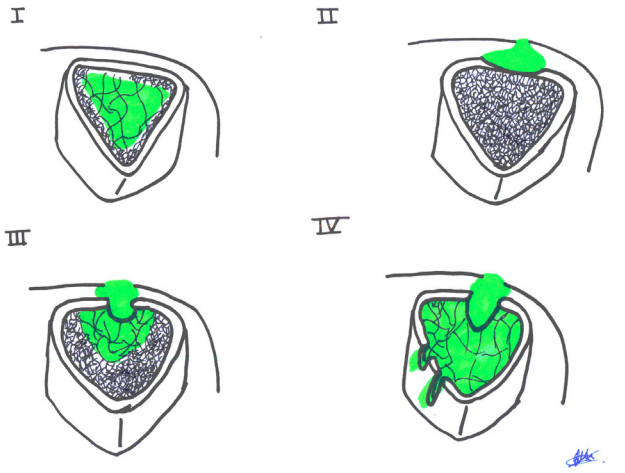

Figure 1 | **Cierny–Mader-Pennick classification of osteomyelitis. Anatomical: I- medullary, II- superficial, III- localized and IV- diffuse. Host immunity: type A host, without comorbidities; type B host, one or two general diseases; and type C host, the risk of surgical treatment exceeds the benefits because of comorbidities.**

Treatment of osteomyelitis involves surgery and antibiotic therapy. Surgery plays a key role especially in chronic osteomyelitis. An aggressive debridement of all necrotic tissues (bone and soft tissue) is essential. After debridement, it could be necessary to stabilize the bone and to provide a suitable soft tissue coverage. Reconstruction techniques provide elements to repair the bone, adding a vascularized coverage that increases antibiotic concentration into the bone and helps its healing. Extended antibiotic therapy without surgery can be curative in haematogenous and vertebral osteomyelitis, especially in children. In the remaining cases, it is a necessary complement to surgery. Usually a combination of antibiotics is necessary to avoid bacterial resistances after extended antimicrobial therapies [4,9–12].

We report here our 21-year experience treating osteomyelitis patients at the Hospital Universitario Central de Asturias (HUCA). Our descriptive study reports the causes, microbiology,

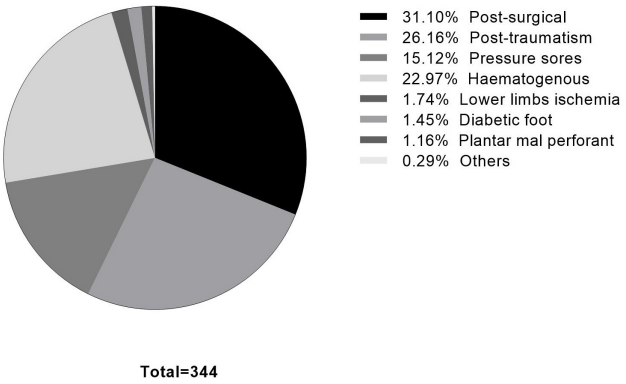

Figure 2 | **Causes of osteomyelitis**

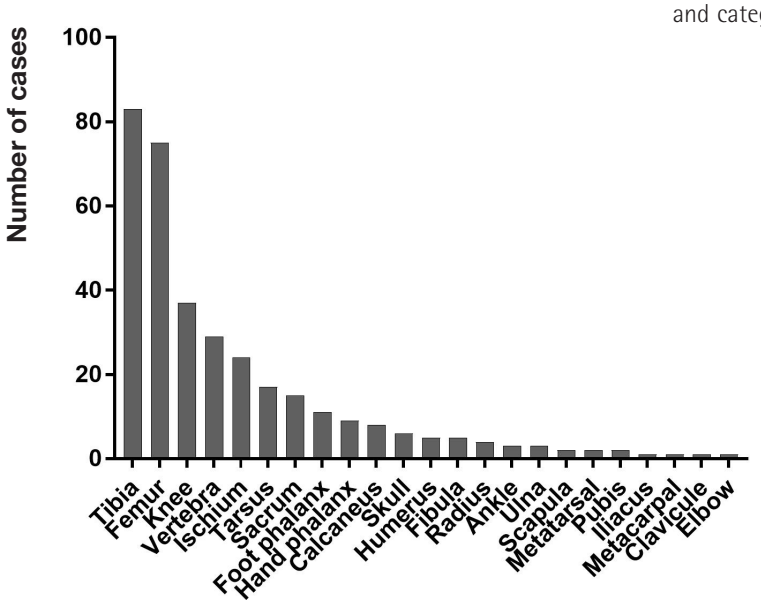

Figure 3 | **Bones affected.**

bone involvement, lab parameters, risk factors and comorbidities, antimicrobial and surgical therapies, cure rates, and relapses in our large osteomyelitis cohort.

MATERIAL AND METHODS

We performed a retrospective study of all diagnosed cases of osteomyelitis/ bone infection between January 1st, 1994 and October 1st, 2015 at the Hospital Universitario Central de Asturias (HUCA) and three other affiliated hospitals from the same region. Demographic data, types of bone infection (classified as hematogenous, post-traumatic, post-surgery, pressure sores, diabetic foot, chronic ischemia of lower limbs, neurophatic foot ulcer or others), bone affected and causal germen were registered. Other data, like osteomyelitis risk factors, analytical tests and image studies were recorded as well. Treatment data, including type and duration of antimicrobials, and type of surgical treatment were carefully registered. Follow-up, relapse and remission rates were also recorded. Relapse was considered when clinical findings or image signs of osteomyelitis reappeared. Osteomyelitis was considered in remission when no relapses were detected after a minimum 12 months of follow-up. Remission time was considered as the time until relapse of bone infection, and when there was no relapse, the follow-up time. The study was retrospective descriptive, with a level of evidence IV

Statistical analysis. Continuous variables are reported as mean ± SD or median (IQR) and categorical variables as n (%). The comparisons between the relapse and non-relapse cases or time free of disease were carried out by the t-test and the chi-square or Fisher exact tests when appropriate, for continuous and categorical variables, respectively. SPSS v.22 (IBM, version 22) software was used for statistical calculations. A P value <0.05 for a two-sided test was considered statistically significant.

RESULTS

Between 1994 and 2015, 402 patients were diagnosed with osteomyelitis at the HUCA Infectious Diseases Unit and their medical charts were reviewed. Fifty-eight were excluded because of lack of confirmation of bone infection or missing key data after their transfer from other affiliated hospitals for surgical therapy. Overall 344 patients, 233 (67.7%) men and 121 (32.3%) women, fulfilled osteomyelitis criteria and were included in the study. Their mean age ± SD was 52.5 ± 18.3 years. The main types of bone infection were post-surgical (107 patients, 31.1%), post-traumatic (90 patients, 26.2%) and haematogenous (52 patients, 23%). Other causes are shown in figure 2. The most frequently involved bone was the tibia (24.1%), femur was the second one (21.8%) with knee joint (femur + tibia) as the third most frequent location (10.8%). Vertebral osteomyelitis was found in 29 patients (8.4%). Other bone locations are shown in figure 3. The bone affected differed according to the type of osteomyelitis. Thus, in post-surgical cases the bone most frequently affected was the femur; in post-traumatic cases was the tibia, in haematogenous osteomyelitis were tibia and vertebrae; and in pressure sores was the ischium followed by sacrum and femur.

Positive cultures were obtained from bone biopsies in 234 cases (68%), blood cultures in 79 cases (23%) and from draining fistulas in 31 cases (9%). *Staphylococcus aureus* was the most frequently agent isolated on monomicrobial infections (29.6% of patients). The second and third most frequently isolated microorganisms were *Pseudomonas aeruginosa* and methicillin-resistant *S. aureus* (4.1% each, respectively). The rate of polymicrobial infection was 35.4%. Many others pathogens were found with a lower frequency, *Staphylococcus epider-*

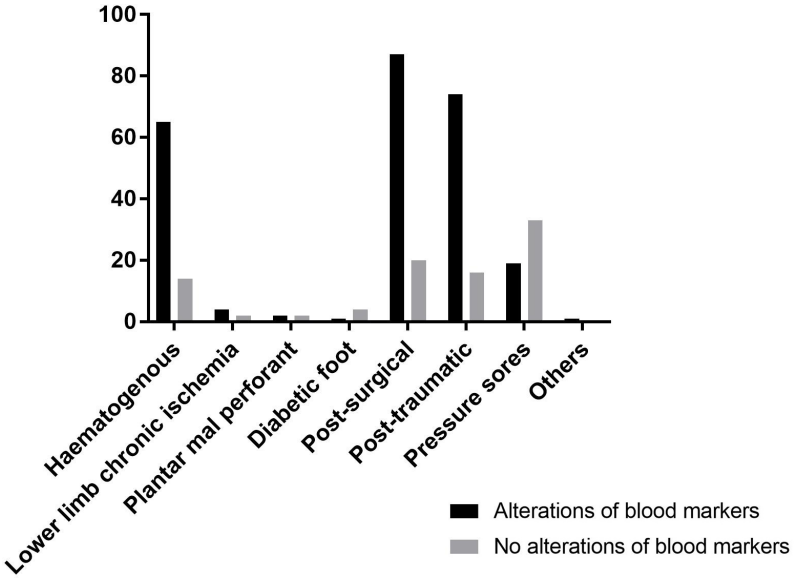

Figure 4 | **Inflammatory blood markers changes according to the osteomyelitis cause.**

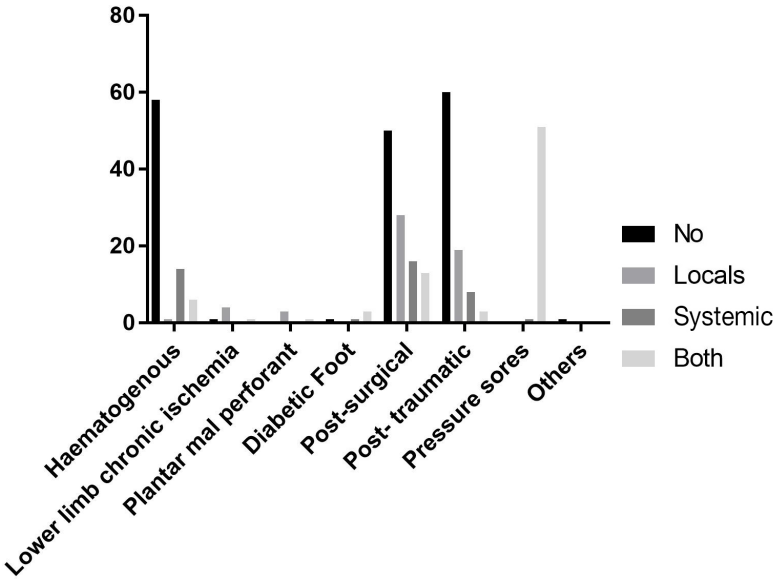

Figure 5 | **Risk factors differences according to the osteomyelitis cause.**

midis (3.2%), *Escherichia coli* (2.3%), and *Enterococcus faecalis*, *Enterococcus faecium*, *Proteus mirabilis*, and anaerobes (<2%). *Mycobacterium tuberculosis* was isolated in 3 cases (0.9%). Overall 22 patients (6.4%) had negative cultures.

Overall, 73.6% of the patients had increased inflammatory blood markers at the diagnosis of osteomyelitis. ESR median value was 54.0 [IQR 27.5-92.0] mm/h and CRP median value was 4.8 [IQR 1.4-11.6] mg/dl. Although there was an elevation of these biomarkers in most of the osteomyelitis patients, there was a statistically significant relationship between inflammatory markers elevation and the type of osteomyelitis, with post-surgical (ESR median value of 56.0 [IQR 26.0-99.0]) mm/h and CRP median value of 15.9 [IQR 2.3-9.5] mg/dl, respectively), haematogenous (ESR median value of 54.0 [IQR 27.5-92.0] mm/h and CRP median value of 4.8 [IQR 1.4-11.6] mg/dl, respectively) and post-traumatic (ESR median value of 47.0 [IQR 22.5-77.3]) mm/h and CRP median value of 3.8 [IQR 0.8-10.0] mg/dl, respectively) osteomyelitis inducing the highest increase of these parameters ($p<0.03$ when comparing ESR values of post-surgical or hematogenous versus post-traumatic osteomyelitis) (figure 4). Image studies, like CT, MRI or nuclear scans, provided the diagnosis of osteomyelitis in 52% of cases when conventional radiography was not diagnostic.

Osteomyelitis risk factors or comorbidities were classified in systemic and local. Among the systemic risk factors, diabetes, rheumatoid arthritis, immunosuppressive therapy or immunodeficiency were found. The most frequent local risk factors were vascular (78 patients, 22.7%) and sensitivity abnormalities (55 patients, 16.0%), and highly-contaminated open bone fractures (38 patients, 11.0%). No osteomyelitis risk factors were found in 171 (49.7%) of the cases, both systemic and local risk factors were observed in 78 (22.7%), only local risk factors in 55 (16%) and only systemic risk factors were found in 40 (11.6%.) patients. The type of risk factors changed significantly according to the osteomyelitis cause ($p<0.001$) (figure 5).

The treatment received by the patients was divided into antibiotic therapy, surgical treatment or both. Antibiotic therapy usually consisted in an intravenous (IV) cycle (median duration of antimicrobials 28.0 [IQR 24-28] days), followed for an oral cycle (median duration of antimicrobials 19.5 [IQR 4-56] days). No differences in the prognosis of the patients according to the need of different antibiotic treatment regimens, IV or oral, were observed. Therapy duration might be biased by the 3 cases of vertebral osteomyelitis treated during 9 months. Overall, 3.8% of patients did not receive IV antimicrobials and for 6.4% of patients the type and duration of antimicrobials were unknown. Regarding IV antimicrobial therapy, 44.5% of cases received one antibiotic, 30.1% two antimicrobials and 15.2% more than 2 antibiotics. The antimicrobials most frequently used as IV monotherapy were cloxacillin (10.8% of all cases), cefazolin (8.4%) and amoxicillin-clavulanic acid (6.7%), and in association vancomycin, ciprofloxacin and clindamycin. The associa-

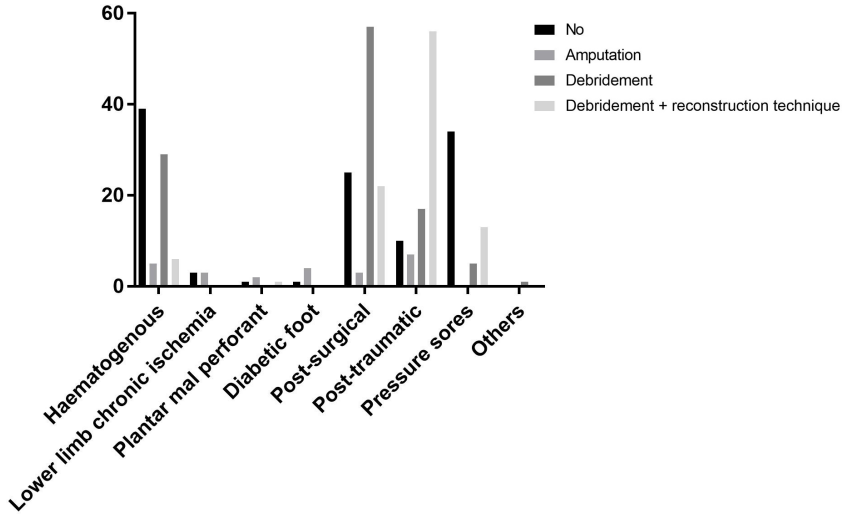

Figure 6 | **Surgical approaches according to the osteomyelitis cause.**

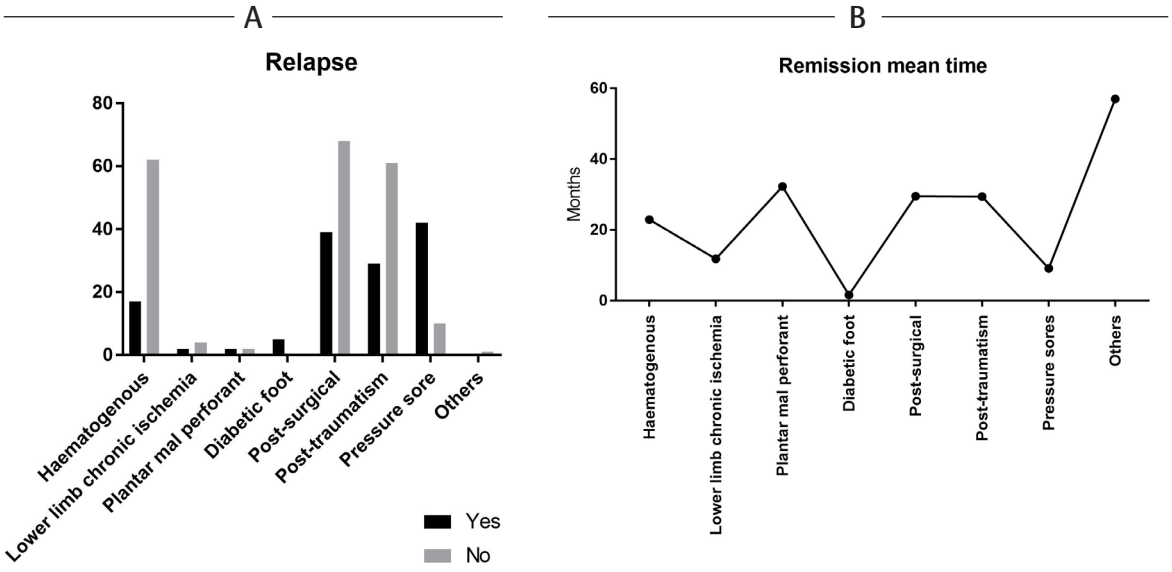

Figure 7 | **Relapse differences (A) and remission mean time (B) according to the osteomyelitis cause.**

tions most commonly used were vancomycin + ciprofloxacin, cloxacillin + gentamycin and clindamycin + ciprofloxacin (2% each). Regarding oral antimicrobial therapy, 39.2% of patients did not receive any oral antibiotic and in 6.1%, the type of antimicrobials and/or its duration were unknown. Overall, 26.7% received oral antimicrobial monotherapy, 21.8% an association of 2 antibiotics and 6.1% more than 2 antibiotics. The oral antimicrobials most used as monotherapy were ciprofloxacin (5.5%), clindamycin (5.2%) and amoxicillin-clavulanic acid (4.4) , whereas rifampicin was the antibiotic most frequently used in combination (14.2%), followed by clindamycin and ciprofloxacin. The oral antimicrobial association most commonly used was rifampicin + clindamycin (5.2%).

In our series, 234 (67.2%) of osteomyelitis patients underwent surgery. Of them, surgery involved only debridement, abscess drainage or joint lavage in 113 (32.8%) patients. Reconstructive techniques, in addition to debridement, were applied in 97 (27.4%). They involved coverage with vascularized tissue, either free or pediculated, from muscle, fasciocutaneous or bone flaps. Partial or total limb amputation was performed in

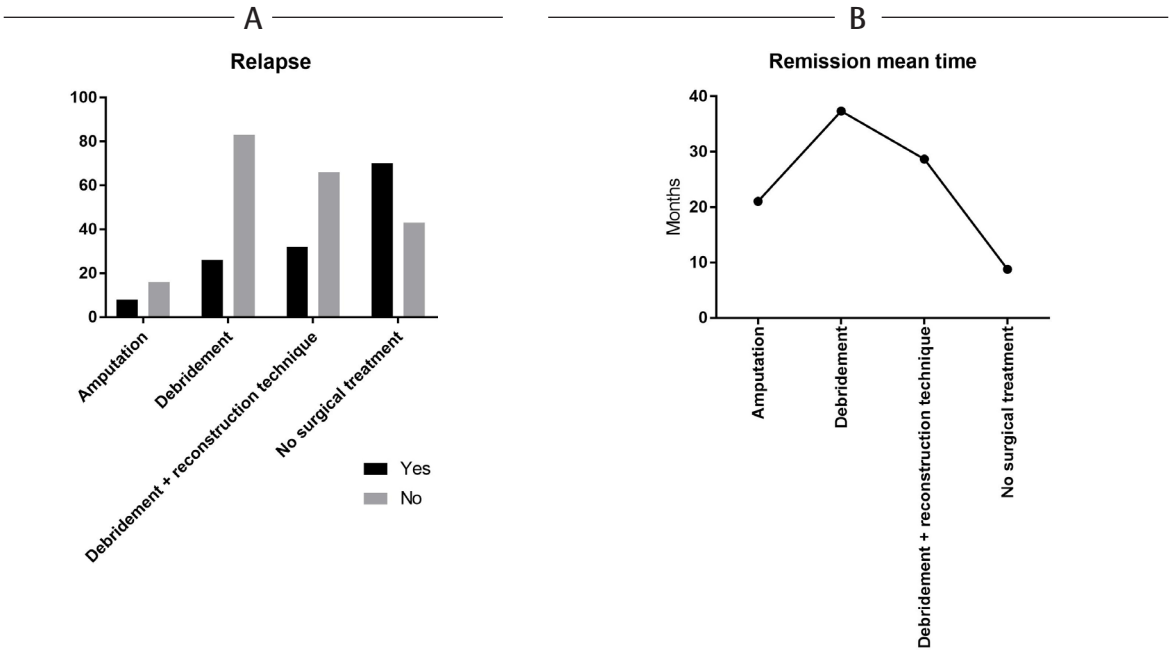

Figure 8 | **Relapse differences (A) and remission mean time (B) according to the surgical treatment received.**

24 (7%) of cases. Surgical treatment significantly differed according to the osteomyelitis cause (figure 6)

The patients' median follow up was 12.0 (IQR 0-48) months. Forty-eight patients (14%) were lost for follow-up, 25 (7.3%) of them were transferred to their original hospital or did not return for follow-up, and the remaining patients died during hospital admission. A total of 23 patients (6.7%) died during the follow up, 11 of them (3.2%) 30 days after hospital admission because of sepsis and/or multi-organ failure related with bone infection. The 12 remaining patients (3.5%) died of other unrelated causes occurred during admission or follow-up. Other severe complications were due to adverse effects of antimicrobials, recurrence of cranial tumor in a patient with cranial osteomyelitis due to previous operation or paraparesis due to spinal cord compression in vertebral osteomyelitis. Main local complications were related to recurrence or persistence of draining fistulae in 42 patients (12.2%) requiring new antimicrobial and/or surgical treatment, and even amputation in 3 patients. Total flap necrosis requiring a second surgery occurred in 8 patients, 4 of them had osteomyelitis recurrence and 2 of these required limb amputation. Partial flap necrosis solved with another type of minor surgery, conventional heal dressings or vacuum therapy occurred in 7 patients, and only one of them had recurrence. Other 7 patients developed pseudoarthrosis, which was infected in only one of them. Four of these pseudoarthrosis patients underwent surgical correction with good evolution. Other complications were episodes of cellulitis, with isotopic scans negative for osteomyelitis and good response to antibiotics, osteoarthritis, joint stiffness, plantar sores, limb shortening or pathologic fractures.

At 12 months of follow up, 224 patients (65.1%) did not show signs of osteomyelitis relapse. On October 1, 2015 when the study data collection was closed 208 patients (60.6%) were still in remission. That means that 16 patients (4.7%) relapsed after 12 months of completing therapy. The remission mean time or time free of disease observed in our patients was 8.0 (IQR 8-36) months. Patients that underwent surgery had significantly less relapses compared to those without surgery (67/234 [28.6%] vs. 69/110 [62.7%], χ^2=34.97, OR [95% CI] 4.19 [2.53-6.98], p<0.0001 by the Yates correction test). Regarding the remission mean time or time free of disease, patients that underwent surgery had a mean of 32.0 ± 36.7 months vs. 7.9 ± 23.3 months for those without surgery (p<0.0001). Although all the types of surgery, amputation, bone debridement and bone debridement + reconstruction were significantly associated with less osteomyelitis relapses, when individually compared to patients without surgery no significant differences in infection relapse rate were observed among the surgical groups (8/24 [33.3%], 31/97 [32.0%] and 28/113 [24.8%], p>0.9). Differences in relapse and remission time according to the type of osteomyelitis and surgical treatment applied are shown in figure 7 and 8.

DISCUSSION

Osteomyelitis is a very complex infection due to its varied etiology and associated factors, and requires a multidisciplinary approach [1,9,13,14]. The diversity of all these elements influences the type of therapy administered and complicates the generalized implementation of a standardized therapeutic

protocol. We report here our experience at the HUCA in the care of osteomyelitis patients during the past 21 years, paying special attention to the etiologic aspects and to the medical and surgical management of osteomyelitis.

Our osteomyelitis series is one of the largest published in the world literature and also has an extended follow-up period [15]. Jiang et al. reported 394 cases of long bone osteomyelitis from China, mostly post-traumatic [16]. Our study involves not only post-traumatic but also other types of bone infection. In our series, post-surgical was the most frequent type, followed by post-traumatic osteomyelitis. Other important causes were haematogenous osteomyelitis or pressure sores. Long bones, particularly tibia, were the bones more frequently affected, although the location was influenced by the origin of the infectious source [17].

S. aureus was the microorganism most frequently involved in osteomyelitis in ours and in previous reports, but nowadays is also common to find osteomyelitis due to multirresistant pathogens or to microorganisms associations. Biofilm is a typical example for these associations and *Staphylococcus spp.* plays an important role in its formation. Biofilm is frequently found in orthopaedic prosthesis infections and its eradication is the main objective of the treatment. Other pathogens isolated on our series were coagulase-negative staphylococci, *Streptococcus* spp, *P. aeruginosa, Enterobacter* spp. and *Enterococcus* spp. Three cases had vertebral osteomyelitis caused by *M. tuberculosis*, an infection commonly reported in other bone infection series, but unusual in our environment [2,4,16–19].

Osteomyelitis manifestations are often very unspecific. Bone infection might be only suspected by the presence of draining fistulas or chronic wounds. Increased inflammatory markers may be of some help, although they are unspecific and show normal values in many cases, especially in chronic or latent infections as in our study [16]. Although many inflammatory blood markers have been studied, only ESR and CRP correlated with the development and evolution of osteomyelitis, as we also observed [20, 21]. Present research lines of our group and others are aimed at establishing a relationship between the carriage of different genetic polymorphisms of cytokines and other proinflammatory molecules and a predisposition for the development of osteomyelitis or its evolution to chronicity [22].

Risk factors associated with osteomyelitis are very important in the evolution and treatment of this infection. Waldvogel and Cierny-Mader-Pennick classifications include an special section devoted to risk factors. Of these, the most important are immunosuppression and poor blood supply [2]. For some osteomyelitis, such as post-traumatic or post-surgical, bone risk factors are not involved in its development, while in others, such as those due to pressure ulcers or in diabetic foot, poor blood supply and immunosuppression play an important role. In our study we have included patients with multiple risk factors and locations, which complicate outcome analysis, especially antimicrobial and surgical therapy success and infection relapse.

The optimal treatment of most osteomyelitis requires in most of the cases the combination of antimicrobial therapy and surgery. Antibiotic therapy is always provided, but the administration route and the duration are controversial. Years ago, very long cycles of antibiotics were commonly used, although modern studies have not proved the benefit of extended antimicrobial therapy [15,20,21,23-28]. In our study the antibiotic therapy was usually divided in two parts, one IV cycle lasting 2 to 4 weeks and an oral cycle lasting 6 to 8 additional weeks, along with surgery. Although the evolution of the patient, among other factors, influenced the duration of treatment, the antibiotic therapy was prescribed and monitored always by the same infection team in this study and, therefore, the intrinsic variability of this parameter was minimized to some extent. No studies have shown which antimicrobial is more effective in osteomyelitis. There are studies designed to prove the efficacy of new antimicrobials in bone infections, but very few studies have compared different antibiotics and routes of administration. In spite of the predominance of *S. aureus* in osteomyelitis, many microorganisms may be involved and antimicrobial combinations with good biofilm and bone penetration are mandatory [15, 20 ,21,23–28].

Surgical treatment is essential in the management of some types of osteomyelitis, but in others, like acute haematogenous osteomyelitis, it might not be necessary. Debridement of all necrotic tissues (bone and soft tissue) is the main surgical=procedure. Bone instability or coverage defects as a consequence of debridement need attention as well, as bone and soft tissue defect reconstruction might influence the outcome. A large number of techniques (bone substitutes with different antibiotics, antibiotic-impregnated cement and beads, flap coverage, bone grafts...) can be used. As with antimicrobials, only descriptive reports of the different surgical techniques and their results have been reported, but no comparative studies of the different techniques have been published so far. Furthermore no studies comparing coverage techniques plus bone debridement versus plain bone debridement, when there is no bone instability or coverage problems, have been reported. We could not find differences regarding osteomyelitis relapses when different types of surgical approaches were compared, amputation, bone debridement and bone debridement + reconstruction in our study. This might be due to the large heterogeneity of our osteomyelitis cases. A more homogeneous cohort including for instance only osteomyelitis of long bone might be more suitable to find differences among osteomyelitis surgical treatments regarding the outcome. We think that providing vascularised tissues with flap reconstruction along with debridement improves the results of surgical treatment. Although our group lacks experience in new and promising treatments, like employment of bioactive glass or other bone substitutes, we plan to incorporate them in the near future as a complement to flap reconstruction [4,9,14,29–34]. There are other techniques that complement antibiotic and surgical approaches, like hyperbaric oxygen therapy. Increasing the oxygen supply to tissues to create a hyperoxic environment may have an antimicrobial effect that could help in refractory

osteomyelitis [35,36]. The main challenge we face today is to ascertain which of these surgical and non-surgical techniques provide the greatest benefit for the cure of the infection and in which type of osteomyelitis would be more efficacious.

In conclusion, osteomyelitis constitutes a complex infection with different causes and many associated factors that complicate its therapeutic approach. Surgery along with adequate antimicrobial therapy are essential components for the cure of most osteomyelitis. Further prospective and comparative studies of different antimicrobial regimens and surgical techniques are necessary to obtain sound data that would allow the elaboration of therapeutic protocols aimed to obtain the best possible results in the management of this difficult-to-treat infection.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest

FUNDING

None to declare

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