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Mycobacterium tuberculosis as cause of therapeutic failure in prosthetic joint infections

Tuberculosis como causa de fracaso terapéutico en infección de prótesis osteoarticulares

Extrapulmonary tuberculosis accounts for almost 20% of tuberculosis representing the osteoarticular tuberculosis between the 0% and 31%.[1] Late-onset disease can appear in patients with a coexisting prosthetic infection that masks the underlying coinfection.[2] Diagnosis is based on epidemiology, image diagnosis, histopathology, and mycobacterial culture, that is not always included if there is no clinical suspicion.[3]

Two patients with prosthetic joint infection and isolation of *M. tuberculosis* were diagnosed between 1990 and 2012, and selected for review. During the study period, 1473 patients were diagnosed with culture-proven tuberculosis. Of these, only two (0.14% of all cases of tuberculosis) were prosthetic joint infections. The Clinical Research Ethics Committee of our hospital approved the study.

Case 1

An 84-year-old man underwent total hip arthroplasty in 2010 because of an intertrochanteric hip fracture. Five weeks after hip replacement, the patient required additional surgery due to septic loosening of the prosthesis. All the implant was removed and delivered to the clinical microbiology laboratory with multiple periprosthetic tissue samples. The patient was empirically treated with vancomycin and ceftazidime. The synovial samples were processed for pathology and microbiology analysis. Histological examination revealed chronic granulomatous synovitis. An acid-fast stain was negative for all periprosthetic tissue samples. Two days after surgery, a methicillin-resistant *Staphylococcus aureus* was detected on all samples. Therapy was then changed to oral trimethoprim/sulfamethoxazole and rifampin.

Two weeks later, *M. tuberculosis* was isolated in cultures of periprosthetic tissue. The patient began therapy with isoniazid (H)–rifampin (R)–pyrazinamide (P)–ethambutol (E), and after 2 months, treatment was changed to HR for another 7 months. After therapy, his analytical parameters have been normalized, but pain still persisted. The patient refused further therapy because of his age and underlying conditions.

Case 2

An 82-year-old woman was admitted due to an acetabular fracture and femoral neck fracture in 1995. Bipolar arthroplasty was performed, and dislocation occurred hours after surgery, with fever and scanty drainage from the wound. A *Corynebacterium* spp growth was observed from a deep tissue culture, and treatment with vancomycin was then initiated during two weeks. Two months after the first surgery, the arthroplasty was changed due to new dislocations. Periprosthetic tissue samples were sent to the clinical microbiology laboratory for culture. However, the samples did not process for histopatological examination. An acid-fast stain was positive for all samples obtained during the surgery. Anti-tuberculous treatment was started with HRP during 2 months, followed by HR. Two weeks later, *M. tuberculosis* was isolated in mycobacterial cultures. The strains were fully susceptible to all first-line antituberculous drugs. At the time the patient was discharged, she had completed 4 months of antituberculous therapy. Unfortunately, the patient was lost to follow-up.

Prosthetic joint infections caused by *M. tuberculosis* usually involve the hip or the knee,[3] and normally related with a local reactivation or occasionally results from haematogenous spread.[4,5] This syndrome is extremely uncommon after total hip or knee arthroplasty, having an incidence of 0.3% of all episodes of prosthetic joint infection.[1,6] Our two cases had also isolation of other organisms that were initially considered to be the cause of infection, which is a rare finding among previously reported cases of PJI tuberculosis.[2] The patients presented persistent clinical signs and symptoms, so a differential diagnosis of tuberculosis is suggested in patients with clinical symptoms that do not disappear despite conventional therapy,[1,3,4,7] as coexistence of *M. tuberculosis* with other bacteria is a possibility.[8] The potential of *M. tuberculosis* to form a biofilm[9] and the data regarding other implant-related infections caused by other mycobacteria, make it reasonable to recommend prosthesis removal if a complete curation is the final goal. All cases were treated with antituberculous therapy, and at least 9 months of therapy are generally assumed to be required.[1]

In conclusion, *M. tuberculosis* prosthetic joint infection can cause therapeutic failure in some cases of properly treated patients. Although this is an uncommon disease, it must be taken into account in order to use specific microbiological methods for diagnosis. The diagnosis of PJI caused by *M. tuberculosis* must include histological examination and microbiological study, and the protocols for PJI should incorporate this recommendation, at least if tuberculosis is a prevalent disease in the country of origin of the patient.[10]

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