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ORIGINAL ARTICLE

Non-bacterial chronic osteomyelitis: experience in a tertiary hospital☆

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Abstract
Introduction: Non-bacterial chronic osteomyelitis (NBCO) is an autoinflammatory disease that presents with recurrent bouts of bone inflammation in the absence of microbiological isolation. It is a diagnosis of exclusion. Its treatment was classically based on the use of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, although nowadays bisphosphonates or anti-tumour necrosis factor-α (anti-TNF) drugs are frequently used with good results. The objective of the study is to describe our experience in the diagnosis and treatment of patients with NBCO.
Patients and methods: Retrospective chart review of patients with NBCO followed up in a tertiary centre between 2008 and 2015.
Results: A total of 7 patients with NBCO were recorded. Four were female and the median age was 10 years (IQR 2). The most common complaint was pain that interfered with sleep in 5 of the patients. Six patients had multifocal lesions at diagnosis. Bone biopsy demonstrated neutrophilic or lymphocytic infiltration and sclerosis in 6 patients. Four patients received antibiotics and NSAIDs without clinical response. Five received a short course of prednisone with an adequate control of symptoms, but only one of them maintained remission after corticosteroid suspension. Five patients received bisphosphonates with disease remission in 3 of them. The other 2 showed an inadequate response to pamidronate and were started on anti-TNF therapy (etanercept, infliximab or adalimumab), remaining asymptomatic at present.

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Conclusions: Our series, although limited, confirms the effectiveness and safety of bisphosphonate and anti-TNF therapy for children with NBCO.

PALABRAS CLAVE
Terapia biológica;
Osteomielitis crónica multifocal recurrente;
Bifosfonatos;
Osteítis

Osteomielitis crónica no bacteriana: experiencia en un hospital terciario

Resumen
Introducción: La osteítis crónica no bacteriana (OCNB) es una enfermedad autoinflamatoria que cursa con brotes de inflamación ósea en ausencia de aislamiento microbiológico. Su diagnóstico es de exclusión. El tratamiento se basaba en la utilización de antiinflamatorios no esteroideos (AINE) y esteroideos aunque cada vez con mayor frecuencia se utilizan bifosfonatos o fármacos contra el factor de necrosis tumoral α (anti-TNFα) con buenos resultados. El objetivo es revisar nuestra experiencia en el diagnóstico y tratamiento de estos pacientes.
Pacientes y métodos: Revisión retrospectiva de las historias clínicas de los pacientes diagnosticados de OCNB entre 2008 y 2015 en un hospital terciario.
Resultados: De un total de 7 pacientes, 4 eran mujeres, con una mediana de edad de 10 años (RIQ 2). El motivo más frecuente de consulta fue dolor que interfería con el sueño en 5 pacientes. Seis presentaron lesiones multifocales al diagnóstico. En 6 se realizó biopsia ósea que demostró un infiltrado neutrofílico o linfocitario y esclerosis. Cuatro pacientes recibieron tratamiento antibiótico y AINE sin respuesta clínica. Cinco pacientes recibieron prednisona, consiguiéndose control sintomático que solo mantuvo uno tras su suspensión. Cinco recibieron bifosfonatos con remisión de la enfermedad en 3. Dos pacientes presentaron una respuesta insuficiente a pamidronato, por lo que recibieron terapia anti-TNFα (etanercept, infliximab o adalimumab) y se mantienen asintomáticos en la actualidad.
Conclusiones: Nuestra serie, aunque limitada, confirma la efectividad y seguridad de la terapia con bifosfonatos y fármacos biológicos en pacientes con OCNB.

Introduction

Nonbacterial chronic osteomyelitis (NBCO), also known as chronic recurrent multifocal osteomyelitis, is an autoinflammatory disease characterised by bouts of bone inflammation in the absence of microbiological isolation. It presents with bone pain, usually to finger pressure, that may or may not be associated with inflammation of the skin and adjacent tissues. Up to 20% of cases are unifocal at the time of diagnosis, which requires a differential diagnosis including bacterial osteomyelitis, trauma, and malignant diseases. When the lesions are multifocal they are usually symmetrical and predominantly affect the metaphyses of the long bones of the lower limbs, but may also involve the pelvis, spine and clavicle. Fever is an uncommon symptom, although patients may develop low-grade fever. The pain can be severe and disabling, and may be associated with functional impairment. This is an infrequent disease of unknown incidence and prevalence that is probably underdiagnosed.[1,2]

The disease is found worldwide, although most of the published case series are from developed countries in Europe, North America and Australia, probably due to their superior diagnostic and therapeutic resources.

The disease is variable in its presentation and clinical course and is a diagnosis of exclusion, so delays in diagnosis are frequent. The abnormal laboratory results that may be associated to it are nonspecific. When they occur, they correspond to signs of systemic inflammation such as anaemia of chronic disease, leukocytosis or elevated acute phase reactants. The literature has described varying degrees of correlation with the histocompatibility agent HLA-B27 (7–21%), which in turn stems from the association of NBCO to inflammatory bowel disease (IBD) and sacroiliitis.[3,4] Since the clinical presentation and imaging findings in NBCO may be nonspecific, cases with unifocal lesions require performance of a bone biopsy to confirm the diagnosis.[1]

Traditionally, treatment was initiated with nonsteroidal anti-inflammatory drugs (NSAIDs), although we now know that this does not achieve adequate symptom control in a high percentage of cases.[5] In the past decade, biphosphonate therapy has risen as the first step in its management, as it not only controls pain, but also induces remission in some cases.[6] Other alternative treatments are based on new developments in molecular biology, which have allowed the detection of the local and systemic elevation of different cytokines, such as tumour necrosis factor alpha (TNFα)[7] or interleukin 1 (IL-1).[8] The inhibition of these molecules, mainly by means of anti-TNFα drugs, has shown promising results.[9,10]