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Case Report

Atypical Clavicular Involvement of Nonbacterial Osteitis: An Orthopaedic Enigma
非典型性鎖骨非細菌性骨炎: 骨科的謎思

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ABSTRACT

Nonbacterial osteitis (NBO) is an underdiagnosed and poorly understood condition caused by sterile inflammation. It can mimic the presentation of many other orthopaedic conditions, for example, osteomyelitis, septic arthritis, or malignancy, in particular for those patients who have unifocal presentation. Because NBO is a diagnosis by exclusion, it poses much difficulty and confusion to many orthopaedic surgeons in treating such disease. Clavicular involvement is common but it is typically present at the medial aspect of the clavicle. We report a case of NBO with atypical clavicular involvement who presented to our orthopaedic clinic with painful swelling in the left shoulder. Appropriate investigations and management are discussed together with literature review.

中 文 摘 要

非細菌性骨炎是一種由無菌性炎症引起的,低診斷率且認識有限的骨科疾病。它與其它許多骨科疾病的表現形式相似,如骨髓炎,化膿性關節炎或惡性腫瘤,並且在單病灶的病人身上更為明顯。由於非細菌性骨炎的診斷主要是基於排除法,這給很多骨科醫生在治療這種疾病時造成許多困難和困惑。鎖骨是非細菌性骨炎好發部位,且通常發生在鎖骨內側。本文報告一例非典型性鎖骨非細菌性骨炎病例。該病人入院時左肩腫脹並伴有疼痛。本文對此病症作了文獻綜述,並探討如何給予適當的檢查和治療。

Introduction

Nonbacterial osteitis (NBO) is a descriptive term referring to a sterile skeletal lesion with nonspecific histological signs of inflammation. It may be unifocal or multifocal involvement with acute, chronic, or recurrent presentation.[1] Various names have been given to these conditions. To name a few: SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome, CRMO (chronic recurrent multifocal osteomyelitis), and chronic sclerosing osteomyelitis. Currently, these conditions are considered to be part of the spectrum of disease with NBO being a unifying component.[2] NBO can manifest at different age and at all sites of the skeleton. Clavicle is a common site of involvement and it is typically reported at the medial aspect.[1] The clinical presentation may mimic many orthopaedic conditions, for example, osteomyelitis, septic arthritis, or malignancy. Many unnecessary investigations and interventions may be given because of uncertain diagnosis. Diagnostic criteria have been proposed to aid the diagnosis and treatment.[1,2]

Case Report

A 13-year-old boy presented 4 years ago with insidious onset of left shoulder pain for 6 months. There was no history of injury and the patient enjoyed good health all along. Physical examination revealed swelling and tenderness at the lateral end of the left clavicle (Figure 1). Other examinations were largely unremarkable except fulminant acne vulgaris. Radiographs revealed an osteolytic lesion at the lateral third of the left clavicle, which measured about 2 cm in size with poorly defined margin (Figure 2). There was associated soft tissue swelling. The initial blood investigations were normal except slight elevation of erythrocyte sedimentation rate (ESR) between 13 mm/hr and 20 mm/hr (normal 0–10 mm/hr). Magnetic resonance imaging (MRI) revealed destructive lesion involving the middle and lateral third of left clavicle with erosive changes in the acromioclavicular joint.

He underwent a biopsy of the lesion, which revealed nonspecific inflammation. All the microbiological examinations, including aerobic, anaerobic, fungal, and acid-fast bacilli, were negative. He was treated conservatively with analgesics. However, follow-up radiographs within 2 months revealed expansion of the lesion at

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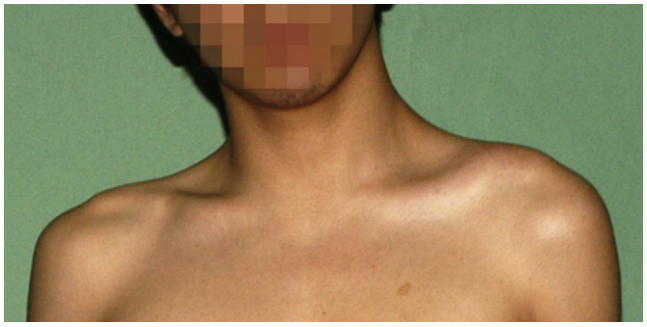

Figure 1. Swelling over the lateral aspect of the left clavicle.

the lateral third of his clavicle. He underwent another biopsy with the histological examination reconfirming the nonspecific inflammation. Skeletal survey was also arranged but did not review any other bony abnormality. Extensive cultures for acid-fast bacilli, fungus, and aerobic and anaerobic organisms were rearranged but were found to be negative. After excluding infection and malignancy, a diagnosis of unifocal NBO was then made. He was treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and followed up regularly. He had occasional episodes of exacerbations, which always responded to NSAIDs. The episodes were less frequent for around 1.5 years after the second biopsy and his radiographs also showed progressive healing with sclerosis. During the exacerbation, the radiographs showed increased bony destruction with lamellated periosteal reaction (Figure 3). Shoulder movements were nearly normal all along and he did not complain of any other joint involvement. Repeated MRI showed consistent findings and blood investigations (complete blood count, C-reactive protein, liver function test, renal function test, antinuclear antibody test, antinuclear antibody, human leukocyte antigen B-27, rheumatoid factor, and urine and blood cultures) were consistently normal except for mild elevation of ESR. He is subsequently under joint follow-up from the paediatric as well as orthopaedic side. The patient remained symptom-free in the past 1 year.

Discussion

The pathogenesis of NBO is largely unknown. It is believed to be an autoinflammatory disorder. This is characterised by recurrent episodes of systemic inflammation often manifested by fever; inflammation of specific tissues, such as joints, skin, gut, and eyes; and the absence of pathogens, autoantibodies, or antigen-specific T-cells.[3] There may be evidence for a genetic basis for NBO but it is still inconclusive.[2,4] Almost any bone can be affected and clavicle is one of the common area of involvement in the adolescents and young adults.[5]

NBO is a diagnosis by exclusion. The differential diagnosis includes juvenile idiopathic arthritis, malignancy, benign bone tumours, suppurative or nonsuppurative osteomyelitis, fracture,

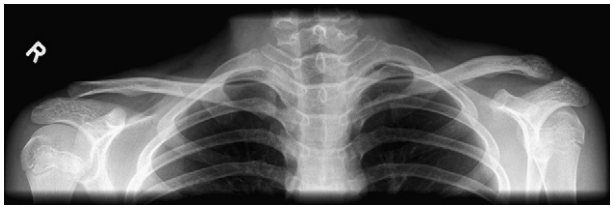

Figure 2. X-ray of the clavicles at the initial presentation showing mixed osteolytic and sclerotic lesion at the lateral end of the left clavicle with hyperostosis.

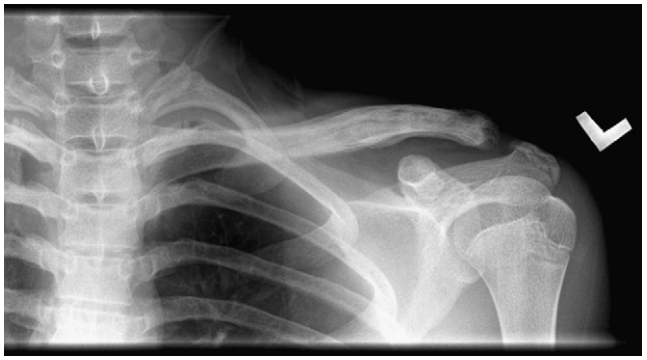

Figure 3. X-ray of the left clavicle showing more extensive osteolytic lesions with periosteal reaction 1 year after the initial presentation. There is more evidence of acromioclavicular joint erosion.

and osteonecrosis.[6] The laboratory parameters are neither consistent nor predictive. Blood investigations may help to rule out other conditions. Indeed, all the blood parameters were persistently negative in our patient except slight elevation in the ESR. For the purpose of establishing diagnosis, Jansson et al[2] have proposed a set of major and minor diagnostic criteria. The major diagnostic criteria include (1) radiologically proven osteolytic/sclerotic bone lesion; (2) multifocal bone lesions; (3) palmoplantar pustulosis or psoriasis; and (4) sterile bone biopsy with signs of inflammation and/or fibrosis and sclerosis. The minor criteria include (1) normal blood count and good general state of health; (2) C-reactive protein and ESR mildly to moderately elevated; (3) observation time longer than 6 months; (4) hyperostosis; (5) associated with other autoimmune diseases apart from palmoplantar pustulosis or psoriasis; and (6) Grade I or II relatives with autoimmune or autoinflammatory disease or with NBO. NBO is diagnosed by two major criteria or one major and three minor criteria. Our patient fulfilled two major and three minor criteria.

Characteristic radiological features of NBO have been described.[1,5] Radiographs of NBO usually reveal poorly defined, mixed sclerotic, and lytic lesions in the metaphysis of the bone. Bone expansion, hyperostosis, and multilaminated periosteal reaction can sometimes be observed. Apart from the mixed lesions seen in the radiographs, computed tomography scan may show multiple small areas of intracortical lysis in the bone. MRI is useful to exclude marrow infiltration caused by malignancy, abscess, and extraosseous mass. Some lesions may not be obvious in the radiographs and marrow oedema evidenced by MRI may be the only positive finding in NBO. It has been noted that the clavicular involvement typically starts in the medial part of the bone and progressive sclerosis and hyperostosis can sometimes be observed. All of these features were present in our patient except that the lesion is atypically found in the lateral end of the clavicle. We were unsure of the diagnosis because of the atypical presentation of the site. We also observe that the lesion becomes more sclerotic during the relatively quiescent phase but becomes more destructive during the painful episodes.

The need for biopsy to establish the diagnosis of this entity may be questionable. Gikas et al,[1] in their study, determined that the features of bone expansion, medullary lytic areas, multilamellar periosteal reaction, bone oedema, and inflammatory soft tissue reaction, when interpreted by an experienced musculoskeletal radiologist can help distinguish NBO from pyogenic osteomyelitis and malignancy. They further argue that if imaging findings along with clinical and biochemical findings are characteristic of NBO, then there is no need to perform a biopsy for histopathological purposes, as the microscopic findings are nonspecific.

It is rather doubtful whether NBO is a self-limiting condition without sequelae because it can have a prolonged clinical course. Huber et al[7] reported a median overall duration of active disease of 5.7 years with more than 25% of patients having persistent activity 12.4 years later. Duffy et al[8] reported noticeable limb deformities and limb length inequality when the patients were followed up till skeletal maturity. We believe that long-term follow-up, at least to skeletal maturity for the paediatric and adolescent patients, is essential.

Antibiotics have been given in the past for NBO. However, since it is now recognised that NBO is a sterile condition, there is no role for antibiotics. NSAIDs are recommended as the first line of treatment to induce good remission patients.[9] For frequent relapses, oral steroids, sulphasalazine, bisphosphonates, methotrexate, colchicine, infliximab, and interferon (alpha and gamma) have been described.[10] Surgery is recommended as the last resort if there is significant morbidity despite appropriate medical therapy.[1] For the management of NBO in paediatric and adolescent patients, we prefer a combined paediatric and orthopaedic management because the paediatricians can help to optimise the medical treatment, whereas the orthopaedic surgeons can observe for any long-term sequelae of the disease, for example, limb deformities. In conclusion, NBO is an underdiagnosed condition, which needs to be kept in mind by the orthopaedic surgeons when dealing with destructive bone lesions. Because of its prolonged clinical course, long-term follow-up is essential to observe for any morbidity as a result of the disease. When the diagnosis is uncertain, further imaging and histological examination are essential to rule out infection and malignancy. Medical treatment is still the first-line treatment.

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