http://dx.doi.org/10.5704/MOJ.1203.005

Non-Bacterial Chronic Recurrent Osteomyelitis of the Clavicle

KL Pan, FRCS, **WH Chan,** MS Orth, **GB Ong*,** MRCP, **M Zulqarnaen**,** MPath, **DK Norlida**,** MPath

Department of Orthopaedics, Universiti Malaysia Sarawak, Kuching ,Malaysia
*Department of Paediatric Oncology, Sarawak General Hospital, Kuching, Malaysia
**Department of Pathology, Universiti Malaysia Sarawak, Kuching, Malaysia

ABSTRACT

This report details the case of a 12-year-old girl with a painful, progressive swelling of the medial portion of the clavicle with no history of trauma or other constitutional symptoms. All laboratory investigations were normal except for an elevated erythrocyte sedimentation rate (ESR). Initial plain radiographs showed a destructive lesion with magnetic resonance imaging showing features of malignancy. Biopsies revealed osteomyelitis, but with negative bacterial cultures and no evidence of malignancy. Treatment with antibiotics did not result in a favourable response. Over time, the swelling increased in size with episodic exacerbations of pain. Follow-up radiographs showed sclerosis and hyperostosis. After five years, this was recognized as non-bacterial chronic recurrent osteomyelitis of the clavicle.

Key Words:
Nonbacterial, chronic recurrent, osteomyelitis, clavicle

INTRODUCTION

Spontaneous swelling of the clavicle that increases in size in a child is an uncommon occurrence. Differential diagnoses include infection, tumour and tumour-like conditions. There are times when laboratory investigation and examination results are in conflict and therapeutic measures do not stop the growth. Early recognition of this nonbacterial osteomyelitis will allay protracted uncertainty. We present the case of a 12-year-old female who was followed up for more than five years with this diagnosis.

CASE REPORT

A 12-year-old girl presented at the orthopaedic clinic in August 2006 with a one month history of spontaneous pain and swelling over the right sternoclavicular region. There was no history of fever or upper respiratory tract symptoms. On examination, there was diffuse tenderness and a hard swollen area. The skin over the swelling was normal and shoulder movement was not affected.

Plain radiographs showed a poorly defined, destructive lesion over the medial third of the right clavicle (Fig 1a). The erythrocyte sedimentation rate (ESR) was 93mm/hr. The total white and differential count was normal, as was the Mantoux test (0 mm). The chest radiograph was clear. With the possibility of a malignant tumour in mind, magnetic resonance imaging (MRI) was performed prior to a biopsy.

The MRI showed a heterogeneously enhancing enlargement of the medial one third of the right clavicle extending to the right sternoclavicular joint (Fig 1b). The radiologist reported the possibilities of an Ewing's or osteosarcoma. At biopsy, the outer cortex was hard and appeared normal. However, the deeper layers showed soft, abnormal, friable tissue. A specimen was sent for bacterial culture but did not yield any bacterial growth. Histopathological examination reported the specimen as being compatible with acute and chronic osteomyelitis after readings by a few pathologists.

Postoperatively, the patient completed a six-week course of fusidic acid and cloxacillin. Unfortunately, follow-up showed that the swelling was getting bigger. A second MRI confirmed an enlarging mass with features suggesting malignancy and a reduced likelihood of osteomyelitis. The ESR was decreased to 38mm/hr, but alkaline phosphatase levels were now elevated at 263U/L. A second biopsy was then performed with findings of only normal appearing bone. There was no more friable tissue as seen in the first open biopsy. The report was similar to the first with no malignancy seen. Features of osteomyelitis were still present, and a second course of fusidic acid and cloxacillin was completed. Seven months later, with the swelling still growing, a third biopsy was performed, with findings of grossly normal bone with no malignancy. Bacterial culture was persistently negative.

The swelling then became quiescent and at follow-up two years later, it was the same size and was asymptomatic. Radiographs at that time showed an enlarged, sclerosed clavicle (Fig 2a). Three years later the swelling became painful again. Plain radiographs showed a new lucency in

Corresponding Author: Pan Kok Long, Dept of Orthopaedics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak, Lot 77, Jln Tun Ahmad Zaidi Adruce, 93150 Kuching, Sarawak Email: klpan@fmhs.unimas.my

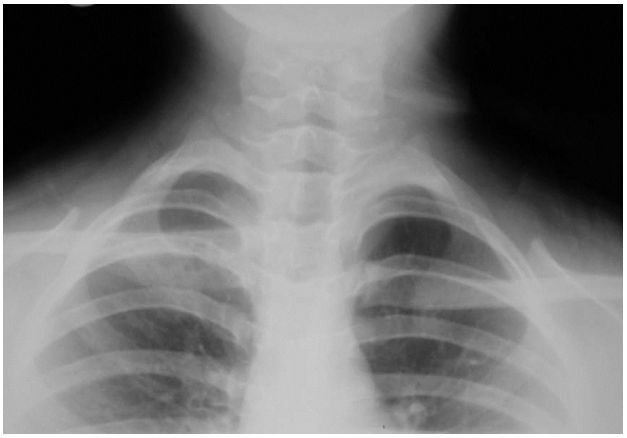

Fig. 1a: Plain radiographs at presentation showing a poorly defined, destructive lesion over the medial third of the right clavicle.

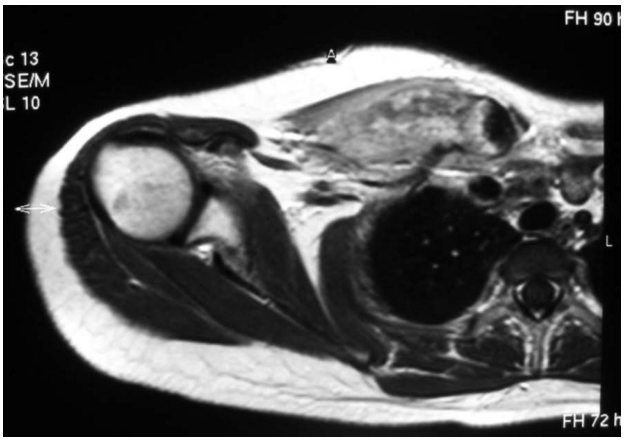

Fig. 1b: Magnetic resonance image (MRI) showing a heterogeneous enlargement of the medial third of the clavicle extending to the right sternoclavicular joint.

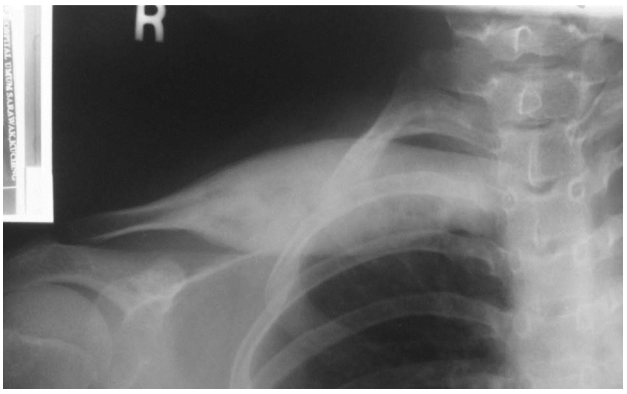

Fig. 2a: Plain radiographs at two years after initial presentation showing an enlarged sclerosed clavicle.

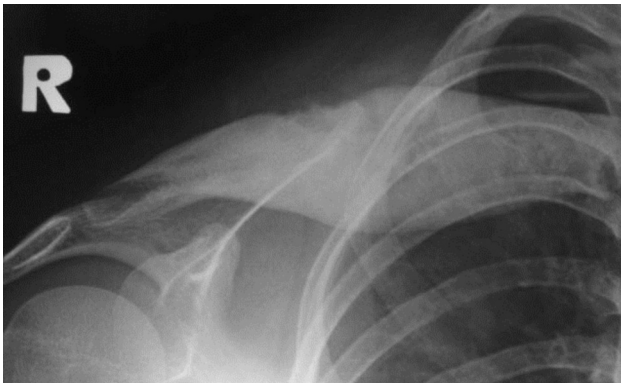

Fig. 2b: Plain radiographs showing a new lucency during a flare-up of symptoms at 3 years after initial presentation.

one area (Fig 2b) leading to another six-week course of antibiotics. At the last follow-up, 5 years after initial presentation (in October 2011) she was well except for a prominent, mildly tender swelling over the right clavicle.

DISCUSSION

For this patient, numerous blood tests, radiographs, MRIs, and three biopsies were performed. Each biopsy showed the diagnosis to be osteomyelitis resulting in multiple, prolonged courses of antibiotics prescribed and completed. Unfortunately, the swelling did not respond to treatment, instead continuing to grow bigger; meanwhile MRIs persistently showed features suggestive of malignancy. It is difficult to explain to a child's parents that a lesion consistently fails to yield any malignant cells or organisms and yet we are not sure of the correct diagnosis. It was not until more than a year had elapsed that we were confident that it was unlikely to be a malignant tumour, and not until five years after initial presentation (amid recurrent episodes of pain and swelling) that we diagnosed nonbacterial chronic recurrent osteomyelitis of the clavicle.

Nonbacterial chronic recurrent osteomyelitis is often called chronic recurrent multifocal osteomyelitis (CRMO). It is a skeletal disorder of unknown aetiology that occurs mainly in children and adolescents. Diagnosis of exclusion is based on the following criteria: (1) lack of a causative organism; (2) absence of abscess formation, fistulae or sequestra; (3) location at an atypical location compared with infectious osteomyelitis with frequent involvement of the clavicle and often multifocal lesions; (4) a radiographic picture suggesting subacute or chronic osteomyelitis; (5) non-specific histopathological and laboratory findings compatible with subacute or chronic osteomyelitis; (6) a characteristic prolonged, fluctuating course with recurrent episodes of pain occurring over several years usually without concomitant systemic manifestations; and (7) sometimes accompanying pustulosis palmoplantaris or acne [1]. Our patient had all the above features except that it was unifocal and she did not have accompanying pustulosis palmoplantaris.

Nonbacterial chronic recurrent osteomyelitis is commonly misdiagnosed as an infection or a neoplasm and unnecessary

aggressive surgical and antibiotic therapy instituted. The incidence of this manifestation is 2.5% of all osteomyelitis cases. It affects mainly young girls with a female/male ratio of 5:1. The median age is 10y (range, 4-14y). Presentation is typically multifocal and runs a prolonged course over 6 months with the patient being healthy between recurrent episodes of pain, swelling and tenderness. There is a characteristic lack of response to antimicrobial therapy. Diagnosis is essentially a process of exclusion. Presentation and radiographic findings can mimic acute haematogenous osteomyelitis, neoplasia, eosinophilic granuloma, osteoblastoma and osteoid osteoma. Patients usually are treated with systemic antibiotics at initial presentation; however, cultures of bone are typically negative [2].

Although aetiology is unknown, nonbacterial chronic recurrent osteomyelitis is considered to be a non-pyogenic inflammatory disease thereby possibly representing a form of seronegative arthropathy. Further, there is typically symptomatic relief following treatment with nonsteroidal anti-inflammatory drugs whereas antibiotics do not have any affect. Magnetic resonance imaging (MRI) is not useful in clavicular lesion presentations (as seen in the case of our patient) but is valuable in cases with tubular bones and in the pelvis presentations [1]. Haddad and colleagues reviewed 15 cases of chronic sclerosing osteomyelitis of the clavicle and found the main symptoms to be pain and swelling. Thirteen cases were at the medial end of the clavicular. Sclerosis was evident on plain radiographs with a periosteal reaction seen in all but 3 cases. No bacterial organisms were grown. Antibiotic treatment was administered for 6 months, and usually resulted in dampened symptoms; this was a baseline minimum before partial clavicular excision was considered. Symptom control was achieved in most cases but recurrences were frequent. Haddad *et al.* concluded that chronic sclerosing osteomyelitis was a diagnosis, which was usually reached late, and for which no universally agreed solution existed [3] .

Most reported cases of CRMO are sporadic, but there is evidence of a genetic component. There is an autosomal recessive syndromic form (Majeed syndrome), which is caused by a mutation. In addition, mice with a mutation on chromosome 18 develop a syndrome resembling human CRMO, suggesting a possible genetic predisposition [4].

CONCLUSION

Early recognition of CRMO can reduce unnecessary and invasive investigative or therapeutic procedures thereby reducing anxiety in both parents and physician. A biopsy will reveal subacute and chronic osteomyelitis with negative bacterial cultures. This condition may run a prolonged, protracted course with exacerbations and increase in the size of the lesion over many years.

REFERENCES

1. Jurik AG, Egund N. MRI in chronic recurrent multifocal osteomyelitis. *Skeletal Radiol.* 1997; 26: 230-8.
2. Deogaonkar K, Ghandour A, Jones A, Ahuja S, Lyons K. Chronic recurrent multifocal osteomyelitis presenting as acute scoliosis: a case report and review of literature. *Eur Spine J.* 2008; 17(2): 5248-252.
3. Haddad FS, Rasquinha VJ, Briggs TWR, Cannon SC. Chronic Sclerosing Osteomyelitis of the Clavicle. *J Bone Joint Surg B* 1999; 81(S III): 301
4. Karaca N, Aksu G, Ozturk C, Gulez N, Kutukculer N. Granulomatous pyoderma preceding chronic recurrent multifocal osteomyelitis triggered by vaccinations in a two-year-old boy. A case report. *Journal of Medical Case Reports.* 2010; 4: 325.