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CASE REPORT

Chronic Recurrent Multifocal Osteomyelitis: A Case Report and Review of Literature

Ostéomyélite multifocale chronique récidivante: Un rapport de cas et revue de la littérature

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ABSTRACT

BACKGROUND: **Chronic recurrent multifocal osteomyelitis (CRMO) is a rare condition of largely unknown aetiology and pathogenesis with variable clinical and radiological features. There are no reports on CRMO to the best of our knowledge; in the West African sub region.**

OBJECTIVE: **To present a case and review the literature on chronic recurrent multifocal osteomyelitis.**

METHODS: **A 13-year-old male presented with a three-year history of recurrent discharging right thigh sinus and an 11-day history of a left shoulder swelling with discharging sinus. Detailed history was obtained and physical examination and radiological and microbiological tests carried out before treatments.**

RESULTS: **There were periodic exacerbations of pain, swelling and discharge over affected areas. He had a short limb gait and shoulder asymmetry. His left shoulder was warm, erythematous and there was decreased range of movement in all directions. Investigations revealed an erythrycyte sedimentation rate (ESR) of 150mm/hr. Wound swabs taken at different times from the right thigh and shoulder sinuses revealed no growth. Radiographs of the left arm, right thigh and hip showed features consistent with chronic osteomyelitis. There were associated destruction of the left hip and soft tissueswelling in the left shoulder. He was principally treated with non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics and dressing of sinuses for three months and had only mild relief of clinical features but no improvement in radiological picture.**

CONCLUSION: **Chronic recurrent multifocal osteomyelitis is a diagnosis of exclusion which is usually under diagnosed because amongst other things, not much is known about it. Successful treatment is difficult to achieve, though some authors have reported good results with combined medical and surgical treatment. WAJM 2011; 30(6): 453–456.**

Keywords: **Osteomyelitis, Bone Inflammation.**

RÉSUMÉ

CONTEXTE: Ostéomyélite multifocale chronique récidivante (CRMO) est une affection rare d'étiologie inconnue et pathogénie avec des caractéristiques cliniques et radiologiques variables. Il n'y a pas de rapports sur OCMR au meilleur de notre connaissance, dans la région ouest africaine.

OBJECTIF: Présenter un cas et revue de la littérature sur la chronique récurrente multifocale ostéomyélite.

MÉTHODES: Un garçon de 13 ans s'est présenté avec une histoire de trois ans de récidive du sinus droit et la cuisse de décharge d'une histoire de 11 jours d'une épaule gauche un gonflement avec décharge du sinus. L'histoire détaillée a été obtenue et l'examen physique et radiologique et des tests microbiologiques effectués avant les traitements.

RÉSULTATS: Il y avait des exacerbations périodiques de douleur, l'enflure et des rejets au cours zones touchées. Il avait une démarche branche courte et à l'épaule l'asymétrie. Son épaule gauche était chaude, érythémateuse et il a diminué l'amplitude des mouvements dans toutes les directions. Les enquêtes ont révélé un taux de sédimentation erythrycyte (ESR) de 150mm/hr. Écouvillons plaies prises à différents moments de la cuisse droite et les sinus épaule a révélé une croissance nulle. Les radiographies du bras gauche, cuisse droite et de la hanche a montré des caractéristiques compatibles avec une ostéomyélite chronique. Il y avait la destruction associée de la hanche gauche et tissueswelling douce à l'épaule gauche. Il a été principalement traité de non-stéroïdiens anti-inflammatoires non stéroïdiens (AINS), des antibiotiques et l'habillage des sinus pendant trois mois et ne disposait que d'un léger redressement des caractéristiques cliniques, mais aucune amélioration dans radiologique image.

CONCLUSION: l'ostéomyélite multifocale chronique récidivante est un diagnostic d'exclusion qui est habituellement sous-diagnostiquée, car entre autres choses, ne sait pas trop à ce sujet. Le succès du traitement est difficile à réaliser, même si certains auteurs ont rapporté de bons résultats avec un traitement médical et chirurgical combiné. **WAJM 2011; 30 (6): 453–456.**

Mots-clés: Ostéomyélite, inflammation d'un os.

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Abbreviations: CRMO, Chronic recurrent multifocal osteomyelitis; **ESR,** Erythrycyte sedimentation rate; **NSAIDS,** Non-steroidal anti-inflammatory drugs; **SAPHO,** Synovitis, acne, palmo-plantar pustulosis, hyperostosis, and osteitis.

INTRODUCTION

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare condition accounting for 2 to 5% of all cases of osteomyelitis.[1,2] It mostly affects children.[1,2] Giedion *et al*[1] first described acquired, culture-negative, multifocal osteomyelitis in children in 1972 and named the syndrome "subacute and chronic symmetrical osteomyelitis." In the original report, the disorder involved the metaphyses of long bones either simultaneously or successively.[1] Subsequent publications reported involvement of additional bone sites and referred to the disorder as chronic multifocal osteomyelitis and chronic recurrent multifocal osteomyelitis (CRMO).[2]

It was once considered strictly a childhood disease, but adults have been diagnosed with it.[2] The disease tends to affect age range 4–14 years, with 10 years as the median and a female preponderance.[3] Its origin and pathogenesis are not entirely clear even though it has been recognized as a clinical entity for almost three decades.[1] It is now classified as an inherited auto inflammatory condition though the exact gene responsible has not been isolated.[3] The clinical and radiological features are variable and the diagnosis is usually one of exclusion.[1,4]

The purposes of this communication are to present a case of CRMO, review the literature, and describe its current management modalities. To the best of our knowledge, this is the first reported case in our sub-region.

Case Report

A 13-year-old boy presented with a three-year history of recurrent discharging right thigh sinus and an 11-day history of a left shoulder swelling with discharging sinus with periods of remission. There was no history of trauma, fever or recent systemic illness. The left shoulder swelling was gradually increasing in size, with associated pain and difficulty in using the arm. He was not known to have with sickle cell disease and there was no family history of chronic recurrent multifocal osteomyelitis.

Physical Examination

Physical examination showed a chronically ill looking young boy in painful distress with a short limb gait and shoulder asymmetry. He was afebrile and had no significant peripheral lymphadenopathy. His left shoulder was swollen, erythematous and warm. There was decreased range of movement in all directions. There were two discharging sinuses on the lateral surface of the mid right thigh but there was no swelling and the thigh was not tender. He was also noticed to have limb length discrepancy with the left limb being shorter by three centimetres and a prominent left hip.

Full blood count results showed Haemoglobin laboratory count of 12.5g/dl, a leucocytosin of 12,000/microlitre with differentials of: polymorphs 57%, eosinophils 2%, lymphocytes 39%, monocytes 2%. There was a markedly elevated erythrocyte sedimentation rate (ESR) of 150mm/hr.

Three wound swabs were taken at different times for microscopy, culture and sensitivity from the right thigh sinuses and from the shoulder sinus and they yielded no significant growth. First swab was taken at initial time of presentation; other two subsequent swabs were taken during periods of exacerbation of symptoms. None of the specimens yielded any significant growth.

His genotype was AA and HIV screening tests were negative. Radiographs of the left arm, left thigh and hip (Figure 1 and 2) showed irregular radiolucencies with surrounding sclerosis in corresponding humerus and femur consistent with chronic osteomyelitis. There was associated destruction of the left hip and soft tissue swelling in the left shoulder.

An assessment of acute exacerbation of multifocal osteomyelitis was made and he was placed on intravenous Flucloxacillin, oral Diclofenac and had the sinus wounds dressed daily while on admission. The patient had only mild relief of symptoms and was seen periodically as an outpatient. He was admitted during other periods of exacerbation of symptoms especially pain and swelling. Admission periods spanned between 10 and 14 days each for control of acute flare up of symptoms. He continued treatment with oral Naproxen after little response with oral Diclofenac for over a month. Presently patient has had antibiotics and NSAIDs for three months with only mild relief of clinical features but no improvement in radiologic picture.

DISCUSSION

Chronic recurrent multifocal osteomyelitis (CRMO) is an inherited inflammatory disease that affects multiple sites, primarily the skeletal system with symptoms similar to osteomyelitis but without an infecting organism[1]. The course of the disease is characterized by periodic exacerbations and remissions but long-term outcome remains unclear[3]. Our patient had periodic exacerbations of multiple site osteomyelitis without any organism implicated. He only showed marginal response to treatment.

Clinical Features

The most common sites affected are the metaphyses of long bones, spine, pelvis, and shoulder girdle.[1,2] The humerus, femur, and hip were affected in the patient being reported.Chronic recurrent multifocal osteomyelitis has however been reported in mertatarsals and mandible.[2] It has been associated with various other overlapping disease entities like palmoplantar pustulosis [3,] and psoriasis. The disease is now considered as part of the synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis (SAPHO) syndrome.[3] Majeed syndrome which consists of CRMO, congenital dyserythropoietic anaemia and inflammatory dermatosis, has also been reported in families.[6]

Chronic recurrent multifocal osteomyelitis is considered strictly a childhood disease, though adults have been diagnosed with it.[2] The disease usually affects 4–14 year olds with predilection for females.[3,6] Though our patient falls within the commonly affected age group, his male gender is not so commonly affected.

Patients may present with a deep aching pain, low grade fever,[2, 7] swelling, occasionally skin redness over the affected bone[3] or joint effusion.[8] Dermatological manifestations may occur and include psoriasis, acne, and pustules on the palms of the hands and soles of the feet[3]. Uveitis and inflammatory bowel

disease have also been described,[1, 9] rarely it may present with spinal deformity.[4] Our patient presented with pain, swelling, deformity and reduction of range of movement over adjoining joints.

Radiological Features

Skeletal manifestations include multiple synchronous or metachronous lesions apparent on plain radiographs. The lesions are lytic and destructive in the early phase, and sclerotic and reactive in the late phase, occurring in any bone.[7,10] Lesions can occur simultaneously or sequentially. The periosteal reaction in the reactive phase can be abundant, multi-layered, and mimic that seen in malignancy.[7,10] Arthritis may be seen in nearby joints.[10] These features were all seen in the radiographs of the patient being reported.

The lesions progress with time, showing sclerosis and hyperostosis.[10] Active lesions may have an onion-skin-like appearance which may mimic Ewing sarcoma or osteosarcoma.[1] Once the process subsides, the affected bones return to near normal appearance if the child is young enough or lesions may persist for as long as 6 years on radiographs.[10] Our patient has however not shown any such return to normal radiologic appearance.

Technetium whole body bone scan is useful for identifying other sites of skeletal involvement. The lesions demonstrate increased uptake on technetium bone scans, even if they are clinically silent.[1] Computed tomography scans and MRIs are helpful in delineating the extent of the lesion, though the findings are non-specific, they are consistent with osteomyelitis.[1] These modalities do not distinguish CRMO from acute bacterial osteomyelitis. Magnetic resonance imaging (MRI) is a useful study for evaluating response to treatment and follow-up,[1, 4] since the need for repeated x-rays, bone scans, and CT scans can cause a significant radiation exposure in a child.

Histopathological Features

Biopsy and sampling of involved bone lesions is frequently necessary.[1,2,11] Biopsy techniques should be meticulously planned to avoid contamination of important structures and avoid creating stress risers in weight bearing bones that could result in pathological fractures. Antibiotic therapy should be delayed until definitive tissue sampling has been accomplished, if possible.[2] Careful sampling of tissues for aerobic and anaerobic culture as well as PCR analysis of the biopsy material should be considered to rule out infectious agents. The histopathological findings show an inflammatory process that varies according to the stage of the disease. Early cases show polymorphonuclear cells and osteoclastic resorbtion of bone, while later cases show lymphocytes, plasma cells, histiocytes, and polymorphonuclear cells.[2]

Our patient had only radiographs with microscopy and culture of discharge from sinuses. This was due to unavailability of other investigation modalities at our centre and reluctance of his parents to give consent for more invasive procedures.

Diagnosis

The diagnosis of CRMO is mainly based on clinical history, examination and radiological features of lesions. Various diagnostic criteria for CRMO have been proposed. Manson *et al.*[12, 13] suggested the following diagnostic criteria:

- Two radiographically confirmed bone lesions.
- At least six months of remissions and exacerbations of signs and symptoms.
- Radiographic and bone scan evidence of osteomyelitis.
- Lack of response to antimicrobial therapy at least one month in duration.
- Lack of an identifiable cause.

Jansson *et al.*[14] proposed criteria for diagnosis of CRMO as part of non-bacterial osteitis (NBO):

Major Criteria

- Radiologically proven osteolytic/sclerotic lesion
- Multifocal bone lesions
- Palmoplantar pustulosis or psoriasis
- Sterile bone biopsy with signs of inflammation and/or fibrosis, sclerosis

Minor Criteria

- Normal blood count and good general health
- C-reactive protein and ESR mild to moderately elevated
- Observation time longer than six months
- Hyperostosis
- Associated with other autoimmune disease apart from palmoplantar pustulosisor psoriasis
- Grade I or II relatives with autoimmune or autoinflammatory disease, or with non-bacterial osteitis.

Patients with at least two major criteria or one major and three minor criteria have non- bacterial osteitis [14]

Treatment

The effective and definite treatment is still impossible. The aim of the treatment is to try to prevent flare-ups and treat them if they occur. Long term treatment is usually required to monitor any growth disturbances in the affected bones. Experience has shown that antibiotic treatment is not effective in dealing with CRMO flare-ups as there is no underlying infection to treat.[1, 2, 4]

Non-steroidal anti-inflammatory drugs (NSAIDs) are the primary choice for effective treatment.[1,3,4,10] Azithromycin has been used because of its anti-inflammatory and immune-modulatory effects.[1] For severe cases, corticosteroids and antimetabolites such as methotrexate have been used.[1,2] Bisphosphonates[15] and sulfasalazine have also been used.[1] Other therapies have been reported, including interferon, azithromycin, tumor necrosis factor.[2,16] Due to the variable nature and rare incidence of this disease, no controlled trials have been performed.[3] Surgical intervention may be indicated in some cases however, aggressive surgical procedures that increase the risk of pathological fracture should be avoided.[10]

Some authors have reported excellent results with combined medical and surgical treatment.[3, 4, 10, 15] Our patient was principally treated with NSAIDS, antibiotics and dressing of sinuses.

Bola Prognosis

The prognosis for these patients is

good. In one study[11] 11 of 23 patients had complete resolution of the clinical findings, at an average of 5.6 years after diagnosis. Six patients continued to have active disease, and the other six had intermittent relapses or chronic pain, while 78% had no physical impairment. In another study,[10] all five patients responded dramatically to treatment with indomethacin, all underwent clinical improvement and radiological lesions disappeared after a mean period of 10.5 months. There were no additional recurrences or new bones affected during a mean follow-up period of four years.

Conclusion

Chronic recurrent multifocal osteomyelitis is a diagnosis of exclusion, usually under diagnosed because amongst other things not much is known about it. Its definitive diagnosis is rather cumbersome because of the barrage of investigation required. Successful treatment is difficult to achieve, though some authors have shown that initiation of therapy early in the disease may lead to full recovery.

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