

Chronic recurrent multifocal osteomyelitis in children

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Abstract

Chronic recurrent multifocal osteomyelitis (CRMO) in children is an inflammatory disorder. It affects mainly the metaphyses of the long bones, in addition to the spine, the pelvis and the shoulder girdle. However, bone lesions can occur at any site of the skeleton. Even though this disease has been recognized as a clinical entity for almost three decades now, its origin and pathogenesis are not entirely clear. No apparent infectious agents are detectable at the site of the bone lesion. No epidemiological data on incidence and prevalence have been published so far. However, incidence might be something around 1:1,000,000, thus reflecting the number of patients followed-up. Clinical diagnosis in an affected child can be difficult because the clinical picture and course of disease may vary significantly. It has been shown that histological examination alone does not allow the distinction of CRMO from acute or subacute bacterial osteomyelitis. Therefore an extensive microbial workup of the tissue biopsy, including PCR-techniques, is essential in order to establish the diagnosis and decide as to the treatment. Non steroid anti-inflammatory drugs (NSAID) are the treatment of choice. In case of frequent relapses oral steroid treatment, bisphosphonates and azulfidine have been used and are reported to be beneficial.

Keywords

Multifocal osteomyelitis, enthesitis related arthritis, psoriasis arthritis, palmoplantar pustulosis

Disease name and synonyms

In previous reports a multitude of labels have been used to describe chronic recurrent multifocal osteomyelitis (CRMO): "chronic sclerosing osteomyelitis" (2), "condensing osteitis" (3, 4), "sclerosis and hyperostosis" (5-7), "primary chronic osteomyelitis" (8) and "pustulotic arthroosteitis" (9, 10). Descriptive histopathological terms have also been used to describe the disease, like "lymphoplasmacellular osteomyelitis" (11, 12). Even though the denomination includes "multiple" and "recurrent", some authors include non-relapsing

unifocal osteolytic lesions in children with no apparent infectious agent detectable at the site of the bone lesion into the diagnosis (13-18). In adults a similar disease has been named "SAPHO-syndrome" (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis) (19, 20). CRMO has been regarded by Kahn *et al.* as the pediatric subset of the SAPHO-syndrome (21,22). Histologically, bone lesions in uni- and multifocal CRMO, as well as SAPHO show similar features (6, 13, 23-26).

Definition

Chronic recurrent multifocal osteomyelitis (CRMO) in children is an inflammatory disorder. It mainly affects the metaphyses of the long bones, in addition to the spine, the pelvis and the shoulder girdle. However, bone lesions can occur at any site of the skeleton.

Differential diagnosis

- Malignancy (osteosarcoma, Ewing's sarcoma, neuroblastoma, rhabdomyosarcoma, leucemia, ([Langerhans cell histiocytosis](#)))
- Osteoid osteoma
- Bacterial subacute osteomyelitis

Clinical manifestations***Skeletal manifestations***

- Unifocal or multifocal, initially osteolytic, later hyperostotic and sclerotic lesions mainly in the metaphyses of the long bones and shoulder girdle, but any bone can be affected. Relapses are frequent even under therapy.
- Arthritis of adjacent and distal joints is frequent. CRMO can be a feature of enthesitis-related arthritis at onset or during the disease course.

Other organ involvement

- Palmoplantar pustulosis, psoriasis or acne conglobata
- Uveitis
- Inflammatory bowel disease

Etiology

Pathogenetically CRMO is linked to enthesitis-related arthritis and psoriatic arthritis. There has been an intense discussion on the putative infectious etiology of CRMO, especially *Propionibacterium acnes* has been postulated to be involved in the pathogenesis. However, in larger cohorts and by using state of the art microbial techniques no apparent infectious agents could be detected at the site of the bone lesion in pediatric patients. Even though this disease has been recognized as a clinical entity for almost three decades now (1), its origin and pathogenesis are not entirely clear.

Incidence and prevalence

No epidemiological data on incidence and prevalence have been published so far. However, incidence might be estimated at 1:1,000,000.

Diagnosis

Clinical diagnosis in affected children can be difficult because the clinical picture and course of disease may vary significantly.

Histologically, bone lesions in uni- and multifocal CRMO, as well as SAPHO show similar features (6, 13, 23-26). Depending on disease course biopsy may show subperiosteal bone formation which is a sign of chronic inflammation with infiltration of leukocytes. In very early lesions granulocytes can be observed, and later on mainly lymphocytes or monocytes. Later stages show fibrotic changes (13). Histological examination alone does not allow distinction of CRMO from acute or subacute bacterial osteomyelitis (13, 26). Therefore extensive microbial workup of the tissue biopsy, including PCR-techniques, is essential in order to establish the diagnosis and decide about treatment.

Disease course

Recently, evolution of CRMO into enthesitis-related arthritis or spondyloarthritis has been documented in three cohorts of children and young adults (18, 31, 34). Inflammatory joint involvement already at the time of diagnosis and during the course of the disease might have been underestimated so far (34). Pathogenetically, CRMO is linked to juvenile arthritis and features of CRMO can overlap features of enthesitis-related arthritis or psoriatic arthritis.

Treatment

Non steroid anti-inflammatory drugs (NSAID) are the treatment of choice.

Therapeutically, antibiotic treatment is considered to be ineffective and treatment with non steroidal anti-inflammatory agents has been reported to be effective repetitively (13, 24, 27-32). In patients with frequent relapses oral steroid treatment (31, 33, 34), bisphosphonates (35, 36) and sulfasalazine (31, 34) have been used and were reported to be beneficial.

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