



Chronic non bacterial osteomyelitis/osteitis (or CRMO)

What is it?

Chronic recurrent multifocal osteomyelitis (CRMO) is the most severe form of chronic non-bacterial osteomyelitis (CNO). In children and adolescents, CNO predominantly affects the metaphyses of the long bones, but inflammatory lesions can occur at any site of the skeleton. Other organs (skin, eyes, gastrointestinal tract, lungs) can also be affected.

How common is it?

The frequency in populations has not been studied in detail. From European national registries of the disease there are estimations available, which state that around 1-5 of 10000 inhabitants might be affected. There is no gender predominance.

What are the causes of the disease?

The causes are unknown. There are hypotheses, that this disease is linked to a disturbance in the innate immune system. Rare diseases of bone metabolism might mimic CNO like hypophosphatasia, Camuratti Engelman syndrome or benign hyperostosis/pachydermoperiostosis.

Is it inherited?

This has not been proven but hypothesized. In fact only a minority of cases is present in a familiar way.

Why has my child got this disease? Can it be prevented?

The causes are unknown so far. Preventive measures are unknown.

Is it contagious or infectious?

No, it is not. In recent analyses no causative infectious agent (like bacteria) has been found.

What are the main symptoms?

The patients usually complain of bone or joint pain; therefore, the differential diagnosis includes juvenile idiopathic arthritis. clinical examination actually can show arthritis in a significant portion of patients. local bone swelling and tenderness is common, limping or loss of function may be present. the disease can have a primary chronic or recurrent course.

Is the disease the same in every child?

It is not the same in every child. Moreover, the type of bone involvement, the duration and severity of symptoms varies from patient to patient and even in the same child if a recurrent course is considered.

Is the disease in children different from the disease in adults?

In general CNO in children resembles that seen in adults. However some features of the disease like skin involvement (psoriasis, acne pustulosa) can be quite different and more

frequent. In adults the disease has been called SAPHO syndrome for synovitis, acne, pustulosis, hyperostosis and osteitis. CNO has been considered the paediatric and adolescent version of SAPHO syndrome.

How is it diagnosed?

CNO/CRMO is a diagnosis of exclusion. Laboratory parameters are neither consistent nor predictive in CRMO/CNO. Radiography of early CNO bone lesions often does not reveal characteristic changes, although, later in the course of disease, osteoplastic and sclerotic changes of long bones of the extremities and the clavicle can be suggestive of CNO. Vertebral compression is also a rather late radiographic sign but further differential diagnoses of malignancy and osteoporosis have to be considered upon presentation of this finding. Diagnosis of CNO must, therefore, rely on the clinical picture in addition to imaging studies.

MRI analysis (with contrast dye) gives further insights into the inflammatory activity of the lesions. We consider technetium bone scans helpful in the initial diagnostic setting, since clinically silent CNO lesions are often present. However, whole body MRI seems to be more sensitive in defining the lesions.

In a considerable number of patients diagnostic imaging alone does not rule out malignancy, and biopsy should be considered, especially since a definite distinction between oncological bone lesions and lesions associated with CNO is often difficult. When choosing the biopsy location, functional and cosmetic aspects must be considered. Biopsies should only be performed for diagnostic purposes and clinicians should not aim to excise the whole lesion; this could lead to an unnecessary functional impairment and scarring. The need of a diagnostic biopsy has repeatedly been questioned in the management of CNO. Diagnosis of CNO seems quite probable if the bone lesions have been present for 6 months or longer and the patient also presents with typical skin lesions. In this case, a biopsy might be omissible; however, a short-term clinical follow-up including repetition of imaging studies is mandatory. Unifocal lesions, which have a solely osteolytic appearance and which involve surrounding tissue structures, must be biopsied to exclude malignancy.

What is the importance of tests?

- a) Blood tests: The laboratory tests, as mentioned before, are not specific in diagnosing CNO/CRMO. Tests like erythrocyte sedimentation rate (ESR), CRP, whole blood count, alkaline phosphatase and creatinine kinase are ordered during a painful episode to see the extent of inflammation and tissue involvement. However, often these tests are inconclusive.
- b) Urine test: not conclusive
- c) Bone biopsy: necessary in unifocal lesions and in cases of uncertainty

Can it be treated or cured? What are the treatments?

Long-term data on treatment predominantly using non-steroidal anti-inflammatory medications (NSAIDs like ibuprofen, naproxen, indomethacin) is available, showing that up to 70% of patients can be cured by a continuous medication lasting up to several years. However, a significant number of patients require more intense medication including steroids, sulfasalazine. Recently, positive treatment results have been reported using bisphosphonates. Chronic treatment-refractory courses have also been reported.

What are the side effects of drug therapy?

It is not easy for parents to accept that their child has to take medication for a long time. They are usually worried about the potential side effects of anti-pain and anti-inflammatory medications. NSAIDS in childhood usually are considered safe drugs with limited side effects like stomachache.

How long should treatment last for?

Treatment duration is depending on the local presence of lesions, their number and severity.

What about unconventional or complementary therapies?

Physical therapy might be of relevance in case of arthritis.

What kind of periodic check-ups are necessary?

Children being treated should have blood and urine tests for at least twice yearly.

How long will the disease last for?

In most patients disease duration is up to several years, in some it is a life-long disease.

What is the long term prognosis (predicted outcome and course) of the disease?

If treated properly a good prognosis is present / can be achieved.

Everyday life

How could the disease affect the child and family's daily life?

The child and the family experience joint and bone problems often over months before the disease is diagnosed. Admittance to a hospital for a differential check up is usually recommended. Regular visits to an outpatient clinic follow after the diagnosis has been made.

What about school? What about sports?

There might be limitations for sport activities especially after biopsy or if arthritis is present. Usually there is no need to limit overall physical activity afterwards.

What about diet?

There is no specific diet.

Can climate influence the course of the disease?

No, it cannot.

Can the child be vaccinated?

Yes, the child can be vaccinated.

What about sexual life, pregnancy, birth control?

Patients with CNO do not have fertility problems. In case the pelvic bones are affected there might be discomfort in sexual activities. The need of medication must be reevaluated during pregnancy.