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## **Chronic non-Bacterial Osteomyelitis/Osteitis (or CRMO)**

Version of 2016

### **2. DIAGNOSIS AND THERAPY**

#### **2.1 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 must 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) provides further insights into the inflammatory activity of the lesions. Technetium bone scintigraphy can be 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 and is currently widely used in clinical practise.

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 malignant bone lesions and lesions associated with CNO is sometimes difficult. When choosing the biopsy location, functional and cosmetic aspects should be considered. Biopsies should only be performed for diagnostic purposes and clinicians should not aim to excise the whole lesion; this could lead to

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unnecessary functional impairment and scarring. The need for 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 avoided; however, a short-term clinical follow-up including repetition of imaging studies is recommended. Unifocal lesions, which have a solely osteolytic appearance and which involve surrounding tissue structures, must be biopsied to exclude malignancy. The use of the clinical chronic nonbacterial osteomyelitis score may avoid unnecessary biopsies. Technique used to perform the biopsy may be different in each centre.

## **2.2 What is the importance of tests?**

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

## **2.3 Can it be treated or cured? What are the treatments?**

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

## **2.4 What are the side effects of drug therapy?**

It is not easy for parents to accept that their child must take medication for a long time. They are usually worried about the potential side effects of painkillers and anti-inflammatory medications. NSAIDs in childhood are generally considered safe drugs with limited side effects such as

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stomach ache. For further information, see the chapter on drug therapy.

### **2.5 How long should treatment last?**

Treatment duration depends on the local presence of lesions, their number and severity. Usually, treatment is necessary for months or years.

### **2.6 What about unconventional or complementary therapies?**

Physical therapy might be relevant in the event of arthritis. However, there is no data on the use of complementary therapy in such diseases.

### **2.7 What kind of periodic check-ups are necessary?**

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

### **2.8 How long will the disease last?**

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

### **2.9 What is the long-term prognosis (predicted outcome and course) of the disease?**

If the disease is treated properly, a good prognosis is present.

3.1 How might the disease affect the child and the family's daily life? The child and the family experience joint and bone problems often over months before the disease is diagnosed. Admission to a hospital for further investigations before starting on treatment is usually recommended. Regular visits to an outpatient clinic for follow-up after the diagnosis are also recommended.

3.2 What about school? What about sports? There may be limitations for sport activities, especially after biopsy or if arthritis is present. Usually, there is no need to limit overall physical activity afterwards.

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3.3 What about diet? There is no specific diet.

3.4 Can climate influence the course of the disease? No, it cannot.

3.5 Can the child be vaccinated? The child can be vaccinated, except with live vaccines when under treatment with corticosteroids, methotrexate or TNF- $\alpha$  inhibitors.

3.6 What about sexual life, pregnancy, birth control? Patients with CNO do not have fertility problems. In the event that the pelvic bones are affected, there may be discomfort in sexual activities. The need for medication must be re-evaluated before considering pregnancy and during pregnancy.