CRMO: The "Osteomyelitis We Haven't Heard Of and Might Overlook"

Definitions

- **CNO (Chronic Nonbacterial Osteomyelitis)** – Chronic nonbacterial osteomyelitis.
- **CRMO (Chronic Recurrent Multifocal Osteomyelitis)** – Chronic recurrent multifocal osteomyelitis, the most severe form of CNO.
- **SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis)** – The adult version of CRMO.

Why Haven't We Heard of It?

CRMO belongs to the relatively "young" group of diseases called **autoinflammatory diseases** (not to be confused with autoimmune diseases!). Informative publications on these conditions have only recently started appearing in Ukraine, and the **diagnosis of CRMO is still somewhat "new" to us**. However, research on CRMO has been ongoing worldwide for about **40 years**.

In Ukraine, CRMO cases are rarely recorded, unlike in Europe and America. However, this is not due to low disease prevalence but rather **limited medical education, lack of physician awareness, and consequently, delayed or incorrect diagnosis**.

What is CRMO?

CRMO, also known as **chronic nonbacterial osteomyelitis (CNO)**, is a **chronic spontaneous systemic autoinflammatory disease** that primarily affects children and is **bone-mediated**. The development of the autoinflammatory process is due to **an innate immune system malfunction**.

Simply put, the immune system of **CRMO patients "attacks" the bones**, causing inflammation even when **no infection is present**. The exact causes of CRMO are still unclear, but in some cases, they are associated with **genetic mutations, particularly on chromosome 18q**. The hereditary nature of the disease has not been definitively established, as it has only been described in isolated family cases. However, research suggests that **interleukins 1 and 10** and **inflammasome activation** play key roles in inflammatory responses.

What Happens to the Bone in CRMO?

Two types of cells are essential for bone development in children:

- **Osteoblasts**, which form bone.
- **Osteoclasts**, which break down bone cells (osteocytes).

Normally, these cells work together to maintain **healthy and strong bones**.

However, in **CRMO**, immune system cells produce proteins that send **signals for osteoclasts to overwork**, leading to **bone inflammation and destruction**. This results in **bone pain with or without swelling**. Over time, **fractures** may occur. Even if the pain decreases with treatment, **inflammation may still flare up periodically**.

Because of this, children with CRMO require **long-term monitoring** by a specialist experienced in treating autoinflammatory diseases, such as a **pediatric immunologist or rheumatologist**.

What Are the Symptoms of CRMO?

CRMO presents as **bone pain**, which can occur **anywhere in the body**. The disease typically affects children between **7–12 years old**, but symptoms can appear **from preschool age to adolescence or even adulthood**.

Children with CRMO may experience:

- **Severe aching bone pain**, **limping**, and **tenderness at affected sites**.
- **Commonly affected areas**: long bones, **clavicle, shoulder girdle, spine, ankles, and feet**.
- **Additional symptoms**: episodic **fever, skin conditions (such as psoriasis, acne, or pustules on the palms and soles)**.
- Some patients may also develop **uveitis** or **inflammatory bowel disease (IBD)**.

While **CRMO symptoms are similar in children and adolescents**, certain features differ:

- **Skin manifestations (scaly patches, pustules, acne) are rare in children**.
- **In adults, CRMO is classified as SAPHO syndrome**, which includes **synovitis, acne, pustulosis, hyperostosis, and osteitis**.

How is CRMO Diagnosed?

CRMO is a **diagnosis of exclusion**. Before confirming it, other conditions must be ruled out, including:

- **Bacterial osteomyelitis**
- **Mycobacterial infections**
- **Malignancies** (leukemia, lymphoma)
- **Systemic diseases** (Langerhans cell histiocytosis)
- **Metabolic bone diseases** (hypophosphatasia, vitamin C deficiency)
- **Other autoinflammatory diseases with bone involvement**

Diagnosis usually requires **multiple tests**:

- **Blood tests**
- **X-rays**
- **Bone scans**
- **MRI** (often whole-body MRI, or targeted MRI of affected areas like the clavicle or ankle)
- **Bone biopsy** (if needed, to rule out infection or cancer)

Why is CRMO Hard to Diagnose?

There is **no single test to confirm CRMO**. Diagnosis relies on:

- **Interpreting inflammatory blood markers**
- **Imaging findings (MRI, CT scans)**
- **Treatment response**

Doctors sometimes misinterpret **bone pain as "growing pains"**, and limping—one of CRMO's hallmark symptoms—can be mistaken for **overuse injuries or minor trauma**. If MRI findings suggest CRMO, **a bone biopsy may be required** to **rule out infection or malignancy**. This process can be **stressful for families awaiting a diagnosis**.

How is CRMO Treated?

CRMO progression varies between patients, and children **respond differently to treatment**. A doctor may need to try **multiple approaches** before finding an effective therapy.

First-line treatment:

- **NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)**
  - **Reduce inflammation and prevent bone destruction**
  - **Block inflammasome activation**, shifting the balance toward anti-inflammatory cytokines

If NSAIDs are **ineffective** or poorly tolerated, or if the patient has **high-risk bone lesions (e.g., spinal involvement)**, **second-line therapies** are used, such as:

- **Short courses of corticosteroids**
- **Methotrexate or sulfasalazine**
- **TNF inhibitors (with or without methotrexate)**
- **Bisphosphonates (e.g., pamidronate)**

The **Childhood Arthritis and Rheumatology Research Alliance (CARRA)** has developed **standardized CRMO treatment guidelines**, recommending a **12-month treatment plan**.

Why is Early Diagnosis and Treatment Important?

✅ **To reduce inflammation**

✅ **To prevent bone damage and deformities**

✅ **To avoid growth abnormalities**

✅ **To relieve pain and improve quality of life**

What is the Prognosis for CRMO Patients?

The prognosis depends on **individual disease course and treatment response**.

- **Some children may require years of treatment**, while others may **eventually discontinue therapy**.
- With **appropriate treatment, quality of life significantly improves**, though **the disease may persist**.
- Regular monitoring is crucial to **adjust treatment and prevent complications**.

Conclusion

Raising **awareness and improving knowledge** about CRMO and **other autoinflammatory diseases** is **essential** for **better diagnosis and treatment outcomes**.

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References

1. CRMO Awareness
2. NOMID Alliance
3. American College of Rheumatology
4. PubMed Study
5. **CARRA Treatment Guidelines for CRMO**