Publisher Correction: Characteristics, Treatment Options, and Outcomes of Chronic Non-Bacterial Osteomyelitis in Children

*Raphaël Kraus**
Ronald M. Laxer

Address

*Hospital for Sick Children, University of Toronto, Toronto, Canada
Email: raphael.kraus@sickkids.ca

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The original version of this article unfortunately contained a mistake in Tables 1 and 2 entries. Some entries of the tables were incorrectly aligned, and the correct presentation of these tables is shown here.

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Table 1. Overview of the molecular pathophysiology of chronic non-bacterial osteomyelitis and related therapeutic considerations

Proposed pathophysiologic mechanism	Associated clinical and translational research evidence	Related therapeutic considerations
Imbalanced cytokine expression	<p>Increased pro-inflammatory cytokines (IL-1, IL-6, IL-20, TNF-α) and decreased immune-regulatory cytokines (IL-10 and IL-19) in CNO patients</p> <p>Stimulation of TLR4 by LPS in monocytes from CNO patients $\rightarrow$ * impaired IL-10 expression and overexpression of IL-6 and TNF-α</p> <p>Reduced activation of the MAPK ERK1 and ERK2 $\rightarrow$ impaired phosphorylation of transcription factor Sp-1 $\rightarrow$ decreased recruitment of Sp-1 to regulatory elements at <i>IL10</i> and <i>IL19</i> promoters $\rightarrow$ under-expression of IL-10 and IL-19</p>	<p>Corticosteroids: reduce expression of NFκB-mediated pro-inflammatory cytokines, including IL-1, IL-6, and TNF-α</p> <p>Anti-TNF-α agents (e.g., ETN, IFX, ADA): abate effects of overexpression of TNF-α</p> <p>Anti-IL-1 agents (e.g., anakinra, canakinumab): abate effects of overexpression of IL-1</p>
Increased inflammasome activation	<p>NLRP3 inflammasome activation $\rightarrow$ production of IL-1β $\rightarrow$ bone inflammation in IL-10-deficient mice</p> <p>Increased NLRP3 and IL-1 mRNA expression in monocytes from CNO patients</p> <p>Inflammasome activity and IL-1β secretion from monocytes from CNO patients reversed by co-culture with recombinant IL-10 or IL-19</p> <p>Familial monogenic disorders associated with CNO (Majeed syndrome [involving <i>LPIN2</i>], DIRA [<i>IL1RN</i>], PAPA [<i>PSTPIP1</i>]) each involve inflammasome activation and increased IL-1</p>	<p>NSAIDs: exert suppressive effect on inflammasomes</p> <p>Anti-IL-1 agents (e.g., anakinra, canakinumab): abate effects of overexpression of IL-1 by inflammasomes</p>
Increased osteoclast activation and differentiation	<p>Imbalanced cytokine expression $\rightarrow$ enhanced interaction between RANK receptor and its soluble ligand RANKL on osteoclasts $\rightarrow$ osteoclast differentiation and activation $\rightarrow$ inflammatory bone loss</p> <p>Mutations in <i>FBLIM1</i> reported in 2 families with CNO; <i>FLBLIM1</i> acts as anti-inflammatory molecule via regulation of RANKL activation</p> <p><i>FBLIM1</i> regulated by STAT3 and STAT3 activated by IL-10; therefore,</p>	<p>Bisphosphonates: inhibit osteoclast activity</p> <p>NSAIDs (via COX enzyme inhibition) and corticosteroids (via phospholipase A1 inhibition) inhibit prostaglandin synthesis, involved in osteoclast activation</p>

Table 1. (Continued)

Proposed pathophysiologic mechanism	Associated clinical and translational research evidence	Related therapeutic considerations
	reduced IL-10 expression → impaired STAT3 activation → altered FBLIM1 expression → osteoclast differentiation and activation	
<p>Table contents modified and extended from (17)</p> <p><i>IL</i> interleukin, <i>CNO</i> chronic non-bacterial osteomyelitis, <i>TLR4</i> toll-like receptor 4, <i>LPS</i> lipopolysaccharide, <i>TNF-α</i> tumor necrosis factor, <i>MAPK</i> mitogen-activated protein kinase, <i>ERK</i> extracellular signal-regulated kinase, <i>Sp</i> signaling protein, <i>NFκB</i> nuclear factor-κB, <i>NLRP3</i> NOD-like receptor family, pyrin domain containing 3, <i>DIRA</i> deficiency of interleukin-1 receptor antagonist, <i>PAPA</i> pyogenic arthritis, pyoderma gangrenosum and acne syndrome, <i>NSAID</i> nonsteroidal anti-inflammatory drugs, <i>RANK</i> receptor activator of nuclear factor-κB, <i>FLBLIM1</i> filamin binding LIM protein 1, <i>STAT3</i> signal transducer and activator of transcription 3, <i>COX</i> cyclooxygenase</p> <p>*→ implies “leads to”</p>		

Table 2. Commonly used treatment options in chronic non-bacterial osteomyelitis in children

Agent	Standard dosage*	Cost†	Toxicity monitoring*	Notable adverse effects*	Special points*
NSAIDs					
Celecoxib (age ≥ 2 years)	10–25 kg: 100 mg/dose twice daily	0.525–42	CBC, AST, ALT, and creatinine prior to initiation and every 6 months during chronic daily use	Gastritis or gastric ulcer	Take with food
Diclofenac	>25 kg: 200 mg/dose twice daily 2–3 mg/kg/day divided 3 times per day, maximum 150 mg/day	9.52		Hepatic or renal toxicity Pseudo-porphyrina	Do not combine with other NSAIDs Avoid in patients with renal dysfunction, thrombocytopenia, liver dysfunction
Ibuprofen	30–40 mg/kg/day divided 3 times per day, maximum 3200 mg/day	0.01–7.76			
Indomethacin	1–3 mg/kg/day divided 2–3 times per day, maximum 200 mg/day	0.33–49.90			
Meloxicam	0.125–0.25 mg/kg/day once daily, maximum 15 mg/day	0.05–34.50			
Naproxen	10–20 mg/kg/day divided 2 times per day, maximum 1000 mg/day	0.13–10.96			
Piroxicam	0.2–0.3 mg/kg/day once daily, maximum 20 mg/day	0.81–15.86			
Glucocorticoids					
Prednisone (or prednisone equivalent) for flare	Maximum 2 mg/kg/day (maximum 60 mg daily) for up to 6 weeks with or without tapering	0.09–110.48	None unless patient has diabetes or hypertension	Weight gain Infection Acne Hirsutism Behavioral change Hypertension Hyperglycemia‡	Take in morning to reduce sleep disturbance Dietary guidance to reduce risk of weight gain
DMARDs					
MTX (PO or SC)	15 mg/m ² /week (maximum 25 mg/week)	18.96–591.61	CBC, AST, ALT, and creatinine prior to initiation, ~1 month after initiation, ~1–2 months after an increase in dose, repeat every 3–4 months	Infection Fatigue Headache Neurologic affects Nausea Vomiting Abdominal pain	SC route may have fewer side effects, better absorption, and improved efficacy at doses >10 mg/m ² Recommend folic acid or leucovorin Avoid live virus vaccinations Consider hepatitis A, B, and C, and varicella screening at baseline Consider TST or IGRA prior to starting Consider hepatitis B screening at baseline
SSZ	50 mg/kg/day up to 3 g/day	0.22–6.00		Hemolytic anemia (G6PD-deficiency)	

Table 2. (Continued)

Agent	Standard dosage*	Cost†	Toxicity monitoring*	Notable adverse effects*	Special points*
TNF-α inhibitors					
ETN	0.8 mg/kg SC weekly or divided twice weekly, maximum 50 mg/week	833.54–1701.11	CBC, AST, ALT, and creatinine prior to initiation, repeat every 13–6 months	SJS DRESS syndrome Injection site reaction (ETN, ADA) Infusion reaction (IFX) Infection (particularly reactivation of latent TB; fungal)	Consider concomitant MTX (may use lower than treatment dosing) TST or IGRA prior to starting, repeat yearly if risk factors present
IFX	5–10 mg/kg IV at 0, 2, and 6 weeks, then every 4–8 weeks	1401.38		Leukocytoclastic vasculitis	Consider screening for histoplasmosis, blastomycosis, coccidioidomycosis in endemic areas
ADA	15–30 kg: 20 mg SC every other week; ≥30 kg: 40 mg SC every other week; May increase to weekly	3334.18–6668.38		Psoriatic rash Demyelinating syndromes (rare) CHF (rare) Other autoimmune diatheses‡	Avoid live virus vaccinations Avoid combinations of biologic agents
Bisphosphonates					
Pamidronate	1 mg/kg/dose monthly (maximum 60 mg); or; 1 mg/kg/dose (maximum 60 mg) for 3 consecutive days every 3 months May use 0.5 mg/kg/dose at the initiation of the treatment Maximum cumulative dose 11.5 mg/kg/year	1.66–70.46	Basic electrolytes, calcium, phosphate, magnesium, and creatinine prior to each monthly infusion or on first day of 3 consecutive infusions	Bone pain Headache Fever Electrolyte abnormalities (particularly hypocalcemia) Osteonecrosis of the jaw (rare; not reported in children) (41)	Continue for minimum of 3 months Daily calcium and vitamin D supplementation Baseline dental evaluation Avoid dental extraction for 4 months following treatment Consider antiemetic as pre-medication Discussion of fetal risk with female patients
Zoledronic acid	0.0125–0.025 mg/kg every 3–6 months (maximum 4 mg/dose) May increase to 0.05 mg/kg/dose	0.57–966.16			
<p><i>NSAID</i> non-steroidal anti-inflammatory drug, <i>CBC</i> complete blood count, <i>AST</i> aspartate aminotransferase, <i>ALT</i> alanine aminotransferase, <i>MTX</i> methotrexate, <i>PO</i> per os, <i>SC</i> subcutaneous, <i>SJS</i> sulfasalazine, <i>G6PD</i> glucose-6 phosphate dehydrogenase, <i>SJS</i> Stevens-Johnson syndrome, <i>DRESS</i> drug reaction with eosinophilia and systemic symptoms, <i>DMARD</i> disease-modifying antirheumatic drug, <i>TST</i> tuberculin skin test, <i>IGRA</i> interferon-γ release assay, <i>TNF</i> tumor necrosis factor, <i>ETN</i> etanercept, <i>TB</i> tuberculosis, <i>CHF</i> congestive heart failure, <i>IFX</i> infliximab, <i>ADA</i> adalimumab</p> <p>* As noted in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) consensus treatment plans (CTPs) for CNO refractory to non-steroidal anti-inflammatory drugs (NSAIDs) and/or with spinal lesions (11)</p> <p>†As reflected by the Average Wholesale Price Per Unit in USD from the Micromedex® RED BOOK® 2019 (53)</p> <p>‡While corticosteroids are associated with many other important adverse effects, we have listed only the most important in the context of treatment duration of a maximum of 6 weeks</p> <p>§Information not reflected in the CARRA CTPs, instead obtained from the Textbook of Pediatric Rheumatology (54)</p>					