Inability to Walk in a Child with Inflammatory Bowel Disease

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An 11-year-old boy was diagnosed with inflammatory bowel disease (IBD), moderate pancolitis, in January 2021 when he presented with bloody diarrhea with failure to thrive. He received oral prednisolone as induction therapy and continued with mesalazine as maintenance therapy. However, due to frequent disease flare ups and ongoing disease activity, his therapy was escalated to infliximab infusion (5mg/kg/dose) at 8 weeks interval which has resulted in the resolution of his gut symptoms. Six months into infliximab initiation , he developed lower back pain, bilateral thigh pain and intermittent difficulties in bearing weight. He reported no fever, joint swelling, or skin rash. The patient was asymptomatic from the gut perspective.

Upon examination, he looked small for age with a weight below the 3rd centile and a height at the 5th centile. He had tenderness over the lower back, bilateral sacroiliac joints, and groin area with normal hip joint movement. He was unable to fully bend his back or bear weight on his legs. His blood tests revealed Hb 10.0 g/dl (reference range 11.4-14), platelet count 800 x10^{9} (reference range 150-450), white cell count 12 x10^{9} (4-12), with a neutrophil count of 7.0x10^{9} (3.5-8), lymphocyte count of 3.0x10^{9}(3-9), albumin 43 g/L (38-54) with normal transaminases and C-reactive protein of 51 (<5) with an ESR of 57 (<9).

He underwent a whole-body MRI [Figure 1].

Informed consent was obtained from the patient's parent.

Questions

1. What is the most likely diagnosis?
2. What are the possible differential diagnoses?
3. How would you manage this boy?

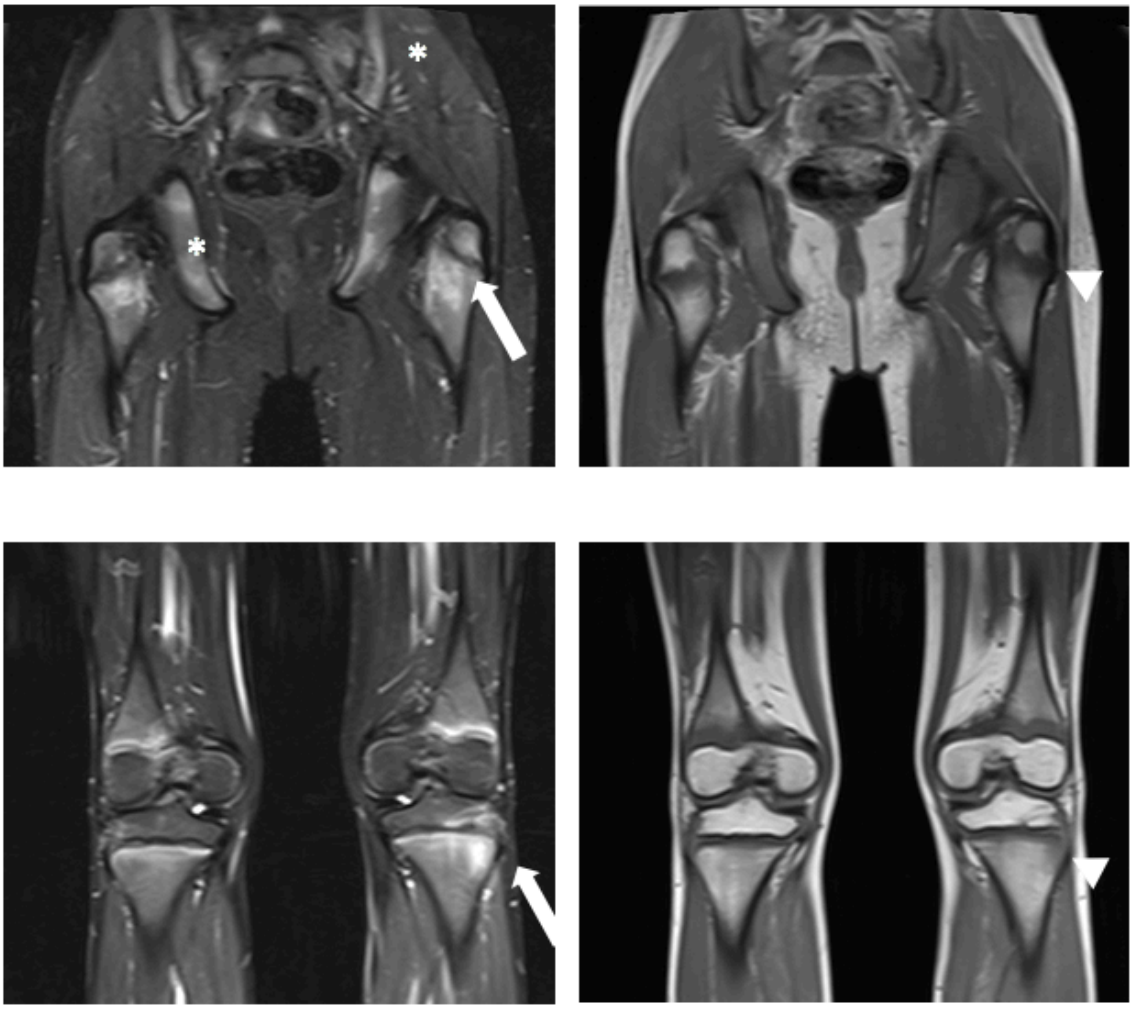

Figure 1: Coronal MRI images of the pelvis/proximal femur, distal femur and proximal tibia. There is edema at the at periphyseal regions of the femur and tibia on short-tau inversion recovery (STIR) images (white arrows). Corresponding low signal changes noted on T1-weighted (T1W) images (arrowheads). Similar asymmetric involvement of the pelvic bones and sacroiliac joints (*). The imaging findings are most concerning for CRMO given the clinical context.

Answers

1. Chronic recurrent multifocal osteomyelitis (CRMO)

2. Infectious osteomyelitis, neoplasms (e.g., leukemia, Ewing sarcoma), Langerhans cell histiocytosis, or other autoimmune/autoinflammatory disorders.

3. Effective control of IBD often leads to an improvement in CRMO symptoms. Treatment options may include oral corticosteroids, methotrexate, sulfasalazine, and tumor necrosis factor-α antagonists.

Discussion

Chronic recurrent multifocal osteomyelitis (CRMO), is one of the extraintestinal manifestation of inflammatory bowel disease (IBD). It is also known as chronic nonbacterial osteomyelitis (CNO), is a rare autoinflammatory bone disorder characterized by recurrent, sterile bone inflammation, primarily affecting the clavicles, pelvis, spine, and long bones.[1-3] It often affects children and adolescents, presenting with a relapsing course of insidious bone pain, localized swelling, and tenderness over the affected areas. The exact etiology remains unknown, but it is believed to involve immune dysregulation. It is proposed that increased release of cytokines from the inflamed gut, such as interleukin-1, interleukin-6, and tumor necrosis factor-α, may modulate bone inflammation in these patients.[4]

CRMO is a diagnosis of exclusion, made after ruling out infectious osteomyelitis, neoplasms like leukemia and langerhans'cell histiocytosis, and other autoimmune/autoinflammatory disorders. The two commonly used diagnostic criteria in pediatric patients are the Bristol and Jansson criteria.[3] These differential diagnoses were ruled out in our patient based on clinical features, and lack of systemic symptoms suggestive of malignancy or infection,

blood tests (including blood cultures), imaging patterns (e.g., multifocal, symmetric lesions on MRI with no abscess or sequestrum formation). Our patient whole-body MRI showed bilateral asymmetric subchondral bone marrow oedema of the sacroiliac joints. The femur shows evidence of peri-physeal oedema on the left side near the greater trochanter and abnormal oedematous changes in the peri-physeal metaphysis of the femur on both sides and similar changes in the proximal tibia bilaterally in keeping with a diagnosis of

Laboratory tests, bone imaging, and bone biopsy are typically required for diagnosis. Radiological findings commonly include one or more osteolytic lesions with sclerotic borders, periosteal reactions, and bone edema. Histopathological findings typically show an inflammatory infiltrate with macrophages, lymphocytes, and plasma cells, along with bone remodeling, fibrosis, and osteoclast-like giant cells, all in the absence of infection. Our patient's parents declined the biopsy and histology examination. While laboratory findings are often normal, elevated inflammatory markers have been observed in some patients.[4]

The treatment for CRMO has not been standardized due to the lack of randomized trials. First-line treatment with NSAIDs is relatively contraindicated in patients with colitis. Treatment options may include oral corticosteroids, methotrexate, sulfasalazine, and tumor necrosis factor-α antagonists. A limited size studies showed that bisphosphonates has substantial disease control.[3,4] Our patient was initially managed with an escalated dose of infliximab at 7.5 mg/kg six weekly and then four weekly. However, over time, he lost response to the treatment and subsequently developed anti-infliximab antibodies. He was then managed with monthly pamidronate infusions, which proved ineffective. Ultimately, he was started on adalimumab, which resulted in the resolution of bone pain and sustained gastrointestinal remission—clinically, biochemically, and histologically.

Paradoxical CRMO refers to the unexpected onset or worsening of CRMO symptoms during treatment with anti-TNFα agents, which are typically used to manage inflammatory conditions, including CRMO itself. It is usually characterized by the emergence or exacerbation of symptoms following the initiation of anti-TNFα therapy, with improvement upon discontinuation of the medication.[5,6] In our patient, paradoxical CRMO is unlikely, as there was no improvement in bone symptoms after stopping the anti-TNFα agent. Although CRMO-related symptoms appeared several months after initiating anti-TNFα therapy, the lack of clinical improvement after withdrawal—along with low infliximab trough levels and the presence of anti-drug antibodies—supports this conclusion

In conclusion, CRMO should be considered in the differential diagnosis for IBD patients presenting with unexplained bone pain, difficulty walking, or abnormal uptake on bone imaging.

Disclosure

The authors declare no conflicts of interest.

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