Case report

Chronic recurrent multifocal osteomyelitis, central retinal artery occlusion and optic neuropathy: A new association

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ABSTRACT

Purpose: To report a patient with chronic recurrent multifocal osteomyelitis (CRMO) complicated by optic neuropathy and central retinal artery occlusion (CRAO).

Observations: CRMO is a noninfectious, inflammatory bone disorder. It is thought to be an autoimmune condition related to an imbalance of pro- and anti-inflammatory cytokines. Retinal vasculitis has been reported in a patient with CRMO but not CRAO or optic neuropathy.

Conclusions: We expanded the list of ophthalmic involvement of CRMO to include CRAO and optic neuropathy.

1. Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare, noninfectious inflammatory disorder, characterized by lytic bone lesions, accompanied by periodic painful exacerbations and remissions. Typically, it is insidious in onset with swelling and tenderness localized over the affected bone. It may occur with or without fever and is a diagnosis of exclusion following bone biopsy. 1–3 There is a single report in the literature of a patient with CRMO who was found to have funduscopic changes consistent with retinal vasculitis. 4 We describe a patient with CRMO and expand the ophthalmic manifestations of this order to include central retinal artery occlusion (CRAO) and optic neuropathy.

2. Case report

A 12-year-old girl developed left-sided lower rib pain. A chest X-ray was normal and she was treated with analgesics. The pain resolved in 1 week. Four months later, the patient spontaneously developed right leg pain without antecedent trauma or illness. An X-ray of her right leg was normal and she was placed in a rigid boot which initially helped, but once out of the boot, the pain returned. This was followed by swelling and a maculopapular, erythematous, nonpruritic rash over her right shin. Magnetic resonance imaging (MRI) showed a stress fracture of the tibia with surrounding inflammation. She was given crutches and instructed to avoid weight bearing.

Two months later, the patient experienced pain in the left medial shin and right wrist. The shin pain worsened to the point where she could not walk. Noncontrast MRI of her left tibia revealed edema in the distal quarter of the tibia without evidence of fracture. She soon
reported pain in her right mid-lower shin and the ulnar side of her right distal forearm. At the same time, she developed episodes of fever up to 103° Fahrenheit lasting 24–48 hours and a rash on her legs and abdomen.

The patient was hospitalized and multiple X-rays of her upper and lower extremities showed a periosteal reaction around the distal portion of the left tibia and right fibula as well as the right distal ulna. There was no evidence of fracture. Laboratory testing revealed a white blood cell count of 14,800 cells/mm³ (normal: 4500–13,500 cells/mm³) with normal differential, hemoglobin of 11.9 g/dL (normal: 12.0–15.0 g/dL), hematocrit of 35.7% (normal: 35–49%), platelet count of 514,000/mm³ (normal: 150,000–450,000/mm³), positive antinuclear antibodies (ANA) (1:160, speckled pattern), elevated Westergren sedimentation rate (ESR) of 51 mm/hr (normal <10 mm/hr), and elevated C-reactive protein (CRP) of 5.0 mg/dL (normal < 1.0 mg/dL). The patient was treated with nonsteroidal anti-inflammatory drugs, primarily naproxen. Repeat CRP was within normal limits, the repeat ESR was 34 mm/hr, and white blood cell count was 6.8 k/mm³. Tuberculin skin test was negative. Alpha-fetoprotein and human chorionic gonadotropin were negative: aquaporin-4-IgG, myelin oligodendrocyte glycoprotein (MOG)-IgG, angiotensin-converting enzyme, Bartonella antibody, Lyme titers, FTA-Abs, p-ANCA, c-ANCA, angiotensin-converting enzyme, lysosome, aquaporin-4-IgG and again MOG-IgG, and hematologic profile has been developed in which IL-10-deficient mice develop in a model has been developed in which IL-10-deficient mice develop in inflammatory bone loss and synovial inflammation.

Chronic non-bacterial osteomyelitis is an autoinflammatory bone disorder. Its more severe form is CRMO which generally affects female children and adolescents with peak onset between 7 and 12 years of age. The incidence is approximately 1:1,000,000 or 2–5% of all osteomyelitis cases. Chronic non-bacterial osteomyelitis is characterized by recurrent attacks of bone inflammation which, at times, leads to bone destruction. This inflammation is associated with pain and often fever and frequently involved bony sites include long bones, the pelvis, vertebral column and the shoulder. Skin involvement in CRMO is not uncommon, as in our patient. Establishing the diagnosis of CRMO often is difficult and requires exclusion of infectious, neoplastic and other inflammatory causes of a bone disorder. The Bristol criteria for CRMO includes bone pain and lytic lesions, sclerosis and new bone formation on plain X-ray or preferably MRI showing bone marrow edema and or bone expansion, lytic areas and periosteal reaction. Also, laboratory testing is without significantly raised CRP. Our patient fulfilled this criteria of CRMO.

The pathology of CRMO is not well understood but appears to be a combination of various genetic risk alleles and environmental factors. It is thought that this leads to an imbalance of pro- and anti-inflammatory cytokines, in particular the interleukins. An animal model has been developed in which IL-10-deficient mice develop inflammatory bone loss and synovial inflammation.

We are aware of only one other report of a patient with CRMO who experienced ophthalmic involvement. A 37-year-old woman with CRMO complained of a visual disturbance in her left eye. She was found to have a cotton-wool spot in her left fundus and fluorescein angiography demonstrated retinal vascular staining in both eyes. These findings were consistent with retinal vasculitis.

Our patient had an extensive evaluation to exclude other disorders that also may be associated with CRAO and optic neuropathy. Etiologies excluded were autoimmune (sarcoidosis, Behçet), hematologic (plasma cell dyscrasia), neoplastic (sarcoma) and infectious (tuberculosis, syphillis). During the initial episode of visual loss, the patient had enhancement of the left optic nerve despite no evidence of optic neuropathy in the left eye. At another point in time, our patient experienced several months of stable 20/20 vision despite having bilateral optic disc atrophy.
edema and enhancement on MRI and normal lumbar puncture. This suggests that there may be a subclinical inflammatory phase prior to vision loss.

Patients with vasculitis-induced optic neuropathy have been reported to have extensive optic nerve and chiasm enhancement on MRI, similar to inflammatory or demyelinating optic neuropathies. High in the differential diagnosis of the recurrent bilateral optic neuropathy with optic nerve enhancement on MRI is neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein associated disease (MOGAD). Our patient had been tested for the aquaporin-4-IgG and MOG-IgG in blood and CSF, both of which were negative. The patient’s optic nerve enhancement involving the full length of the optic nerve on MRI is similar to patients with MOGAD. Thus, it might be useful to include CRMO in the differential diagnosis of NMOSD and MOGAD.

In conclusion, we have expanded the spectrum of ophthalmic complications of CRMO to include CRAO and optic neuropathy. While this bone disorder is rare, it behooves clinicians caring for these patients to be attuned to any visual complaints.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None.

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References

1. Gicchino MF, Diplomatico M, Granato C, et al. Chronic recurrent multifocal osteomyelitis: a case report. Ital J Pediatr. 2018;44(1):26.
2. Buch K, Thaesen ACB, Brons C, Schwarz P. Chronic non-bacterial osteomyelitis: a review. Calcif Tissue Int. 2019;104(5):544-553.
3. Roderick MR, Sen ES, Ramanan AV. Chronic recurrent multifocal osteomyelitis in children and adults: current understanding and areas for development. Rheumatology. 2018;57(1):41-48.
4. Shanmugam VK, Philipotts M, Brady T, et al. Retinal vasculitis with chronic recurrent multifocal osteomyelitis: a case report and review of the literature. BMC Rheumatol. 2019;3:29.
5. Hofmann SR, Kapplusch F, Girschick HJ, et al. Chronic recurrent multifocal osteomyelitis (CRMO): presentation, pathogenesis, and treatment. Curr Osteoporos Rep. 2017;15(6):542-554.
6. Nepal P, Alam SI, Sajid S, Sapire J, Ojjii V. Rare presentation of chronic recurrent multifocal osteomyelitis of the Iliac wing mimicking Ewing’s sarcoma. SA J Radiol. 2021;25(1):2030.
7. Sklar EM, Schatz NJ, Glaser JS, Post MJ, ten Hove M. MR of vasculitis-induced optic neuropathy. AJNR Am J Neuroradiol. 1996;17(1):121-128.
8. Siatkowski RM, Scott IU, Verm AM, et al. Optic neuropathy and chiasmopathy in the diagnosis of systemic lupus erythematos. J Neurol Ophthalmol. 2001;21(3):193-198.
9. Prasad S, Chen J. What you need to know about AQP4, MOG, and NMO. Semin Neurol. 2019;39(6):718-731.