A case of Reiter’s disease exacerbated by lithium

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Abstract
Reiter’s disease is characterized by the triad of peripheral arthritis, urethritis, and conjunctivitis. A 38-year-old male, who was on treatment with lithium for mania, presented to us with all features of this triad. He was previously diagnosed and treated as seronegative arthritis. However, his symptoms persisted despite therapy. His skin lesions regressed only once lithium was stopped. Lithium is known to exacerbate or precipitate a multitude of dermatological conditions. However, there is no previous reported association of lithium exacerbating preexisting Reiter’s disease. We report this case as it is the first known association of its kind.

Key words: Arthritis, lithium, Reiter’s disease

INTRODUCTION
Reiter’s disease is defined as an episode of peripheral arthritis of more than 1 month duration, occurring in association with urethritis and/or cervicitis. Its defining feature is initiation by infection, usually in the genitourinary or gastrointestinal tract.[1]

The efficacy of lithium in mania has revolutionized the treatment of bipolar disorders.[2] The lithium intake has been implicated with a number of cutaneous adverse effects; however, the exacerbation or precipitation of Reiter’s disease in particular has not been mentioned in previous case reports.

We report a case of lithium-exacerbated Reiter’s disease hitherto unreported.

CASE REPORT
A 38-year-old male presented with discharge and ulcer over genitals since 1.5 years, pain over the knee joint and small joints of the hands, blurring of vision, pain and discharge from both eyes, and pain over the soles of the feet. He was diagnosed with mania 1 year after the onset of these symptoms and started on oral lithium. Four months after therapy, he developed multiple reddish raised lesions over the face, hands, and legs.

On examination, he had crusted, psoriasiform lesions over the face, legs, chest, and back [Figure 1]. Thick yellowish scales were present over the scalp. Nails showed subungual hyperkeratosis. He also had bilateral conjunctival congestion and balanoposthitis over the glans with subprepuccial discharge [Figure 2].

Investigations revealed a total leukocyte count of 20,600/cm²; erythrocyte sedimentation rate (ESR) was 120 mm (first hour) and C reactive protein (CRP) level was 50.7 mg/l. HLA-B27 was found to be positive. Rheumatoid factor, anti-streptolysin O, anti-nuclear antibody, HIV, hepatitis B surface antigen, and serological test for syphilis were negative. Serum lithium levels showed a normal value of 0.25 meq/l. An X-ray of the pelvis showed evidence of right-sided sacroilitis. Skin biopsy showed a large macropustule, with features of psoriasiform dermatitis [Figure 3].

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Lithium was stopped immediately on admission and replaced by olanzepine and lorazepam. Two weeks after admission, he was started on oral methotrexate 7.5 mg weekly, increased to 20 mg/week; sulfasalazine 500 mg twice daily, oral prednisolone 20 mg/day, analgesics, and topical beclomethasone dipropionate were also administered. Improvement was seen 6 weeks after starting treatment. Considering the severity of disease and the ethical implications, a reintroduction of lithium was not considered. On discharge, his skin lesions had completely regressed; however, the arthritis persisted. Treatment was continued for a period of 4 months. On follow-up visit, repeat blood investigations showed a decrease in the total count and ESR (38 mm in the first hour).

DISCUSSION

Reactive arthritis is characterized by nonspecific arthritis, aseptic urethritis, and conjunctivitis or uveitis. A number of studies have reported an association between Reiter’s disease and polymorphism of HLA B27. Associations with HLA-B7, -Bw60, -B39 and recently -B-51 have been reported. Management includes aspirin or other nonsteroidal anti-inflammatory drugs for arthritis, topical salicylic acid and steroids for cutaneous lesions, and antibiotics for urethritis depending on culture results.

Lithium which is FDA approved for the treatment of acute mania and bipolar illness was first discovered by Johan August Arfvedson in 1817, and the reported prevalence of cutaneous adverse effects varies from 3.4% to 45%. Most of the cutaneous adverse effects occur at therapeutic serum levels, which is in contrast with acute lithium toxicity. Most side effects encountered with lithium are not sufficiently severe to warrant discontinuation of therapy; nevertheless, some acute reactions and some chronic adverse cutaneous effects which are resistant to treatment do necessitate discontinuation. Lithium has been implicated in the exacerbation or precipitation of preexisting skin disorders and also in the induction of dermatoses de novo. However, there is no reported case in the literature till date of lithium exacerbating preexisting reactive arthritis.

Lithium is known to cause an increase in the total circulating neutrophil mass and also accelerates neutrophil production and allows unimpeded neutrophil migration into skin lesions. The mechanisms of lithium-induced neutrophilia are proposed to be due to the inhibition of adenyl cyclase, glycogen synthase kinase-3, decreased myoinositol turnover, and inhibition of sodium channels. These in turn decrease the cAMP-mediated process which may promote epidermal proliferation as well as leucocytoclastic activities resulting in a psoriasiform dermatitis. Reiter’s disease is considered neutrophilic dermatosis, and increased...
neutrophil chemotaxis has been shown in patients with reactive arthritis.\textsuperscript{[13]} Hence, it is logical to conclude that lithium administration can exacerbate reactive arthritis.

Our patient presented with conjunctivitis, urethritis, arthritis, enthesitis, and sacroilitis. He was diagnosed with seronegative arthritis previously and treated with systemic steroids and analgesics without much improvement. His skin lesions and urethritis completely regressed only once lithium was stopped. We report this case due to its rare occurrence and since there is no such previous reported association in the literature.

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