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LETTER TO THE EDITOR

# Reactivation of inflammatory monoarthritis during dupilumab treatment used for prurigo nodularis

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Dupilumab is a humanized monoclonal antibody which specifically targets interleukin-4/interleukin-13 receptor and is primarily indicated for the treatment of atopic dermatitis, although it has been shown to be efficacious in various disorders including asthma, chronic rhinosinusitis, prurigo nodularis.[1] Herein, we report an extraordinary case related to the exacerbation of inflammatory arthritis in a patient under dupilumab treatment for prurigo nodularis.

An 18-year-old woman with a history of allergic rhinitis and atopic dermatitis, presented for her pruritic lesions. The pruritic nodules started from the lumbar area nine years ago and subsequently spread to entire body. Topical corticosteroids, oral antihistamines, systemic corticosteroids, and methotrexate were prescribed with no long-term benefits. Dermatological examination revealed hyperkeratotic plaques involving the trunk and extremities. Histopathological evaluation of the lesions was compatible with the diagnosis of prurigo nodularis. She was started on oral cyclosporine 200 mg for seven months; however, within the last month of cyclosporine treatment, her complaints increased, leading us to switch to dupilumab. Although her clinical manifestations and pruritus improved, she developed mild right knee swelling, warmness, and arthralgia after the first maintenance dose following the loading dose. Upon questioning, we recognized that the patient developed reactive arthritis in the right knee, when she was 10 years old. Until now, she stayed asymptomatic. She was consulted to rheumatology department and effusion was detected by right knee ultrasonography and arthrocentesis was performed which revealed no bacterial growth. Elevated C-reactive protein and erythrocyte sedimentation levels were noted. Rheumatological markers were all negative. Right knee magnetic resonance imaging showed moderate effusion along with synovial proliferation consistent with synovitis; no periarticular erosion, osteitis or ligamentous anomaly were detected (Figure 1). She was diagnosed with dupilumab-induced exacerbation of inflammatory arthritis and was started on oral diclofenac and intraarticular steroid injection which resulted in symptomatic relief. Therefore, dupilumab treatment was continued.

Dupilumab is the first biological agent approved for the treatment of refractory

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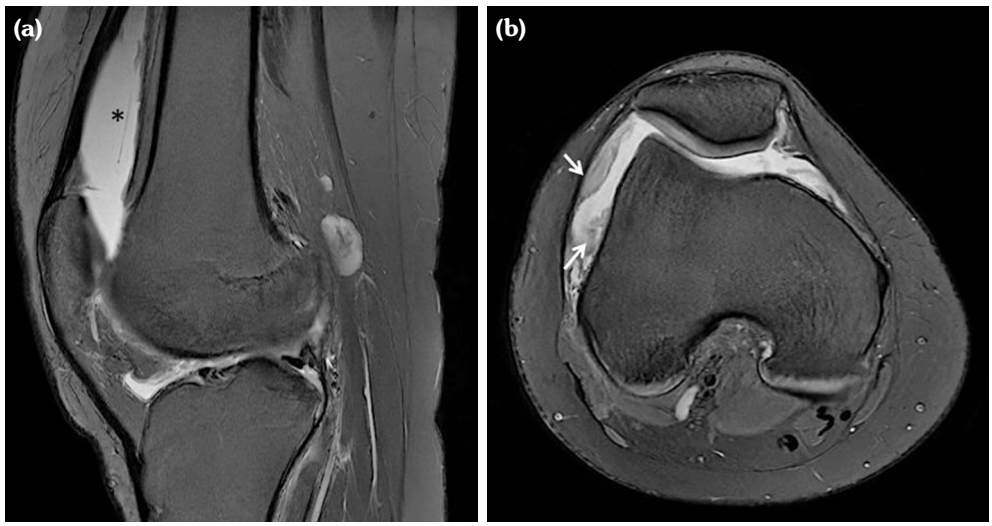


**Figure 1.** A **(a)** sagittal and **(b)** axial proton-density weighted image with fat-saturation showing moderate effusion (asterisk) and synovial proliferation (arrows) compatible with synovitis. No evidence for osteitis or periarticular erosion. Also note the reactive enlarged lymph node in popliteal fossa.

atopic dermatitis. Similar to the other biological agents, dupilumab is reported to have various side effects.[2] Most commonly reported side effect was conjunctivitis, followed by headache, muscle/joint pain, and injection site reactions.[2] Inflammatory arthritis is an underrecognized complication of dupilumab. De Wijs et al.[3] reported a case of acute inflammatory polyarthritis observed in an atopic dermatitis patient after one month of dupilumab therapy. Willsmore et al.[4] described a possible relationship between new-onset seronegative arthropathy, enthesitis, and dupilumab. The pathogenesis of dupilumab-induced arthritis is unknown; however, the blockage of interleukin-4 and interleukin-13 may increase the levels of inflammatory cytokines such as tumor necrosis factor alpha and interleukin-6.[5] Furthermore, inhibition of T helper (Th)2 pathway, may potentially cause compensatory activation in Th17 pathway which is related to peripheral spondyloarthritis and inflammatory arthritis.[4]

In conclusion, we emphasize the fact that exacerbation in inflammatory arthritis can be encountered during dupilumab treatment. Dermatologists should be aware of this rare side effect of dupilumab and an urgent rheumatological consultation must be sought for proper diagnosis and treatment.

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