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Multifocal Myositis and Elevated CPK associated with the use of Ustekinumab for Hidradenitis Suppurativa

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Dear Editor, ustekinumab (UST) is a human interleukin (IL)-12/IL-23 monoclonal antibody that has been approved by the Food and Drug Administration (FDA) to treat moderate to severe plaque psoriasis, psoriatic arthritis, and Crohn's disease. Off-label use of UST has shown promising results for hidradenitis suppurativa (HS) in patients that have failed therapy with adalimumab, the only FDA approved treatment for HS.[1] Common adverse reactions of UST include headache, fatigue, and upper respiratory tract infections and are generally mild.[1] We report a patient with poorly controlled HS who experienced new onset myositis during treatment with UST.

Our patient was a 49-year-old female with a three-year history of Hurley Stage III HS and a past medical history which included metabolic syndrome and class I obesity. She had no prior personal or family history of autoimmune disorders. Moderate improvement of HS was seen with adalimumab and infliximab, however, both were discontinued due to complications from polymicrobial, multidrug resistant infections. Despite promising results after three rounds of CO_2 laser excision and surgical deroofing, she continued to have an average of one to two acute HS flares per month. To further maintain and stabilize flares between CO_2 laser therapy sessions, subcutaneous UST was initiated at a standard dose of 90 mg administered at weeks 0, 4, and 12. The patient initially tolerated UST and noticed a reduction in frequency of HS flares, but shortly after the third injection, the patient reported significant functional limitation due to palmar erythema, myalgia, swelling of the proximal

extremities, and generalized muscle weakness. An electromyography (EMG) was abnormal, demonstrating low amplitude and short duration motor units with normal recruitment in the bilateral bicep muscles and longer duration motor units in the extensor carpi radialis and lateral gastrocnemius muscles. There was no evidence of muscle membrane irritablility, making an underlying inflammatory condition unlikely. These findings along with an elevated creatine phosphokinase (CPK) three times the normal limit were consistent with a mild, non-irritable drug-associated myositis. The timing to onset of symptoms was 2 days after the third (12th week) injection. Upon discontinuation of UST, CPK levels normalized with resolution of symptoms 12 weeks from symptom(s) onset.

This case demonstrates the unexpected development of multifocal myositis associated with the use of UST in an HS patient. Drug-induced myositis (DIM) is defined as muscle damage, and/or muscle breakdown due to direct myotoxicity, indirect damage, or an immunologically induced inflammatory reaction.[2] Manifestations of DIM include myalgias, generalized symmetrical weakness, and proximal muscle soreness.[2] Diagnosis is based on the clinical examination and diagnostic tests such as CPK levels, autoantibodies, EMG, and muscle biopsies. Symptoms are typically temporary and reversed by drug discontinuation. The clinical resolution of symptoms after discontinuation of UST therapy, with no evidence of muscle membrane irritability per EMG findings, in addition to a negative family and personal history of autoimmune disorders does not support the diagnoses of inflammatory and/or autoimmune myopathies.

According to Eudraviligance, there has been 9 previously reported cases of UST associated myositis.[3] The FDA adverse event reporting system, MedWatch, has 14 documented cases of UST associated myositis since 2012, including 3 that were disabiling and 4 that led to hospitalization.[4] Naranjo's algorithm score supports a probable adverse drug reaction given the previous reports of this occurance in pharmacovigilance databases, the temporal sequence of events, and having no other reasonable explanation of this event from our patient's clinical history and characteristics. Concomitant medications in this patient included metformin, colchicine, spironolactone, and zinc. Of those medications, colchicine has been previously associated with myopathy, although this presentation is

usually slow and painless after prolonged treatment. Our patient was taking 0.6 mg of colchine daily for the past two years and continued taking colchicine during this episode of myositis. Colchicine myopathy risk is increased with concominant use of CYP3A4 inhibitors, including macrolide antibiotics, cyclosporine, -azoles, and protease inhibitors.[5] Chronic kidney disease (CKD) is a major predisposing risk factor, leading to plasma colchicine toxicity. Our patient denied a history of CKD at onset of DIM related symptoms.[5]

UST associated myositis is rarely reported outside of pharmacoviligiance databases and has not been previously reported during off-label use for HS. Given the growing use of UST for the management of refractory HS, it is important for clinicians to consider the potential adverse effect of myositis. Further research is needed to evaluate the pathophysiology and prevalence of UST associated myositis.

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