Psoriasis Treatment in Patients With Sickle Cell Disease

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PRACTICE **POINTS**

- Tumor necrosis factor α contributes both to the vascular inflammatory state seen in sickle cell disease as well as the cycle of inflammation seen in the development of psoriasis.
- Tumor necrosis factor α inhibitors may be the drug of choice for patients with both psoriasis and sickle cell disease.

Plaque psoriasis is a chronic inflammatory disease driven by the proliferation of T cells and the production of several immunomodulators such as tumor necrosis factor (TNF) α. Tumor necrosis factor α plays a key role in multiple inflammatory conditions, including psoriatic arthritis, rheumatoid arthritis, and hidradenitis suppurativa. We present a patient with plaque psoriasis and sickle cell disease who began treatment with the TNF-α inhibitor adalimumab. With this treatment, the patient had improvement in both psoriasis and sickle cell disease symptoms. Tumor necrosis factor α inhibitors may be the drug of choice in patients with both psoriasis and sickle cell disease.

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Plaque psoriasis is a chronic inflammatory disease with a complex pathogenesis. Cutaneous dendritic cells drive the activation and proliferation of T cells with production of several immunomodulators, such as tumor necrosis factor (TNF) α, IL-17, IL-12, and IL-23. Because multiple systemic therapies are efficacious, treatment selection depends on side-effect profiles, availability, and patient preference. Activation of the TNF-α pathway is not unique to psoriasis. Tumor necrosis factor α plays a key role in multiple inflammatory conditions, including psoriatic arthritis, rheumatoid arthritis, and hidradenitis suppurativa. One study in mice demonstrated that TNF-α drives endothelial and vascular wall dysfunction in sickle cell anemia. In this study, use of the TNF-α blocker etanercept in mice with homozygous sickle cell anemia (HbSS) disease resulted in amelioration of TNF-mediated clinical features shared by sickle mice and humans.[1]

Sickle cell anemia is caused by a structural defect in hemoglobin that results in hemolysis and chronic anemia. The most common type of hemoglobin in adults without sickle cell anemia is HbAA. Homozygous sickle cell anemia patients carry 2 abnormal S alleles, whereas in sickle cell trait, patients carry both the S and normal A alleles (HbSA). Hemoglobin C is a structural variant of HbA that results in lower solubility in red blood cells. Patients with hemoglobin SC disease (HbSC) have S and C alleles.[2] We present a case of a patient with moderate to severe plaque psoriasis and heterozygous sickle cell anemia treated with adalimumab.

Case Report

A 31-year-old woman presented with moderate to severe plaque psoriasis (70% body surface area) and HbSC. She reported chronic dull arthralgia in the ankles that was worse at night. Radiographs of the feet and ankles showed erosive changes of the distal tarsal row and metatarsal bases. The diffuse bone pain had gradually worsened over the years and was treated by hematology with ibuprofen and ketorolac. At presentation, her HbSC pain was 8/10 on a visual analog scale. She described her sickle cell pain crises as sharp 10/10 pain in the back, elbows, and ankles, associated with mild edema lasting

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1 to 2 days. Radiographs of the spine, hands, and ankles were unremarkable.

Adalimumab was chosen as a systemic therapy for psoriasis based on the potential for improvement in HbSC. Within 17 weeks of starting adalimumab, the psoriasis body surface area decreased from 70% to 40%, and the HbSC pain decreased from 8/10 to 4/10 at 8-week follow-up and to 0/10 at 17-week follow-up. After initiation of adalimumab, she reported decreased use of pain medication with no sickle cell pain crises.

Comment

Tumor necrosis factor α blockers are commonly used for moderate to severe plaque psoriasis. To our knowledge, there have been no reported human studies showing TNF-α blockade as a potential treatment of sickle cell disease. Increased levels of TNF-α have been shown to contribute to the onset of sickle cell crises and severity of sickle cell disease by playing an integral role in the development of vascular wall dysfunction and ischemia.[3] Inflammatory mediators in HbSS disease, such as heparan sulfate from the endothelial glycocalyx and heme from hemolysis, act on monocytes to release TNF-α.[1] Through this effect on the endothelium, TNF-α impedes blood flow during sickle cell crisis, leading to worsening ischemia and resultant painful infarction.[3] Analysis of cytokine levels in HbSS patients showed significantly ($P<.05$) elevated levels of TNF-α during sickle cell crises and at baseline in comparison to nondiseased controls (HbAA), indicating a possible role of TNF-α in the pathogenesis of the crisis state.[3] These studies suggest that TNF-α inhibition may reduce the initiation of vaso-occlusive crisis and decrease the subsequent ischemia related to a sickle cell crisis.

Although these findings were observational and limited to a single patient, the 50% decrease in pain level and use of pain medications reported to her hematologist independent of her dermatology visits coincided with the initiation of adalimumab. Although radiographs showed possible psoriatic changes of the distal metatarsal row, her described sickle cell pain and pain crises were atypical for psoriatic arthralgia. Tumor necrosis factor α inhibitors could be the drug of choice to treat patients with psoriasis with concomitant HbSS or HbSC disease due to the blockade of a common inflammatory mediator. Further studies are indicated to analyze the in vivo role of TNF-α inhibition in sickle cell disease.

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