Thalamic stroke in a young adult with severe psoriasis refractory to adalimumab

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INTRODUCTION

Recent cohort studies and meta-analyses suggest that psoriasis is an independent risk factor for stroke.[1,2] Tumor necrosis factor-alfa (TNF-α) antagonists such as infliximab, adalimumab, and etanercept are effective biological agents in the treatment of moderate-to-severe psoriasis.[3] The role of these agents in preventing cardiovascular complications and stroke in patients with psoriasis is less understood. Here we describe the case of a young man with severe psoriasis refractory to adalimumab, presenting with thalamic stroke.

Abbreviations used:

CRP:	c-reactive protein
Hs:	high sensitivity
TNF-α:	tumor necrosis factor-alfa

CASE REPORT

The patient is a 40-year-old man with history of plaque psoriasis and psoriatic arthritis for 12 years refractory to conventional immunomodulatory therapy, including methotrexate and etanercept. Twenty months before the current presentation, he was started on a 40-mg biweekly dose of adalimumab and a 10-mg daily dose of prednisone. Although the symptoms were better controlled with adalimumab, the disease course was complicated by 3 flares last year. The adalimumab dose was increased to 40 mg weekly 6 months ago. In addition, he was being considered for intravenous infliximab treatment. Before treatment and during relapse, involved body surface area was 20%. Psoriasis Area and Severity Index was 18, and during remission the Psoriasis Area and Severity Index was 5. Cellulitis developed on his right elbow, and adalimumab was stopped temporarily. Two weeks later, he presented with a 3-day history of progressive right-sided weakness, numbness, and slurring of speech. The clinical presentation was characterized by psoriatic skin lesions on his trunk and lower limbs (Fig 1) accompanied by arthralgia and swelling of the metacarpophalangeal joints of both hands.

On neurologic examination, the patient had complete right hemiparesis, right-sided upper motor neuron facial palsy, and right-sided hemianesthesia with impaired touch and pain sensation. Vital signs, complete blood counts, and basic metabolic panel results were normal; his body mass index was 22.5. A computed tomography scan of the head was not revealing, and contrast-enhanced magnetic resonance imaging showed an infarct in the left thalamus and perithalamic white matter (Fig 2).

Because stroke is uncommon in this age group, he was evaluated for thrombotic disorders, autoimmune vasculitis, and structural heart disease. Coagulation profile, including prothrombin time, partial thromboplastin time, thrombin time, and fibrinogen levels, was normal. Factor V Leiden phenotype was absent. The autoimmune markers antinuclear antibody, c—antineutrophilic cytoplasmic antibody, p—antineutrophilic cytoplasmic antibody, anticyclic citrullinated peptide, and lupus anticoagulant were negative. Echocardiogram with bubble study excluded thrombus and intracardiac shunts and carotid Doppler excluded atheromas. Serum high-sensitivity (hs)—C-reactive protein (CRP) level was chronically elevated and did not show evidence for acute exacerbation of systemic inflammation (Fig 3).

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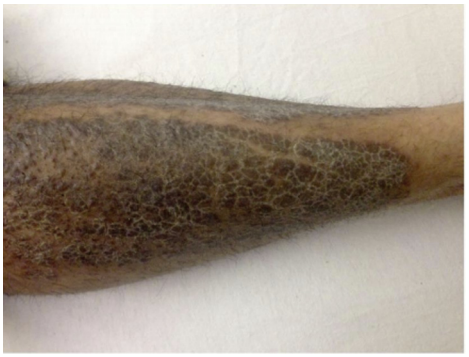

Fig 1. Psoriatic skin lesions observed on patient's right lower limb.

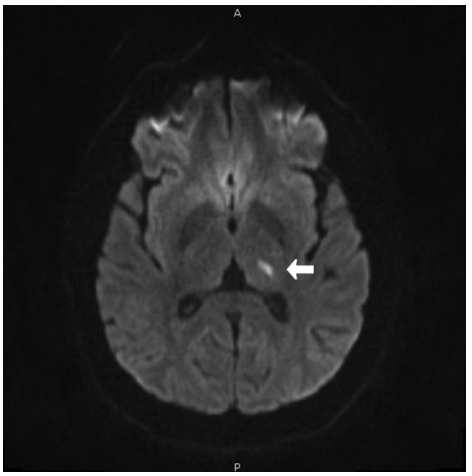

Fig 2. Diffusion-weighted magnetic resonance imaging of the brain shows lacunar infarct in the left thalamus (*arrow*).

Tissue plasminogen activator was not administered, as the patient was out of the 3- to 4.5-hour window. Consequently, he was conservatively treated with aspirin, Plavix, and physical therapy. He recovered rapidly and by day 8 of hospitalization, both motor and sensory signs were resolved without any residual impairment.

DISCUSSION

Thalamic stroke in this patient is consistent with occlusion in the inferolateral artery affecting the venteroposterolateral and venteroposteromedial nuclei of the thalamus.[4] The major risk factors for thalamic stroke are hypertension, atherosclerosis, embolism, and vasculitis. Based on the clinical presentation, radiologic evidence, and chronic elevation of hs-CRP, we believe that the cause of stroke was likely thrombosis of the inferolateral artery caused by progressive vascular inflammation. From earlier studies, it is clear that psoriasis is a systemic inflammation that could lead to increased

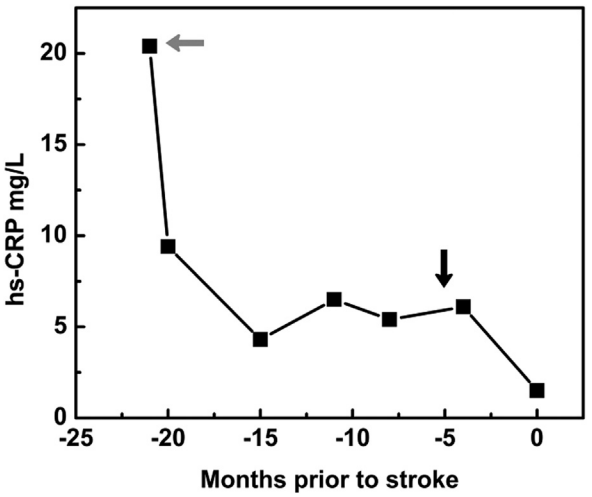

Fig 3. Trend in hs-CRP level. *Grey arrow* points to the initiation of adalimumab treatment. The *black arrow* represents the point at which the dose was doubled.

predisposition for atherosclerosis and metabolic syndrome.[5] Additional risk factors for stroke gradually developed in this patient during the disease course. Hypertension was diagnosed 5 years ago and diabetes mellitus 2 years ago. It is important to note, however, that his hypertension and diabetes (hemoglobin A1C, 7.2%) were well controlled with medical therapy and lifestyle modifications.

Adalimumab is a potent anti-inflammatory agent that inhibits the inflammatory mediator TNF-α, which is implicated in the pathogenesis of psoriasis. Therefore, it is important to understand the role of TNF-α inhibitors in preventing serious systemic complications of psoriasis including myocardial infarction and stroke. This subject has been extensively reviewed by Nguyen et al.[6] Overall, studies found mixed results: certain studies found that TNF-α inhibitor therapy lowered cardiovascular complications and death, and others found no effect compared with placebo or methotrexate.[6] TNF inhibitor therapy has also been found to reduce inflammatory markers such as CRP, and increase high-density lipoprotein. The probable mechanism for reducing cardiovascular risk is improving endothelial function and preventing plaque rupture. In contrast, biological therapy with anti—interleukin-2/23 agents (ustekinumab and briakinumab) has resulted in increased cardiovascular adverse events, although the study may not be powered to make strong conclusions. In this patient, treatment with adalimumab resulted in significant reduction in the level of hs-CRP, a major biomarker of systemic inflammation (Fig 3). However, such a reduction was not enough to prevent stroke. It is

important to note that the level of hs-CRP reduction attained would still categorize him as having moderate risk (10%–20%) for coronary heart disease in the next 10 years based on Centers for Disease Control and Prevention/American Heart Association guidelines.[7] There are no specific guidelines for stroke prevention or a target inflammatory biomarker level to reduce cardiovascular risk factors in this patient population, and it is not clear whether more aggressive treatment would have altered the progression of psoriasis-related complications in our patient. Along with clinical remission, targeting hs-CRP levels based on Centers for Disease Control and Prevention/American Heart Association guidelines to reduce cardiovascular risk factors would be an interesting hypothesis to test. We anticipate that it would be an important area of investigation for the future, and this case report further emphasizes the need for such research.

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