Combined biologic therapy for the treatment of psoriasis and psoriatic arthritis: A case report

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Psoriasis has both cutaneous and systemic manifestations. Psoriatic pathogenesis is driven by chronic, immune-mediated inflammation.[1,2] Multiple cormorbidities of psoriasis, such as obesity, diabetes, hypertension, and dyslipidemia predispose to cardiovascular disease. Furthermore, psoriasis alone may represent an independent cardiovascular risk factor.[3]

Biologic therapies specifically targeting inflammatory pathways have emerged in the management of psoriasis. Given the role of chronic inflammation in both psoriasis and cardiovascular disease, the impact of these therapeutic agents on cardiovascular risk has been of research interest. To date, the data suggest an overall reduction in risk for cardiovascular events with tumor necrosis factor—alpha inhibitors and a neutral effect for ustekinumab, an IL-12/23 inhibitor.[1,4,5] Fewer data exist to corroborate the relationship between ustekinumab and cardiovascular risk, and concern still exists for an increased susceptibility to major adverse cardiovascular events.[1,6-8] There are limited data guiding the combination of biologic agents in the management of psoriasis and psoriatic arthritis.

CASE REPORT

We present a 62-year-old man with the metabolic syndrome: obesity (body mass index, 47), type 2 diabetes mellitus, hypertension, and hypercholesterolemia and a 15-year history of severe plaque psoriasis and psoriatic arthritis involving the distal and axial skeleton. The patient did not respond to several prior treatments including topical corticosteroids, narrow-band ultraviolet B phototherapy, cyclosporine, infliximab, and adalimumab. He began taking etanercept, 50 mg once weekly, combined with methotrexate administered as a 25-mg subcutaneous weekly dose. Significant clearance of psoriasis and the diminution of arthritis ensued. However, lack of affordability necessitated a switch from subcutaneous to oral methotrexate taken at 20 mg weekly. This formulation change resulted in increased gastrointestinal intolerability and a significant return of psoriasis. He was instructed to discontinue use of both etanercept and oral methotrexate, and ustekinumab, 90 mg, was administered subcutaneously at weeks 0 and 4. The psoriasis rapidly cleared, yet the arthritic and enthesopathic symptoms returned. Unbeknownst to the treating practitioner, the patient restarted etanercept, 50 mg weekly, for approximately 4 weeks before his next office visit. At that visit, the patient displayed completely clear skin and had no symptoms of psoriatic arthritis. The patient stated that he never felt better and insisted on maintaining the 2-biologic regimen, which was guardedly permitted by the physician and covered by his insurance plan.

Approximately 5 months after initiation of the combined regimen, the patient experienced unstable angina. The patient had no previous history of coronary artery disease but had several risk factors including metabolic syndrome and a paternal family

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history of cardiovascular disease. He underwent percutaneous coronary intervention with placement of drug-eluting stents. Additionally, dual antiplatelet pharmacologic therapy with clopidogrel and aspirin was initiated. For management of his comorbidities, he maintained an antihypertensive regimen, atorvastatin for dyslipidemia and insulin and metformin for glycemic control. At a 1-month follow-up visit, he remained free of angina, and both the psoriasis and psoriatic arthritis remained under good control with the continuation of concomitant etanercept and ustekinumab.

DISCUSSION

This patient, receiving concomitant treatment with ustekinumab and etanercept, experienced a great reduction in both the signs and symptoms of psoriatic disease. In this case, ustekinumab effectively cleared the psoriasis, whereas etanercept treated the symptoms of psoriatic arthritis. A solitary case report does not represent enough data to advocate the routine use of combination biologic regimens. However, a customized approach to the management of psoriasis always is necessary. This patient, who did not respond to multiple other approaches, experienced dramatic improvement in disease control with the combined regimen. However, he experienced a cardiovascular event that cannot be definitively attributed to the therapies. It remains unclear whether biologic therapy, particularly ustekinumab, which was new to the patient and temporally associated, or the combination of ustekinumab and etanercept played an exacerbating role in the cardiovascular adverse event or whether the angina represented an unrelated consequence of the longstanding metabolic syndrome. Regardless, he is receiving antiplatelet therapy and pharmacologic therapy for hypertension, dyslipidemia, and diabetes to help prevent future cardiovascular sequelae. Although both biologic agents were covered by the patient's health insurance, issues related to cost effectiveness obviously make this approach to therapy impractical for most. In this instance, after an extensive discussion of the potential risks and benefits, both the patient and the treating physician have opted for the continuation of the combined biologic therapy. Close monitoring of the patient will ensue.

REFERENCES

1. Hugh J, Van Voorhees AS, Nijhawan RI, et al. From the Medical Board of the National Psoriasis Foundation: The risk of cardiovascular disease in individuals with psoriasis and the potential impact of current therapies. *J Am Acad Dermatol*. 2014;70(1):168-177.
2. Henseler T, Christophers E. Disease concomitance in psoriasis. *J Am Acad Dermatol*. 1995;32(6):982-986.
3. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. *JAMA*. 2006;296(14):1735-1741.
4. Wu JJ, Poon KY, Channual JC, Shen AY. Association between tumor necrosis factor inhibitor therapy and myocardial infarction risk in patients with psoriasis. *Arch Dermatol*. 2012; 148(11):1244-1250.
5. Gordon KB, Langley RG, Gottlieb AB, et al. A phase III, randomized, controlled trial of the fully human IL-12/23 mAb briakinumab in moderate-to-severe psoriasis. *J Invest Dermatol*. 2012;132(2):304-314.
6. Tzellos T, Kyrgidis A, Trigoni A, Zouboulis CC. Association of ustekinumab and briakinumab with major adverse cardiovascular events: An appraisal of meta-analyses and industry sponsored pooled analyses to date. *Dermatoendocrinol*. 2012; 4(3):320-323.
7. Ryan C, Leonardi CL, Krueger JG, et al. Association between biologic therapies for chronic plaque psoriasis and cardiovascular events: a meta-analysis of randomized controlled trials. *JAMA*. 2011;306:864-871.
8. Tzellos T, Kyrgidis A, Zouboulis CC. Re-evaluation of the risk for major adverse cardiovascular events in patients treated with anti-IL-12/23 biological agents for chronic plaque psoriasis: a meta-analysis of randomized controlled trials. *J Eur Acad Dermatol Venereol*. 2013;27(5):622-677.