Psoriasis and the Metabolic Syndrome

Psoriasis is an inflammatory skin disease, but in many ways it is a disease that goes beyond the skin. Moderate to severe psoriasis has, in fact, proven to be a much more complex systemic disease. With the advent of biologic therapies as a viable modality for treating moderate to severe disease some 10 to 15 years ago, we have learned much about the immunologic components of psoriasis and the extent to which it is associated with various other disease states and conditions. In particular, within roughly the past decade, researchers have dug deeper into the link between psoriasis and the metabolic syndrome. This has raised many questions, not only about the etiology of psoriasis but also what constitutes an appropriate clinical intervention for severe disease. This coupled with the sensitivities to biologic safety profiles—largely stemming from the withdrawal of efalizumab from the market and the halted clinical trials for briakinumab—has caused some concern regarding the use of biologics in psoriatic populations. However, a careful review of clinical studies tells a very different story about the safety and utility of these therapies.

EXPLORING THE DATA

Many studies over the last several years have probed the link between psoriasis and the metabolic syndrome. For example, one notable study revealed a number of increased associations among psoriasis patients when compared to non-psoriatic patients. In a 40-49 age group, psoriatic patients were much more likely to have diabetes compared to the control group.¹ In addition, in the 50-59 age group, nine percent of the psoriatic patients had hyperlipidemia, compared to just two percent in the control group. In the same age group, 20 percent of psoriatic patients had hypertension, compared to four percent in the control group.¹ This dovetails with a 2007 prospective evaluation of a Nurses Health Study, which revealed a correlation between elevated body mass index and psoriasis.²

A particularly compelling prospective, population-based cohort study published in the Journal of the American Medical Association in 2006 looked at over half a million patients based in the United Kingdom, in which 127,139 had mild psoriasis and 3,837 has severe psoriasis.³ It found that the adjusted relative risks of myocardial infarction (MI) in patients with psoriasis based on patient age was five-fold higher in the 20s age range, four-fold higher in the 30s age range, and two-fold higher in the 40s age range in patients with severe psoriasis.³ Given the increased risk of these conditions in psoriatic patients, it is no surprise that men and women with severe psoriasis die between 3.5 and 4.4 years sooner than patients without psoriasis, on average.⁴

While much work remains to understand the systemic and immunologic aspects of the disease, early evidence shows that treating with biologic agents may decrease the pro-inflammatory and pro-atherogenic factors and subsequently decrease the incidence of heart attacks and strokes noted in psoriatic patients.

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THE ROLE OF TNF
The pathophysiology of the correlation between severe psoriasis and the metabolic syndrome may lie in the pro-inflammatory molecules that trigger psoriasis. That is to say, tumor necrosis factor (TNF) alpha is also a pro-atherogenic molecule inducing atherosclerosis, thereby increasing the incidence of heart attacks and strokes in psoriatic patients. The logical question therefore becomes: Does effective anti-psoriatic treatment affect cardiovascular comorbidity? Several studies have investigated this question and the results are quite compelling.

A recent study assessed whether patients with psoriasis treated with TNF inhibitors have a decreased risk of MI compared to those not treated with TNF inhibitors. In total, 1,673 psoriatic patients received a TNF inhibitor for at least two months, as compared to 5,075 psoriatic patients who had not been treated with TNF inhibitors. The mean duration of follow up was 4.3 years and the median duration of TNF treatment was two years. After adjusting for MI risk factors, the TNF inhibitor-treated group had 50 percent fewer MIs than the non-TNF inhibitor-treated group. Per 1,000 patient years, the incidence of MI in the TNF-treated group was three, as compared to four in the oral treatment/phototherapy group, and seven in the topical therapy group. The investigators concluded that the use of TNF inhibitors for psoriasis was associated with a significant reduction in MI risk when compared with topical therapy. In addition, the use of TNF inhibitors was associated with a non-statistically significant lower MI rate as compared with oral agents and phototherapy.

Along similar lines, another study determined the impact of anti-inflammatory therapy on the risk of MI in psoriasis. Researchers assessed 25,554 American patients receiving systemic therapy or phototherapy and did not find a reduced risk of MI in either group. In light of the previous data, this suggests that biologic therapy may be an independent factor in the reduction of MI risk in psoriasis patients. Supporting this thesis are the compelling results from the recent Janssen PSOLAR registry, which examined the results of unadjusted rates of major adverse cardiac events (MACE) per 100 patient years based on exposure to therapy within 90 days of therapy administration. The findings revealed a rate of 0.30 for biologic therapy and 0.45 for non-biologic therapy. For any duration of exposure, the rates were 0.30 for biologic therapy and 0.55 for non-biologic therapy.

CONCLUSION
As an ophthalmologist observes retinopathy and refers the patient for diabetic evaluation and care, noting psoriasis should lead dermatologists to make cardiovascular evaluations. While much work remains to understand the systemic and immunologic aspects of the disease, early evidence shows that treating with biologic agents may decrease the pro-inflammatory and pro-atherogenic factors and subsequently decrease the incidence of heart attacks and strokes noted in psoriatic patients. More generally, the growing data identifying specific links between psoriasis and the metabolic syndrome, along with data indicating the efficacy of TNF inhibitors in decreasing associated risks, suggests that dermatologists should play a central role in coordinating with primary care physicians and other specialists in the overall health maintenance of these patients.

Dr. Bagel has served as consultant, researcher, or speaker for Amgen, LEO, Abbott, Janssen, Galderma, and GlaxoSmithKline.

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