By DIANA MAHONEY New England Bureau

**Arthritis by Sherry Boschert San Francisco Bureau**

**San Francisco — Ucerated skin lesions in three patients with refractory pyoderma gangrenosum shrank and reepithelialized after 10-11 weekly treatments with granulocyte and monocyte adsorption apheresis (GCPA).**

Three patients were being treated concurrently with prednisone and cyclosporine, sulfalessazine, or cyclophosphamide, so it’s difficult to sort out the exact benefit of granulocyte and monocyte adsorption apheresis (GCPA). It’s significant, however, that the lesions had not healed with prior treatment with these medications and others, and clinicians were able to discontinue the drugs or reduce the dosages after GCPA.

**Discontinuing the troublesome medication may not always be possible, necessitating clinical ingenuity.**

Drugs for Rheumatoid Diseases Trigger Skin Woes

BY SHERRY BOSCHERT San Francisco Bureau

**SFO** — Use of several agents for the management of arthritis and other diseases seen by rheumatologists can induce cutaneous reactions that require referral to a dermatologist, said Dr. Peter W. Heald at a dermatology conference sponsored by the University of Vermont.

Because these drug-aggravated conditions often present as known diseases but frequently have different underlying mechanisms and treatment responses, diagnosis and management can be problematic, according to Dr. Heald, professor of dermatology at Yale University, New Haven, Conn. Also, the condition the suspect drug is prescribed to treat may make it inadvisable to discontinue the medication. To help unmask some of the dermatologic imposters, Dr. Heald presented a series of clinical cases from his own practice along with management pearls gleaned from personal experience and recent literature.

**Interferon-Induced Cytokine Psoriasis**

Cytokine psoriasis—a subset of psoriasis with a unique clinical appearance and therapeutic response—appears with some frequency around 1990, not coincidentally around the time treatment with interferon for hepatitis C became more common, Dr. Heald said. "Over the past decade, we’ve started seeing tons of patients who are 1-2 months into interferon therapy coming in with psoriasis that’s just gone crazy. They have acute, irritated, oozing lesions, sometimes with pruritus and often associated with palmar lesions and acral dermatitis," he said. Of interest, the psoriatic lesions are not local to the interferon injection sites, but rather are all over the body and, if the patient has or is prone to psoriatic arthritis, that will be induced or aggravated as well.

Although the exact underlying mechanism for this is not fully understood, psoriasis is thought to be an immune-mediated disease with a cytokine profile predominantly of the Th1 helper cell, type 1 (Th1) subset. Presumably, interferon-α triggers psoriasis by activating dendritic cells and T cells involved in the pathogenesis of the condition, according to Dr. Heald. "I’m not a big believer in interferon inducing new causes; it is more likely that interferon causes problems in people who are prone to psoriasis or who have a mild case," he said. "If you’ve got a condition where you’ve already got a Th1-mediated process going on in the skin, and you feed that interferon, it’s going to cause problems."

The plan for managing this type of psoriasis is to treat the patients while they are completing their course of interferon therapy. "The usual regimen is etanercept—I start them on 50 mg twice a week—with or without prednisone for rapid onset of relief," Dr. Heald said. "In my experience, the response to etanercept for this type of psoriasis is even better than [it is for] regular psoriasis." At the end of the interferon course, patients can be safely tapered off of the etanercept, he said.

An important consideration in the management of these patients, said Dr. Heald, is to involve the treating physician in the decision process. "Let them know that you are going to start treatment and that you’re comfortable using the anti-tumor necrosis factor therapy."

**Antimalarial Psoriasis**

"I recently saw a patient who started on an antimalarial medication to treat symptomatic polyarthritis with psoriasis. Within 2 weeks of starting the drug, he began to develop what I call a ‘fill-in-the-gap’ type of psoriasis, in which erythema develops in between preexisting plaques," Dr. Heald said. "We’ve seen a bunch of these cases because for a while at our Veterans [Affairs] hospital a patient had to fail an antimalarial before getting approval for treatment with a biologic for psoriatic arthritis.”

To manage this condition, "we stop the drug immediately and switch over to something that can treat both psoriasis and psoriatic arthritis" and possibly a prednisone taper," Dr. Heald said. "I don’t think psoriasis patients should ever be put on antimalarials. Hydroxychloroquine inhibits epidermal transglutaminase activity, which leads to irregular keratinization and dermoeperidermal detachment and cleft formation. In psoriasis, this leads to an erythrodermic form of the disease."

**Efalizumab-Induction Psoriasis**

Most dermatologists have legions of hap hazard psoriasis patients thanks to the efficacy of biologics for continuous control of their conditions, "but there is one little side to this that has not been published enough: the possibility of psoriasis exacerbation when treatment is interrupted," said Dr. Heald, who has had patients weeks and even months after stopping efalizumab therapy whose psoriasis returns with a vengeance, following two or three missed doses. "One of my patients went on a trip and forgot his medication for 3 days. He experienced an unbelievably quick, abrupt aggravation with lots of pruritic new lesions and oozing lesions," Dr. Heald said. "It’s unclear what’s behind this, but it’s possible that with an interruption in therapy ‘all those cells go barreling back into the skin and create this abrupt syndrome.”

"To manage the reaction, ‘I have sometimes tried getting prednisone or cyclosporine in there right away just to get immediate control because these patients get so bad so quickly, and then [I] start another form of therapy.'"

**Interferon: Pyoderma Gangrenosum**

Although not common, the development of virulent pyoderma gangrenosum-type ulcers at the interferon injection sites of some patients receiving the drug for multiple sclerosis or hepatitis C, "appears to be the result of interferon aggravating one of the TH1 types of inflammatory processes that typically occurs within 3 months of starting the therapy," Dr. Heald said. Biopsies of the affected areas may show neutrophil infiltrates of vasculitis.

"Because patients and their neurologists love the drug, they’re not going to stop it, so they will want you to help manage them through it,” Dr. Heald said. This is particularly true for patients with multiple sclerosis. "Patients who are staying on interferon for MS can’t just do it. They do have to do interferon trials, triamcinolone injections, which I’ve had the most success with.”

**Vitiligo and Imiquimod**

Topical imiquimod can induce local interferon-γ release and vitiligo hyperpigmentation. "In patients prone to vitiligo, the imiquimod triggers an immunomodulating event that may enhance a latent cell-mediated process,” Dr. Heald said. "In the patients I’ve treated with it, nobody has developed vitiligo all over. It’s been localized to a small area of imiquimod application.”

"Use one of the other topical immunomodulator drugs, he said.

Infliximab and Lupus Erythematosus

Four months on infliximab appears to bring out subclinical lupus in a small percentage of patients with preexisting anti-nuclear antibodies. "I’ve had about a half-dozen patients who are on infliximab for rheumatoid arthritis coming in with a lupus-like syndrome of arthralgia, flat, scaly skin lesions that tend to be mostly on the face and arms,” Dr. Heald said. "The mechanism for the condition is a little bit murky, but what’s clear is that in some instances, you have to stop the drug. You can’t treat through this.”

Alternative treatment options include methotrexate or ciclosporine. "You want to stay away from the anti-TNF family in general,” he said, noting that once infliximab therapy is withdrawn, the skin lesions tend to clear in 2-3 months.

**Apheresis Healed Refractory Pyoderma Gangrenosum Lesions**

**BY SHERRY BOSCHERT San Francisco Bureau**

**SOF** — Dr. Mariko Seishima and her associates at Ogaki Municipal Hospital, Japan, reported a case of pyoderma gangrenosum healed with prior treatment with these medications and others, and clinicians were able to discontinue the drugs or reduce the dosages after GCPA. Dr. Seishima and her associates reported in an abstract at the annual meeting of the American Academy of Dermatology.

All three patients were being treated concurrently with prednisone and cyclosporine, sulfalessazine, or cyclophosphamide, so it’s difficult to sort out the exact benefit of granulocyte and monocyte adsorption apheresis (GCPA). It’s significant, however, that the lesions had not healed with prior treatment with these medications and others, and clinicians were able to discontinue the drugs or reduce the dosages after GCPA.

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