Nicotine for Pyoderma Gangrenosum

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 35-year-old man with no past medical illness developed bloody diarrhea with up to 12 loose stools per day and abdominal pain in February 1984. He had smoked 1 pack of cigarettes per day for 16 years until he stopped smoking 2 months prior to the onset of his illness. In March 1984, he was hospitalized because of toxic dilatation of the colon (toxic megacolon). Treatment consisted of intravenous fluids and electrolytes, broad-spectrum antibiotics, and corticosteroids. After the condition had slowly improved, he was released on a daily dosage of 40 mg of prednisone, 4 g of sulfasalazine, and 800 mg of cimetidine. Findings of colonoscopic and sigmoidoscopic examinations with biopsies were inconclusive, and he was diagnosed as having active nongranulomatous colitis similar to inflammatory bowel disease, without being able to differentiate between ulcerative colitis and Crohn disease. He subsequently had short remissions with only minimal activity and many relapses with severe symptoms. He was treated with 1.5 to 3 g/d of sulfasalazine, and 50 to 100 mg/d of azathioprine, as well as intermittent courses of prednisone. Cimetidine, iron, and vitamins were also administered.

We first saw the patient in July 1985 for 2 multiloculated necrotic ulcers on both legs surrounded by a raised, thickened, undermined bluish edge. The diagnosis of pyoderma gangrenosum was made clinically. Therapy with 60 mg/d of prednisone was started and gradually reduced to 25 mg/d of prednisone over 1 year, after which the ulcers healed. In July 1992, he again developed pyoderma gangrenosum on 1 leg and underwent a similar treatment and course over nearly 1 year until the ulcer had completely healed.

In August 1995, there was an exacerbation of his bowel symptoms together with pyoderma gangrenosum on his left leg. Therapy consisted of blood transfusions and 30 mg/d of prednisone, in addition to the sulfasalazine and azathioprine regimens. His bowel symptoms but not his cutaneous lesions improved gradually, and prednisone was slowly tapered within 5 months to 12.5 mg/d. In March 1996, azathioprine was stopped on his request. However, the pyoderma gangrenosum did not respond to this treatment; rather, the cutaneous situation in August 1996 was about the same as it had been 1 year earlier.

THERAPEUTIC CHALLENGE

Currently available treatment for pyoderma gangrenosum is far from satisfactory. Only 2 major drugs, corticosteroids and cyclosporine, have proved effective in the treatment of pyoderma gangrenosum. Unfortunately, they may be poorly tolerated and are associated with significant adverse effects. While the intestinal symptoms of our patient responded favorably to systemic corticosteroid therapy, his cutaneous symptoms responded only very slowly for the first 2 attacks and not at all for his last one.

Our challenge was to devise an alternative safe and effective treatment.

SOLUTION

Therapy with topical nicotine was started. The patient was instructed to apply a 10-mg nicotine patch directly on the ulcer and replace it every 24 hours. Systemic treatment was continued, except that the prednisone dosage was lowered to 10 mg/d.

There was a dramatic improvement of the cutaneous lesions with this regimen. The ulcer became smaller and less inflamed within 2 weeks and cleared up completely within 4 weeks, leaving only postinflammatory hyperpigmented scars.

Treatment with nicotine patches was discontinued 1 month later. Within 2 weeks, the same symptoms recurred, with an exacerbation of the bowel symptoms together with pyoderma gangrenosum on his left leg. He was treated with 60 mg/d of prednisone, in addition to sulfasalazine and 100 mg/d of azathioprine. With this treatment, the bowel symptoms improved rapidly and prednisone was tapered within 2 months to 10 mg/d. We saw the patient 2 weeks later (the prednisone dosage was then 30 mg/d); there was a large, oozing, inflamed ulcer...
on his left leg. Treatment with nicotine patches was reintroduced, and the ulcer healed again within 3 months. We did not observe any adverse effects during therapy with the nicotine patches.

**COMMENT**

Ulcerative colitis is largely a disease of nonsmokers. Ex-smokers often acquire the disease within a few years of stopping the habit. Patients who smoke intermittently often experience improvement of their symptoms during periods of smoking. Based on these observations, several trials have been conducted in an attempt to treat patients with nicotine in various forms. In most of the open studies, smoking, nicotine chewing gum, or nicotine patches appeared to improve symptoms of this inflammatory bowel disease. This result has also been confirmed in a recent double-blind, controlled trial with transdermal nicotine patches.

Pyoderma gangrenosum is well known to be associated with ulcerative colitis. It responds to similar treatment modalities, such as systemic corticosteroid and immunosuppressive drug therapy. Therefore, it is logical to assume that pyoderma gangrenosum would benefit from nicotine therapy, as has been shown for ulcerative colitis. There are only a few reports of such treatment for this dermatosis. The reason for this might be the rarity of the disease, estimated at 3 cases per 1 million population per year. However, we believe that lack of awareness of this form of therapy among dermatologists is the main reason for the scarcity of studies on this therapeutic modality.

Herein we describe a patient with pyoderma gangrenosum who responded twice to topical nicotine within 4 weeks and 3 months, respectively, without any adverse effects. It is noteworthy that his bowel disease appeared for the first time 2 months after he stopped smoking. Furthermore, his pyoderma gangrenosum and bowel symptoms appeared shortly after withdrawal of treatment with nicotine patches.

Transdermal nicotine patches may be associated with local cutaneous and systemic adverse effects. The most frequently reported events have been central nervous system effects (headache, dizziness, and fatigue), sleep disturbances (insomnia and nightmares), cardiovascular effects (increased blood pressure, heart rate, and peripheral vasoconstriction), and gastric disturbances (constipation, flatulence, nausea, vomiting, dyspepsia, and taste perversion). There have also been reports of sweating, muscle and limb pain, paresthesia, increased cough, and palpitations. Because of the pharmacokinetic profile of transdermal delivery systems (slow rate of absorption of nicotine and low, stable plasma nicotine concentrations), systemic adverse events are usually mild and do not often lead to discontinuation of therapy.

However, with the use of nicotine patches on multiple open lesions, the possibility of reaching higher and even toxic plasma nicotine concentrations should be seriously considered and symptoms of nicotine overdose carefully monitored.

Undoubtedly, large randomized clinical trials are more significant than case reports on encouraging therapeutic results in individual patients. However, before conclusive data can be provided, we believe that early sporadic reports are effective for dissemination of the information and are often followed by a plethora of such communications. Finally, it may be that efficacy will be noted only in those patients with a similar history, i.e., inflammatory bowel disease onset following cessation of smoking.

Presented in part at the Ninth Zagazig International Conference of Dermatology and Venereology, Cairo, Egypt, December 7, 1996.

**REFERENCES**