# An Eruption Secondary to Intravenous Immunoglobulin Therapy

Diya F. Mutasim, MD; Pranav B. Sheth, MD

*A 42-year-old woman presented with a recurrent eruption over the distal extremities. Lesions formed a few days after initiation of intravenous immunoglobulin (IVIg) therapy and lasted 2 to 3 weeks after therapy completion. Results of a histologic examination revealed parakeratosis, exocytosis, and spongiosis. The clinical and histologic findings are similar to previous reports. The mechanism of this eruption is not known.*

Intravenous immunoglobulin (IVIg) therapy has been used for several neurologic disorders, immune deficiencies, hematologic and autoimmune diseases, and dermatologic conditions such as dermatomyositis and autoimmune bullous disorders.[1,2] IVIg therapy, often effective in patients who have failed other therapies, is relatively safe; however, its use may be limited because it is rather expensive. Therapy is usually given in daily infusions for a few consecutive days every month. The number of cycles given depends on the disease and on the response to therapy. Multiple side effects reported secondary to IVIg therapy include systemic symptoms such as headache, myalgia, fever, chills, nausea, and cardiovascular manifestations. Hypersensitivity and anaphylactic reactions, hemolytic anemia, viral hepatitis, renal failure, thrombotic events, alopecia, and skin eruptions also have been reported.[2] Skin reactions secondary to IVIg therapy include urticaria, pruritus, petechiae of the extremities, and eczematous lesions of the palms and soles.[1-4] We report a case involving a characteristic cutaneous eruption following IVIg therapy for chronic inflammatory demyelinating polyneuropathy.

From the Department of Dermatology, University of Cincinnati, Ohio.
Reprints: Diya F. Mutasim, MD, Department of Dermatology, University of Cincinnati, PO Box 670592, Cincinnati, OH 45267-0592 (e-mail: diya.mutasim@uc.edu).

## Case Report

A 42-year-old white woman with chronic inflammatory demyelinating polyneuropathy was treated with IVIg daily for 5 consecutive days. She developed lesions over her palms and soles 3 days after initiation of therapy. The lesions were markedly pruritic and occasionally painful. The patient also reported a petechial eruption over her extremities. She used a class I topical steroid ointment (betamethasone dipropionate) with no significant improvement. She did not develop any other adverse effects secondary to IVIg therapy. She had had 5 previous episodes of IVIg therapy approximately 1 year apart. During each episode, she developed similar palmoplantar lesions a few days after initiation of therapy. The lesions resolved 2 to 3 weeks after completion of therapy. Severity of the cutaneous eruption varied among different courses of IVIg therapy. The patient did not receive any medications or over-the-counter agents during the course of IVIg therapy. She used cetirizine daily for seasonal allergies.

Results of a skin examination showed an eruption on both palms (significantly more on the right side than the left), soles (left involved more than right), and insteps. The eruption consisted of discrete and coalescing erythematous papules and papulovesicles ranging in size from pinpoints to 1 mm (Figure 1). In addition, pinpoint petechiae were present on the legs and dorsal feet. A biopsy specimen obtained from the left inner foot showed a small focus of parakeratosis with serum crust; an underlying superficial intraepidermal spongiose vesicle; exocytosis; and a focal, dense lymphocytic infiltrate in the underlying papillary dermis. An eccrine duct was present within the inflammatory focus (Figure 2).

## Comment

Although IVIg therapy is generally safe, several side effects have been reported. These include cutaneous effects such as urticaria, pruritus, petechiae, and palmoplantar eczematous lesions.[1-4]

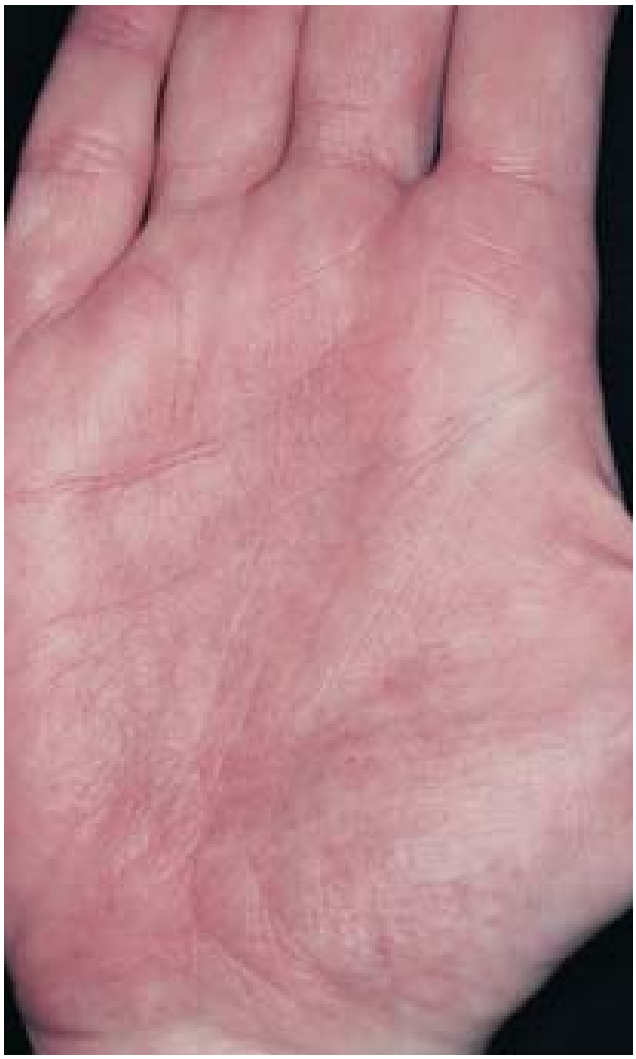

**Figure 1.** Numerous pinpoint erythematous papulovesicles on the right palm.

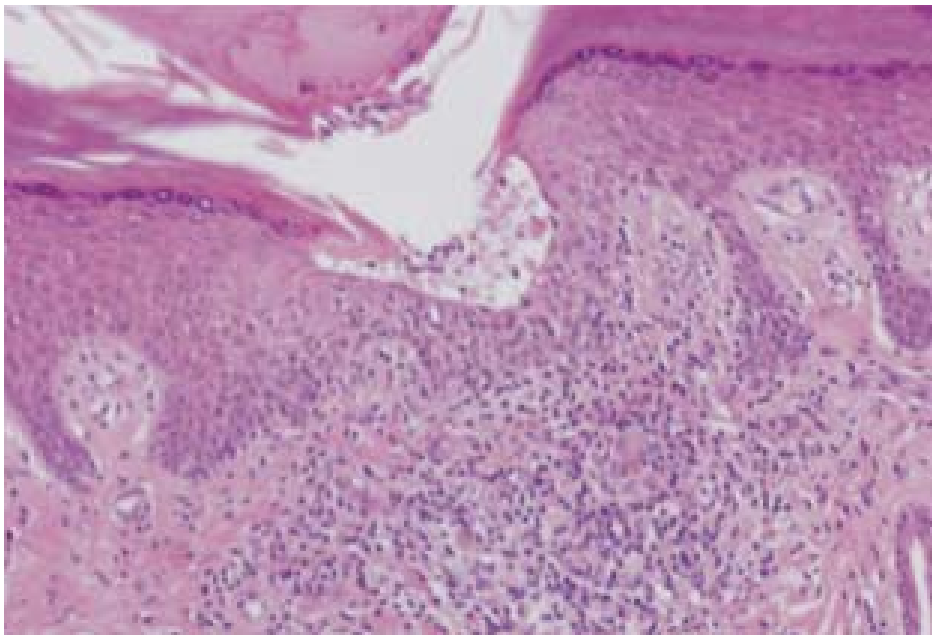

**Figure 2.** Parakeratosis with serum, spongiosis, exocytosis, intraepidermal microvesicle, and superficial dermal lymphocytic infiltrate adjacent to eccrine duct (H&E, original magnification ×200).

CONTINUED ON PAGE 38

CONTINUED FROM PAGE 36

In a retrospective study,[4] 3 of 23 patients who had neurologic disorders and who were treated with IVIg developed a vesicular eczematous eruption over the hands—a development similar to that experienced by our patient. No other drugs were taken by any of the 3 patients immediately before, during, or after treatment. Lesions resolved within 3 weeks. All 3 patients developed a skin reaction after the first cycle of IVIg therapy. IVIg therapy was discontinued for these 3 patients because of fear of a more generalized skin eruption. Twelve of the 23 patients were exposed to several cycles of IVIg therapy without any adverse cutaneous effects.[4]

The etiology of adverse cutaneous effects secondary to IVIg therapy is not clear. Multiple factors have been suggested, including infusion rate, commercial source of IVIg product, and underlying disease.[4] The mechanism of the adverse effects is also not clear. Suggested factors include complement activation by aggregated immunoglobulin molecules, antigen–antibody reaction, contaminants, and stabilizers used during manufacturing.[2] Our patient's observation of the consistent recurrence of the eruption after each IVIg cycle raises the possibility of individual susceptibility to the reaction. Our patient never experienced similar cutaneous lesions before initiation of IVIg therapy. Primary involvement of areas rich in eccrine glands (palms and soles) and the histopathologic presence of an eccrine duct suggest involvement of eccrine glands in the pathogenesis of the skin lesions. It is possible that a component of the IVIg product is preferentially excreted through the eccrine glands, thus predisposing to the unique distribution of the eruption.

In summary, we report a case with unique cutaneous findings secondary to IVIg therapy. Because IVIg therapy is being used more frequently in dermatologic practice, dermatologists should be aware of this not uncommon cutaneous adverse effect.

## REFERENCES


1. Dalakas MC. Intravenous immune globulin therapy for neurologic disease. *Ann Intern Med*. 1997;126:721-730.
2. Duhem C, Dicato MA, Ries F. Side-effects of intravenous immune globulins. *Clin Exp Immunol*. 1994;97:79-83.
3. Yockey SMD, Ahmed I. Intravenous immunoglobulin–induced lichenoid dermatitis: a unique adverse reaction. *Mayo Clin Proc*. 1997;72:1151-1152.
4. Iannaccone S, Sferrazza B, Quattrini A, et al. Pompholyx (vesicular eczema) after i.v. immunoglobulin therapy for neurologic disease. *Neurology*. 1999;53:1154-1155.