

Hypersensitivity vasculitis occurring in a patient receiving immunotherapy

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Although it is generally accepted that IT is not associated with significant long-term adverse effects, the question of IC disease caused by allergy injections is unresolved. Some authors have suggested that significant levels of ICs can occur during IT,^{1, 2} whereas other authors have provided evidence to the contrary.^{3, 4} The common practice of stopping IT after 5 years takes into account the remote possibility of development of IC disease.

BRIEF CASE REPORT

A 59-year-old white man was first observed with symptoms of perennial allergic rhinitis and prostatism exacerbated by chronic antihistamine use. His past medical history was positive for eczema and hyperlipidemia, for which lo-

Abbreviations used

IT: Immunotherapy

IC: Immune complex

vastatin had been prescribed 6 months previously. Physical examination revealed only mild hyperemia and edema of the nasal turbinates and a cloudy posterior pharyngeal discharge. Skin testing revealed significant positive results to all local trees, weeds, grasses, house dust mite (*Dermatophagoides farinae*), smuts, and molds. IT was initiated at a dose of 1:100,000 wt/vol in paired injections to the above antigens.

Approximately 72 hours after the sixth injection (week 3, dose 0.40 cc, 1:100,000 wt/vol), the patient complained of a pruritic rash involving the abdomen, thighs, and lower legs. The rash partially subsided but continued to exacerbate 2 to 3 days after each subsequent pair of injections. After the twelfth injection (week 6, cumulative dose 0.52 µg of protein nitrogen), IT was stopped because of this convincing association. Lovastatin was also stopped at this time. Ex-

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FIG. 1. Mixed lymphocytic and polymorphonuclear leukocytic infiltration of blood vessel wall.

amination revealed an erythematous maculopapular eruption that blanched with gentle pressure. A skin biopsy specimen revealed a mixed lymphocytic and leukocytoclastic vasculitis (Fig. 1) consistent with an IC process.

The following laboratory analyses were performed: complete blood cell count, sequential multiple analysis-12, sedimentation rate, and urinalysis were normal. Tests for rheumatoid arthritis and antinuclear antibody were twice negative; rapid plasma reagin, antistreptolysin titer, and C-reactive protein were negative. Serum IgE was 42.8 IU/ml (5 to 100 IU/ml), and a serum protein electrophoresis was normal. C3, C4, and total hemolytic complement were within the limits of normal. Hepatitis B surface antibodies were present, but surface antigen, Be antigen, core and Be antibodies were negative. Cryoglobulin and Raji cell assay were negative.

Two months after IT and lovastatin were stopped, the rash subsided, although a curious head and neck photosensitivity has persisted. Administration of lovastatin was restarted after 5 months without incident.

DISCUSSION

Allergen IT dates back to 1911 and has been used successfully to treat large numbers of patients throughout this century. Studies of the efficacy of this treatment abound, but studies of the long-term safety of IT (except for immediate reactions) are sparse. Levinson et al.³ found no rheumatoid factor or antinuclear antibody generation, no complement consumption, no Coombs' antibody activity, and no C1q binding activity during maintenance IT. Stein et al.⁴ confirmed these findings and extended them to include absence of proteinuria or cryoglobulinemia during long-term IT.

To the contrary, Phanuphak and Kohler,² in 1980, reported six patients who developed a systemic vasculitis (polyarteritis nodosa) during IT. Five of these patients had evidence of circulating ICs to include cryoglobulinemia, increased C1q binding, or complement consumption. These authors concluded that the injected antigens were indirectly responsible for the systemic arteritis, presumably by inducing antibodies with cross-sensitivity to endogenous host antigens.

One notable similarity between the series by Phanuphak and Kohler² and the patient reported here is the

onset of the vasculitic symptomatology early in the course of IT. Three of their six patients experienced a rash as a presenting feature, all within the first 3 months of beginning IT. Had IT not been promptly stopped in this case, it is conceivable that the patient might have experienced a more severe (i.e., necrotizing) vasculitis.

Although there was some evidence of IC generation in most of these patients,² it is not surprising that two screening tests for ICs were negative in the patient reported here. The amount of injected allergen was far less in this case than in the series by Phanuphak and Kohler.² Evidence for IC generation (greater than control) was absent in a total of 91 patients receiving maintenance IT in the series by Levinson et al.³ and Stein et al.⁴

In summary, a middle-aged man experienced a cutaneous nonnecrotizing vasculitis after 6 weeks of IT. The rash consistently exacerbated 2 to 3 days after weekly paired IT injections for a period of 4 weeks. The rash was steroid resistant but responded after 2 months of avoiding IT and lovastatin. Rechallenge with lovastatin failed to reproduce the rash. No evidence of IC generation was obtained. Although the usual duration of time for generation of ICs is 7 to 14 days, previous sensitization may shorten this interval.⁵ Although the true nature of this hypersensitivity vasculitis remains unknown, it appears possible that injected aeroallergens were at least indirectly responsible.

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