Hypergammaglobulinemic Purpura of Waldenström

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Hypergammaglobulinemic purpura of Waldenström is a rare syndrome that includes recurrent episodic purpura occurring mainly on the lower extremities and dorsum of the feet. The hallmark of this condition is polyclonal hypergammaglobulinemia primarily composed of IgG. Although the condition generally is benign, it may herald an underlying connective tissue disease or hematologic malignancy. We report a case of a 47-year-old woman with episodic purpura of 3 years' duration associated with Raynaud phenomenon.

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Case Report

A 47-year-old woman presented with lower extremity pain and swelling of 3 years' duration followed by a bright red, petechial eruption. She was otherwise in good health and denied any constitutional symptoms, joint pain, dry mouth or eyes, or new medications. She did, however, report symptoms of Raynaud phenomenon.

Physical examination revealed innumerable, 3- to 5-mm, bright to dusky red macules diffusely distributed on her lower legs (Figure 1). A complete blood cell count showed anemia and her erythrocyte sedimentation rate was 70 mm/h (reference range, 1–15 mm/h). She had an antinuclear antibody titer of 1:640 and was SS-A (Sjögren syndrome antigen A) positive. Her rheumatoid factor was 261 U (reference range, <20 U). Cryoglobulin and hepatitis C virus screens were negative. Serum protein electrophoresis and serum immunofixation showed polyclonal hypergammaglobulinemia with an IgG level of 2650 mg/dL (reference range, 562–1585 mg/dL).

A cutaneous biopsy specimen was obtained for histologic analysis (Figure 2). Histologic sections showed a perivascular infiltrate composed of lymphocytes, numerous polymorphonuclear leukocytes showing karyorrhexis, and a few admixed eosinophils. The vessels were intact without evidence of fibrinoid necrosis. There were extravasated red blood cells in the dermis and admixed within the inflammatory infiltrate. Iron-stained sections for hemosiderin were negative.

Prior to diagnosis, the patient had tried using compression stockings that exacerbated her eruption and concomitant pain. She reported that when she lied down overnight her rash completely resolved and recurred the following day while working. She did not undergo any treatment for this condition and was referred to an oncologist for further evaluation. The patient was subsequently lost to follow-up.

Comment

Hypergammaglobulinemic purpura of Waldenström is a rare syndrome that includes recurrent episodic showers of petechiae occurring mainly on the lower extremities and dorsum of the feet. The petechiae may be induced or exacerbated by prolonged increases in hydrostatic pressure, such as by standing or walking for long periods or by wearing constrictive stockings.[1-4] The lesions present bilaterally but are asymmetrical and typically show a fairly constant pattern in a given patient.[4] They can be associated with edema and burning or tingling sensations.[5,6] Hypergammaglobulinemic purpura of Waldenström most commonly occurs in women. It may be a primary syndrome or associated with other disorders, such as Sjögren syndrome, hepatitis C virus, rheumatoid arthritis, Raynaud phenomenon, and multiple myeloma.[5]

The differential diagnosis includes hypersensitivity vasculitis, Henoch-Schönlein purpura, essential

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The authors report no conflict of interest.

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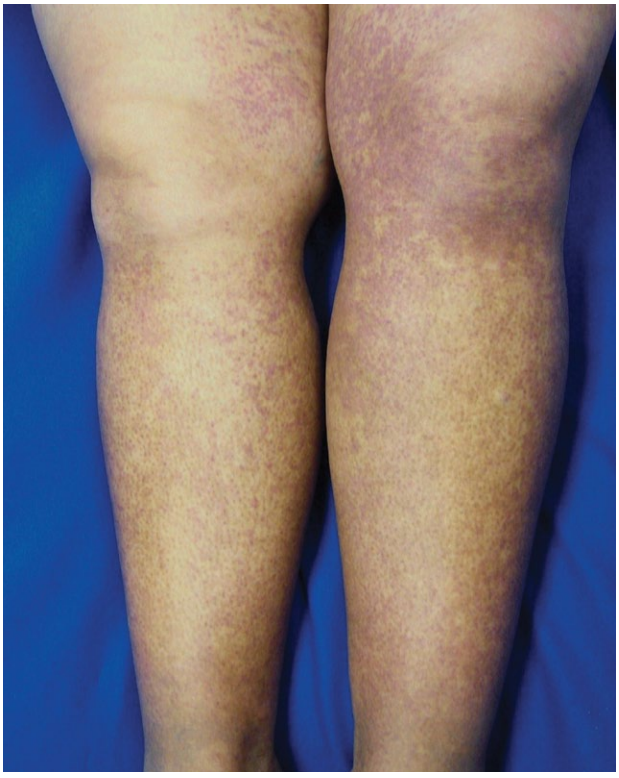

Figure 1. Innumerable, bright to dusky red macules on the lower legs.

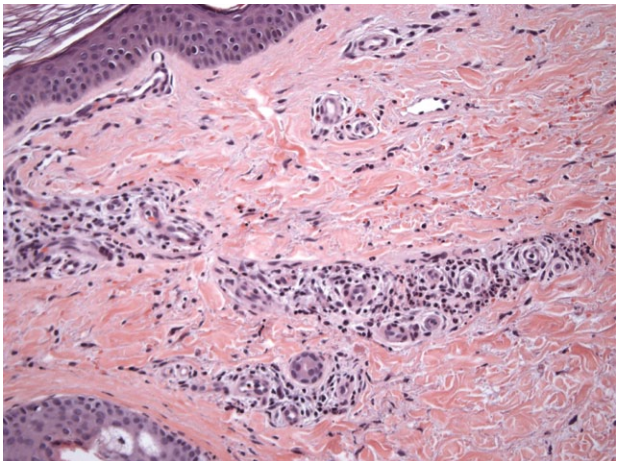

Figure 2. Punch biopsy showed a perivascular lymphohistiocytic infiltrate, numerous polymorphonuclear leukocytes showing karyorrhexis, and a few admixed eosinophils (H&E, original magnification ×40).

mixed cryoglobulinemia, hypocomplementemic vasculitis, vasculitis secondary to collagen vascular diseases, certain infections, and malignancies.[3]

Serum protein electrophoresis demonstrates polyclonal hypergammaglobulinemia with IgG being the bulk of the protein. Occasionally, increased amounts of IgA are found and IgM is normal or decreased.[5] Almost all patients have an elevated erythrocyte sedimentation rate, are rheumatoid factor positive, and have antibodies to SS-A/Ro.[4,5] Antinuclear antibodies, proteinuria, antithyroglobulins, and leukopenia also may be found.[1,2] Mild hypochromic anemia also is a common finding. Cryoglobulins usually are absent.[3]

The exact pathogenesis of the development of purpura in this disease is not clear; however, excessive production of polyclonal immunoglobulins may be responsible.[7] Histologic examination usually shows a perivascular infiltrate of mononuclear cells with fragmentation of nuclei in the superficial dermis. Deposits of immunoglobulin and complement have been described in the capillary walls on immunofluorescence.[4,7]

The disease generally is benign but chronic. However, hypergammaglobulinemic purpura of Waldenström may herald an underlying connective tissue disease or hematologic malignancy, such as multiple myeloma. Generally, no specific treatment is needed, but tests should be conducted to rule out an underlying connective tissue disease.[5] Anecdotal reports of treatment with colchicine with or without steroids or hydroxychloroquine sulfate showed marked response.[1,3] Chlorambucil, indomethacin, thioguanine, dipyridamole, and aspirin have been used with some success.[4] Ironically, compression stockings that can exacerbate the purpura also have been shown to improve patient comfort.

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