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Hypergammaglobulinemic purpura of Waldenström—Unusual and impressive case in a patient with myeloma: A case report

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Abstract

Background: Hypergammaglobulinemic purpura of Waldenström is an uncommon disease, which presents mostly in women on the lower extremities. It is sometimes associated with underlying immune dysregulation. Sjögren syndrome is the most common association; however, rare occurrences of the self-resolving syndrome with lymphoma or myeloma have been reported.

Case Summary: We describe an unusual and impressive presentation of hypergammaglobulinemic purpura of Waldenström in an elderly female patient with myeloma. Notably, the patient did not have any concurrent connective tissue diseases. Despite her florid presentation, her hypergammaglobulinemic purpura of Waldenström spontaneously resolved within a few days.

Conclusion: Hypergammaglobulinemic purpura of Waldenström is a self-resolving but recurrent syndrome, which may be associated with autoimmune disorders or rarely myeloma. Early diagnosis of the syndrome may avoid unnecessary treatment interventions and should prompt screening for underlying diseases.

Keywords

Leukocytoclastic vasculitis, purpura, Waldenström, hypergammaglobulinemia

Introduction

Hypergammaglobulinemic purpura of Waldenström (HGPW) is characterized by recurrent purpura on the lower extremities, increased erythrocyte sedimentation rate (ESR), and polyclonal gammopathy.[1] The syndrome is primarily seen in middle-aged women and may be brought on by prolonged increases in hydrostatic pressure including heat exposure, tight-fitting clothing, and extended periods of standing.[2] It is typically mild and self-limiting and is considered an unusual form of chronic leukocytoclastic vasculitis (LCV). The rash resembles that seen in so-called exercise-induced vasculitis. HGPW may be primary or secondary, and in older adults, it is often secondary to an underlying immune dysregulation or granulomatous condition.[1] Sjögren syndrome is the commonest association; however, rare occurrences of lymphoma or myeloma have been reported.[1,3–8] A common link between these disease entities is polyclonal immunoglobin formation with immune complex deposits in blood vessels of the lower limbs.[1] The differential of HGPW includes non-inflammatory purpuras like pigmented purpuric dermatosis, as well as other forms of LCV. Herein is presented an unusually florid case of HGPW, associated with myeloma, that nevertheless resolved spontaneously in several days.

Case report

An 80-year-old female with a 2-year history of myeloma was admitted for urosepsis. She received one dose of intravenous ceftriaxone and a second dose 48 h after. No other medications were started during her admission. Her

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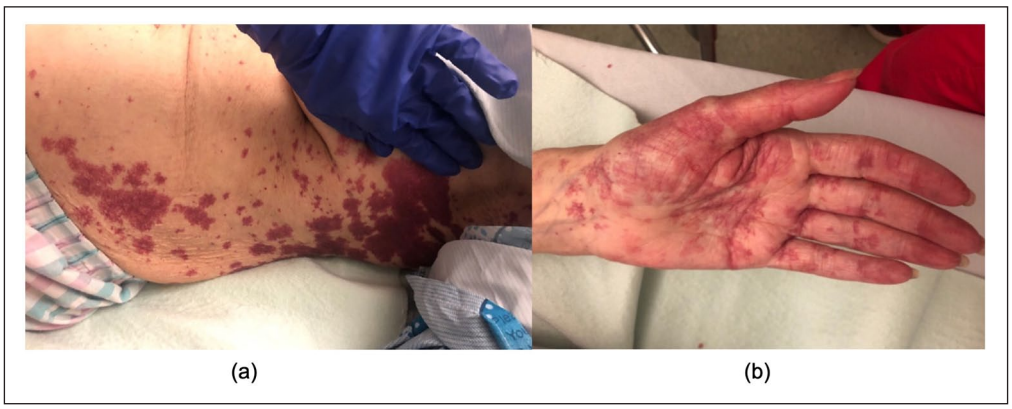

Figure 1. (a) Stellate and annular purpura on dependent areas of torso. (b) Stellate purpura on the patient's left palm.

immunoglobulin (Ig) IgA kappa myeloma had been treated with cyclophosphamide and prednisone 16 days earlier. Her medical history included atrial fibrillation, anemia, coronary artery disease, dyslipidemia, and a remote stroke without residual deficits. She had no known concurrent connective tissue disease.

During the first 24 h of her admission, she developed rapid onset of a non-painful, non-pruritic purpuric eruption on the trunk and extremities. From collateral history, the patient had developed a similar eruption around the time of her myeloma diagnosis 2 years prior, which had self-resolved and was not associated with any new medication.

On examination, the patient had strikingly bright-red non-blanching non-palpable macules and patches, some stellate and annular on the palms, dorsal hands, arms, medial upper thighs, and extensively across the dependent regions of her central back and flanks. Notably, the feet and legs were spared (Figure 1).

The clinical differential included small vessel vasculitis, capillary fragility syndromes like systemic amyloidosis or scurvy, early disseminated intravascular coagulation, Majocchi-Schamberg syndrome, and petechiae from platelet deficiency or dysfunction.

Blood work revealed elevated IgA, but low IgG and IgM. Serum free kappa light chains were very high, and there was a monoclonal gammopathy (Table 1). Skin biopsy showed abundant extravasated red blood cells within the papillary and superficial dermis, with perivascular and interstitial neutrophils and focal fibrinoid necrosis of vessels (Figure 2). Direct immunofluorescence showed C3 and fibrin around the superficial dermal vessels but no IgG, IgA, or IgM. These findings were compatible with LCV.

The eruption began to fade spontaneously and had cleared completely within 10 days. There were no residua. The clinical features and course, hematologic and biochemical results, and histopathology suggested a diagnosis of HGPW. The diagnosis was furthermore supported with the rapid resolution of the purpura and the possible history of a previous similar episode.

Table 1. Relevant laboratory investigations.

Immunoglobulins	
IgG	1.6 g/L (7–16)
IgM	<0.1 g/L (0.4–2.3)
IgA	18.4 g/L (0.7–4)
Serum free light chains	
Kappa	385.5 mg/L (3.3–19.4)
Lambda	2.9 mg/L (5.7–26.3)
Kappa: Lambda ratio	132.93 (0.26–1.65)
White blood cells	4.4 x 10^9/L (3.5–10.5)
Platelets	73 x 10^9/L (130–380)
Hemoglobin	100 g/L (115–155)
Rheumatoid factor	Negative
Antinuclear antibodies	Negative
Serum protein electrophoresis	Monoclonal IgA gammopathy

Discussion

HGPW usually presents clinically with mild itch, burning or tingling, and petechiae or purpura localized to the lower part of the legs.[6,9] This syndrome preferentially affects middle-aged women with skin findings resolving on their own within several days.[6,10,11] Laboratory investigations often reveal elevated levels of immunoglobulins, either IgG, IgM, or IgA or a combination. Additional findings can include leukopenia, anemia, and the presence of rheumatoid factor (RF).[6,9]

Although HGPW is often associated with hypergammaglobulinemia, the pathogenesis remains unclear. A more specific feature may be the finding of immune complexes including IgG and IgA RF, which are believed to be involved in the development of the disease.[8] Although our patient had a negative RF, standard RF assays only assess for the presence of IgM RF and do not detect for IgG or IgA RFs. The pathology of HGPW may reveal mild perivascular lymphocytic infiltrate and erythrocyte extravasation, or LCV as was seen in the present case (Figure 2).[1]

Diagnosis of HGPW may prompt screening for hematological and rheumatological disease owing to underlying

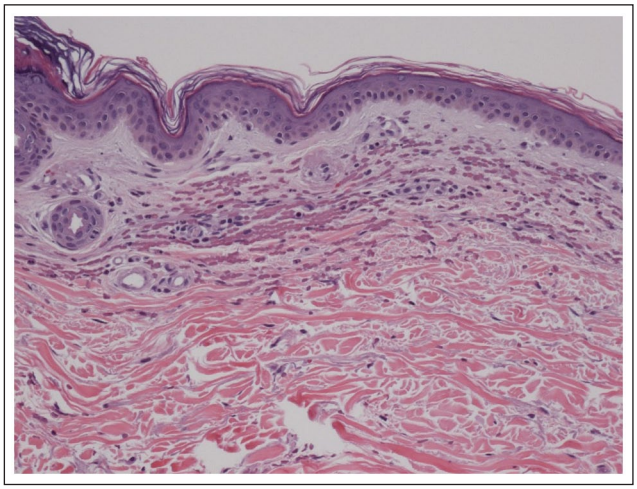

Figure 2. Extensive red blood cell extravasation in upper dermis, with perivascular neutrophils and focal fibrinoid necrosis of the small vessel wall (hematoxylin & eosin, 20× original magnification).

Table 2. Selected disorders associated with hypergammaglobulinemic purpura of Waldenström.

Henoch-Schonlein purpura[14]
Lymphoma[8]
Myeloma[3–5]
Rheumatoid arthritis[6]
Sarcoidosis[14–17]
Sjögren's syndrome[6,7]
Systemic lupus erythematosus[12,13]
Tuberculosis[14,18]

associations, especially Sjogren's syndrome, lupus erythematosus and rheumatoid arthritis.[1,6,7,12,13] Less common associations include granulomatous disorders like sarcoidosis and tuberculosis (Table 2). Notably, our patient had an underlying diagnosis of myeloma but no other known connective tissue diseases. HGPW associated with myeloma is very rare with only several cases previously reported to our knowledge.[3–5] In a report by Savin, a patient had recurrent episodes of extensive self-resolving purpura involving the extremities prior to their diagnosis of myeloma.[5] Rogers and Welch described a male patient who had hypergammaglobulinemic purpura a decade prior to his diagnosis of myeloma.[4] Shalit et al. reported a case of a male patient who was admitted for recurrent purpura. Skin biopsy showed IgA deposition in blood vessels. Two years prior to their admission, the patient also had an asymptomatic finding of IgA type lambda monoclonal gammopathy.[3] The patient presented in the current case report had been diagnosed with monoclonal gammopathy of undetermined significance approximately 5 years prior to her first similar episode of purpuric lesions. She was diagnosed with multiple myeloma 2 years later.

The diagnosis of HGPW can be challenging as it can mimic other hemorrhagic disorders. Its predominance in women and common presentation of recurring episodes of self-resolving non-palpable petechiae and purpura without systemic symptoms may aid diagnosis. Treatment of HGPW is not always necessary but includes avoidance of triggers and wearing of support stockings; aspirin, colchicine, and dapsone have also been used. Many cases are idiopathic, but associations include autoimmune, granulomatous, and hematological disorders as well as lymphoma and myeloma.[3–5,8] Therefore, screening for underlying disorders at the initial presentation of HGPW is important.

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Informed consent

The patient provided informed consent for publication of the case report and images.

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