SKIN

BRIEF ARTICLE

Cryoglobulinemia Type I in Patient with History of Monoclonal Gammopathy of Unknown Significance: A Case Report

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ABSTRACT

Cryoglobulinemia is a form of vasculitis causing inflammation of the blood vessels due to aggregated proteins that clump together at cold temperatures, causing damage to skin, muscles, nerves, and other organs. An elderly black female presented with superficial ulceration with overlying eschar within areas of retiform purpura of her bilateral thighs present for 8 months. She was previously diagnosed with vaso-occlusive disease before presenting to our clinic for further evaluation and management. Upon investigation, we have concluded that the patient has cryoglobulinemia type I.

INTRODUCTION

Cryoglobulinemia vasculitis (CV) is a rare immune complex-mediated inflammation of blood vessels caused by proteins called cryoglobulins that precipitate from an individual's serum or plasma at temperatures lower than 37°C.[1] Due to the rarity of disease, heterogeneity of clinical presentations, and other associated lymphoproliferative disorders or infections, cryoglobulinemia can often be misdiagnosed before a correct diagnosis and treatment plan is made.[2] Here we describe a case of cryoglobulinemia type I in a patient with history of monoclonal gammopathy of unknown significance (MGUS), cold induced urticaria, and other comorbidities.

CASE REPORT

A 69-year-old black female presented to the dermatology clinic with a past medical history of monoclonal gammopathy of unknown significance (MGUS), cold induced urticaria, hypertension, hyperlipidemia, and diabetes mellitus. History of present illness is significant for an 8-month history of dark discoloration associated with pain and bruising on her bilateral thighs. The patient stated the area worsened over time since her initial presentation. The patient denied fever, unexplained weight loss, myalgias, arthralgias, malaise, or enlargement of lymph nodes.

She underwent previous evaluation at another clinic 2 months prior which included a shave biopsy from her right anterior proximal thigh that showed showed vaso-occlusive disease with focal areas of epidermal necrosis, multiple small vessels with fibrin thrombi, minimal associated inflammation, with no evidence of leukocytoclasis. The patient was given

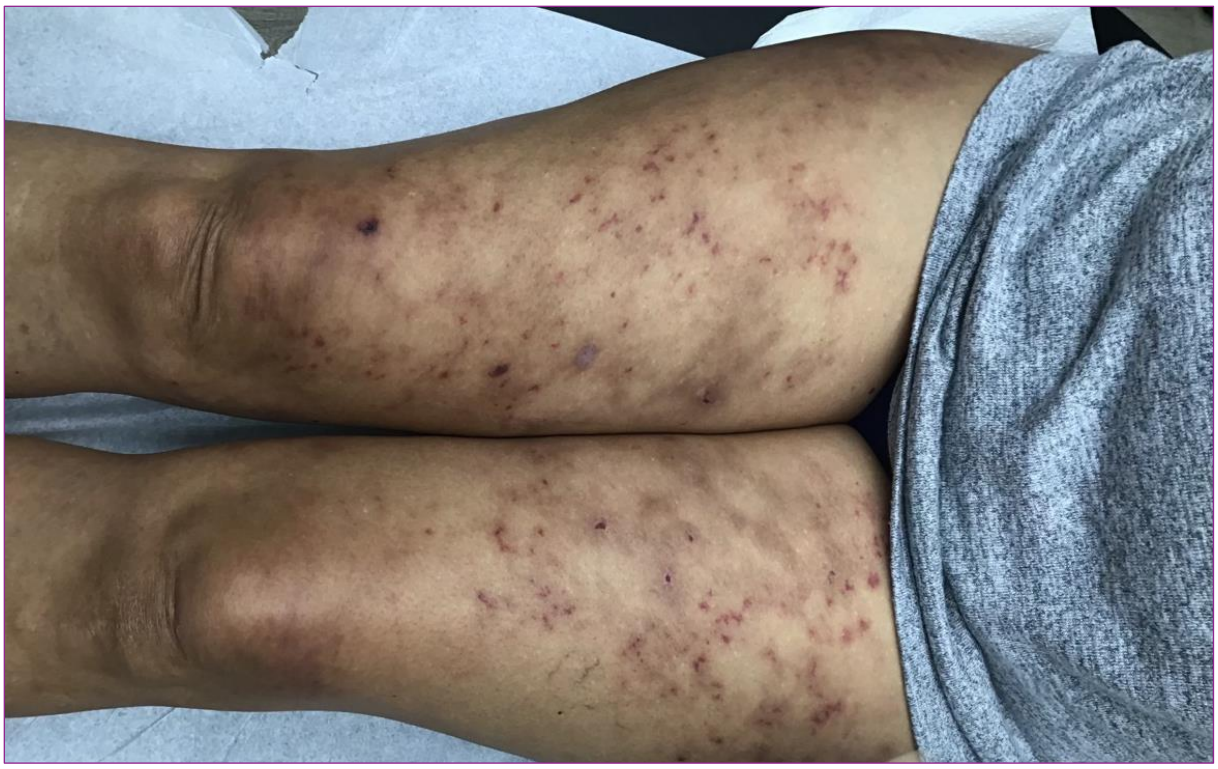

Figure 1. Superficial ulceration with overlying eschar within areas of retiform purpura of bilateral thighs.

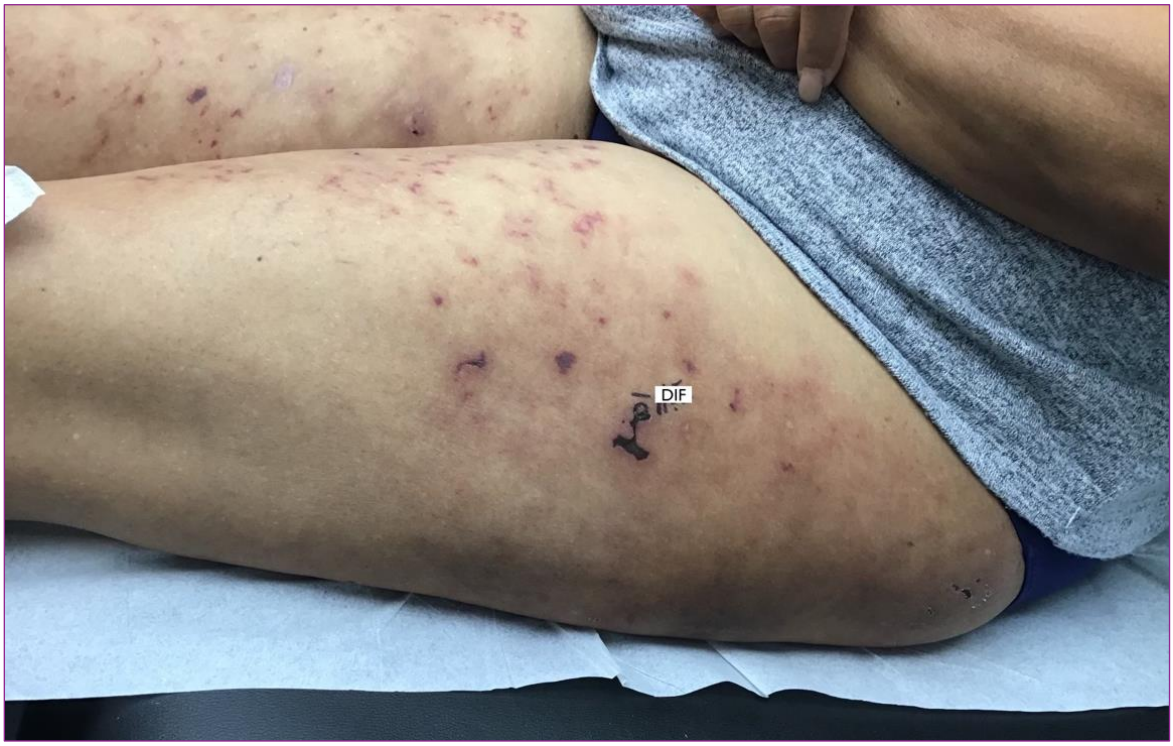

Figure 2. Site of 4mm punch biopsy on left thigh.

triamcinolone acetonide 0.1% topical cream twice daily with minimal improvement.

Physical examination showed superficial ulceration with overlying eschar within areas of retiform purpura of bilateral thighs (**Figure 1**). Two 4 mm punch biopsies were taken from her bilateral thighs (**Figure 2 and 3**). H&E from the right thigh showed non-inflammatory thrombosis compatible with cryoglobulinemia type I. Biopsy of the left thigh stained with DIF revealed intravascular deposition of IgM, C3, and fibrinogen in the papillary vascular plexus with no deposition of IgG or IgA. The immunofluorescent pattern of single monoclonal antibody deposition (IgM without IgG) is suggestive of cryoglobulinemia type I.

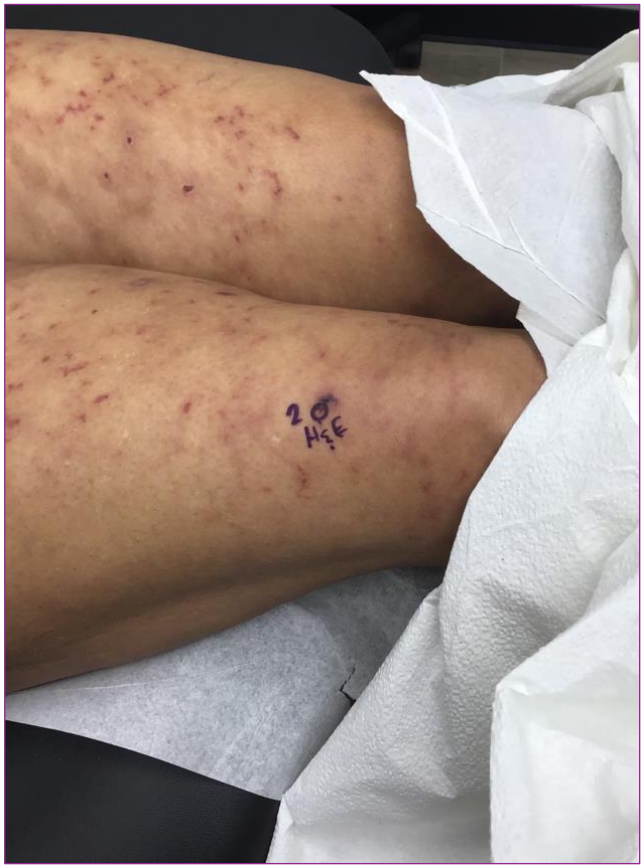

Figure 3. Site of 4mm punch biopsy on right thigh.

Laboratory work including ANA, Rheumatoid Factor (RF), Hepatitis Panel (Hepatitis B and C), Hepatic Function Panel, Complement Components (C3C and C4C), and Total Complement were ordered. Labs revealed negative ANA, RF, and Hepatitis Panel (B and C); Complement Component C3C of 133 mg/dL (normal 83-193 mg/dL), Complement Component C4C of 5L (15-57 mg/dL), and Total Complement (CH50) of <13 L (range 31-60 U/mL) that was verified by repeat analysis.

She was referred to hematology-oncology for further management and was treated with rituximab and a prednisone taper. At the 4 month follow up, she finished treatment and did well with no recurrence of symptoms. Her laboratory values identified IgG 1100, IgA 237, IgM 36, a free light chain Kappa Lambda ratio of 0.34, and a cryoglobulin serum level of 36. To date, she continues to be monitored by hematology and oncology for her cryoglobulinemia Type I and MGUS.

DISCUSSION

Cryoglobulinemia can be divided into type I, II, or III. Type I consists of monoclonal immunoglobulins, whereas type II and type III, also referred to as mixed cryoglobulinemia, is a combination of polyclonal immunoglobulins with both monoclonal immunoglobulins and rheumatoid factor activity.[3]

The most predictive measure for cryoglobulinemia is based on the measurement of cryoglobulin coupled with low C4 complement level. Our patient had both a low C4 and total complement level, suggestive of cryoglobulinemia.

Most CV patients have chronic hepatitis C, a finding more common in mixed

cryoglobulinemia.[4] Mixed cryoglobulinemia is often associated with infections such as hepatitis B, hepatitis C, and HIV, autoimmune diseases such as SLE and Sjogren's and lymphoproliferative disorders. However, our patient was unique in that she developed cryoglobulinemia vasculitis in the absence of hepatitis B and C.

In the absence of hepatitis C infection, non-infectious origins such as lymphoproliferative disorders are commonly diagnosed among patients with CV.[5] Lymphoproliferative disorders, B cell diseases, and plasma cell dyscrasias such as multiple myeloma and monoclonal gammopathy of undetermined significance (MGUS) are more common in cryoglobulinemia type I.[3] Our patient was previously diagnosed with MGUS before the development of her CV, findings consistent with type I cryoglobulinemia. A French nationwide survey published by Terrier B, et al. found that out of 64 patients with cryoglobulinemia type I, 28 patients also had a diagnosis of MGUS.[3] Another study published by the British Journal of Hematology also found that out of 64 patients, 40% also had a diagnosis of MGUS.[6]

The immunofluorescent pattern of single monoclonal antibody deposition (IgM without IgG) is suggestive of cryoglobulinemia type 1 whereas mixed cryoglobulinemia is composed of polyclonal immunoglobulins. In our patient, immunofluorescence showed deposition of only IgM with no evidence of leukocytoclastic vasculitis, a finding which is normally seen in mixed cryoglobulinemia.[7] Type II and III (mixed) cryoglobulinemia can also be associated with rheumatoid factor (RF) activity which was negative in our patient. These biopsy and laboratory findings further suggest that this presentation is more likely cryoglobulinemia type I.

Type I cryoglobulinemia only accounts for 10-15% of people with cryoglobulinemia whereas mixed constitutes the rest.[8] Type I is most associated with cutaneous involvement including recurrent episodes of purpuric eruptions, livedo reticularis, acrocyanosis, Raynaud's syndrome, and even severe infarction skin necrosis.[9-11] Renal and neurologic involvement are more frequent findings in patients with mixed cryoglobulinemia, findings not seen in our patient.[8]

Based on presenting symptoms, physical exam findings, pathophysiology report from biopsy along with laboratory results, and current literature on cryoglobulinemia, we affirm and believe that this patient has cryoglobulinemia type I secondary to MGUS who was successfully treated with rituximab and a prednisone taper.

Consent: Patient consent was received prior to initiation of this case report and for usage of the photos and medical information within.

Conflict of Interest Disclosures: None

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