Annals of Clinical Case Reports

Case Report
Published: 19 Dec, 2022

Hyperviscosity Syndrome Multiorgan System Failure in Multiple Myeloma

Mahmoud A[1], Rana P[1,2], Beilani T[3] and Ismaiel IM[4]*

[1]*Department of Internal Medicine, St. Joseph's University Medical Center - New Jersey, USA*

[2]*School of Medicine, St. George's University - Grenada, West Indies*

[3]*College of Osteopathic Medicine, Kansas City University - Kansas City, USA*

[4]*Department of Pulmonary and Critical Care, St. Luke's University Hospital - Bethlehem Campus, USA*

Abstract

Hyperviscosity is typically seen in patients suffering from diseases such as Waldenström macroglobulinemia or sickle cell, however, is a rare occurrence in Multiple Myeloma (MM). Here we report an unusual case of a patent with MM who originally presented septic but was discovered to be suffering from hyperviscosity syndrome. Since multiple pathologies can be found in these types of patients, they may resemble a coagulopathy or infectious etiology. It is imperative to avoid diagnostic and treatment delays to avoid morbidity and mortality by exploring serum viscosity and obtaining biopsies of any lesions that may be present when hyperviscosity syndrome is on the differential. Unfortunately, in this patient, this discovery was too late, and he continued to deteriorate. He was found to have multiorgan failure and was transferred to comfort care.

Introduction

Hyperviscosity syndrome is a complication of monoclonal and polyclonal disorders associated with increased serum protein content such as plasma cells in Multiple Myeloma (MM), and white blood cells in Waldenström macroglobulinemia, and immunoglobulins in cryoglobulinemia. Classic hyperviscosity syndrome presents with the triad of easy bruising/bleeding, visual disturbances, and neurological deficits. The increase in viscosity results in decreased circulation and hypoperfusion which can result in devastating sequela [1]. We report a case of multiorgan system failure in a patient with MM with type I cryoglobulinemia causing hyperviscosity syndrome.

Case Presentation

An 80-year-old male with a past medical history of multiple myeloma status post-chemotherapy, presented with pancytopenia, sepsis secondary to Methicillin-Susceptible *Staphylococcus aureus* bacteremia of unknown source, and multiple purpuric rashes of the lower extremities. The hospital course was complicated by worsening sepsis and acute kidney and liver failure. He was intubated due to worsening encephalopathy and hypoxia. Renal replacement therapy was initiated. Work up was negative for thrombotic thrombocytopenic purpura and haptoglobin level was normal. Brain imagining was negative for acute changes. A transesophageal echocardiogram was negative for cardiac vegetations. Serum viscosity was elevated to 2.06 (Normal: 1.4-1.8). Serum was positive for Type I cryoglobulin. A skin biopsy showed leukocytoclastic vasculitis with intravascular deposits consistent with cryoglobulinemia. Due to the patient's severe symptomatic cryoglobulinemia with multiorgan failure, Total Plasma Exchange (TPE) was initiated. Skin lesions progressed into significant excoriations and large ulcerations with persistent bacteremia. Despite multiple sessions of TPE and broad-spectrum antibiotic therapy, he continued to deteriorate. The family decided to transition him to comfort care.

Discussion

Hyperviscosity efficacy syndrome is a hematological and oncological emergency caused by elevated blood viscosity resulting from an increase in serum proteins, red blood cells, white blood cells, platelets, or abnormally shaped cells. This reduced flow can have dangerous consequences throughout the body including hypertension, abnormal bleeding, sepsis, visual and auditory deficits, and organ failure due to hypoperfusion and cell aggregation.

Hyperviscosity is a complication of disorders associated with increased serum protein

OPEN ACCESS

Correspondence:
Anas Mahmoud, Department of Internal Medicine, St. Joseph's University Medical Center, 703 Main St, Paterson, NJ 07503, New Jersey, USA, E-mail: dranasmah@gmail.com

Received Date: *16 Nov 2022*
Accepted Date: *15 Dec 2022*
Published Date: *19 Dec 2022*

Citation:
Mahmoud A, Rana P, Beilani T, Ismaiel IM. Hyperviscosity Syndrome Multiorgan System Failure in Multiple Myeloma. Ann Clin Case Rep. 2022; 7: 2364.

ISSN: 2474-1655.

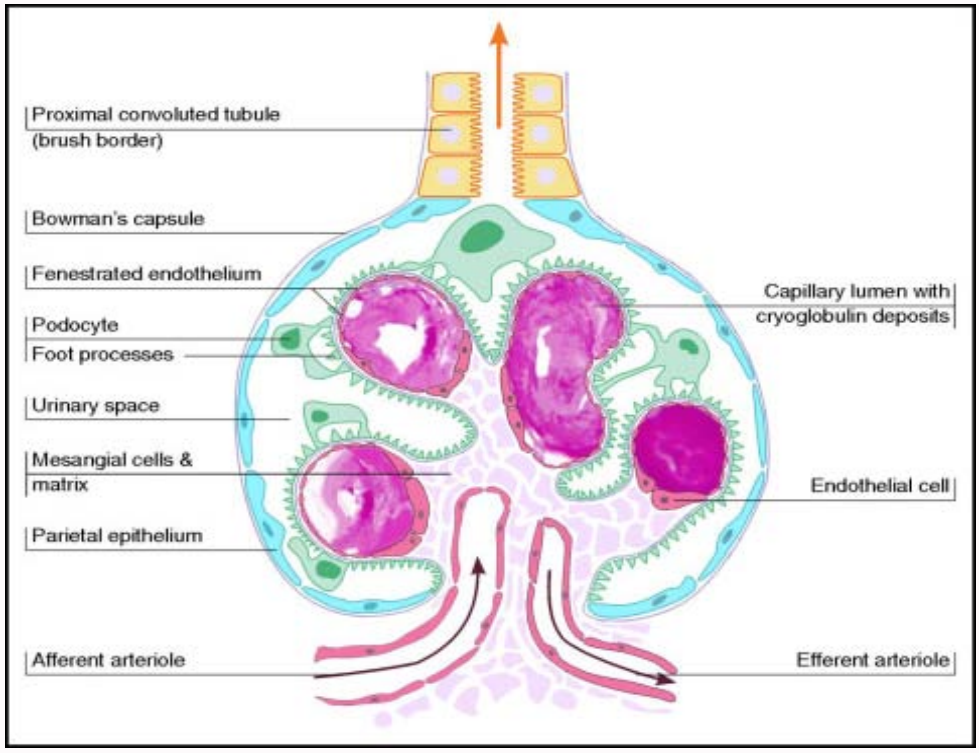

Figure 1: Schematic illustration of vascular occlusion in type I cryoglobulinemia, demonstrating glomerular intracapillary thrombi [6].

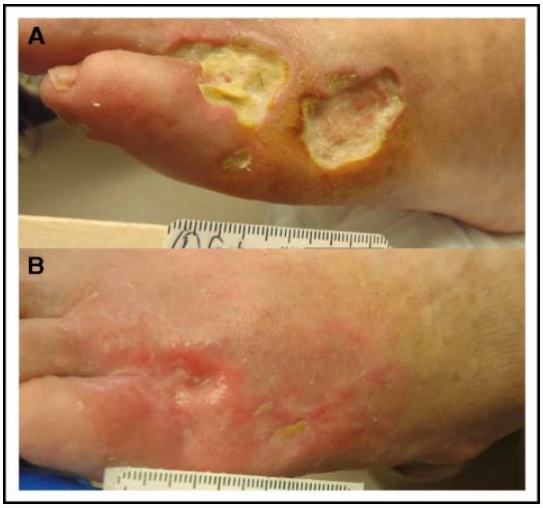

Figure 2: (A) Three skin ulcers at the anterolateral dorsum of the left foot in a patient with newly diagnosed WM-associated mixed cryoglobulinemia. (B) The ulcers healed within 3 months from initiation of definitive therapy for WM [6].

content such as in Multiple Myeloma (MM), Waldenström macroglobulinemia, and cryoglobulinemia or cell deformity as seen in Sickle cell disease and spherocytosis. Hyperviscosity is symptomatic in about 10% to 30% of Waldenström macroglobulinemia cases, however, is a rare occurrence in MM reported in only 2% to 6% of cases [2] (Figure 1).

A small subset of MM cases are associated with cryoglobulins, in particular, type I which are made of a specific immunoglobulin. Cryoglobulinemia is a form of life-threatening vasculitis with the presence of abnormal proteins that precipitate in cold temperatures or at room temperature in high quantities [3]. It may manifest as skin lesions in 50% of cases (Figure 2) and neurologic and renal involvements in 47% and 30% of cases [4,5]. Asymptomatic cryoglobulinemia doesn't warrant treatment, however, in symptomatic patients, treatment with immunosuppression should be initiated promptly and be directed against the underlying disorder (Figure 3).

The pathogenesis process of cryoprecipitation is not completely understood, however, differs depending on the type of cryoglobulinemia. Type II and III cryoglobulinemia involves the formation of immune complexes between the crystallizable Fc portion of the polyclonal IgG and IgM (rarely IgG or IgA) rheumatoid factors. Type I, on the other hand, the monoclonal component undergoes crystallization and aggregation due to temperature and concentration changes [3]. This can lead to small blood vessel occlusion without much inflammatory response (Figure 1).

Diagnosis of cryoglobulinemia is typically made clinically with the presence of cryoglobulins in the serum. When detected, measurement of the relative volume of the precipitate to total serum volume should be recorded as the cryocrit which will correlate with symptomatic disease. However, there is a poor correlation between cryocrit and the response to treatment [3]. Monitoring cryocrit during TPE might, however, help assess the response to therapy and determine the length of treatment [6]. There is controversy over whether whole blood viscosity or serum viscosity should be used for definitive diagnosis, but most clinical laboratories measure the viscosity of the serum component of blood. Viscosity is measured in the unit of centipoise (cp). The normal range of serum viscosity can be from 1.4 cp to 1.8 cp, with water being 1.0 cp.

In a study with eighty-six patients with cryoglobulinemia who underwent repeated clinical evaluation during the course of their

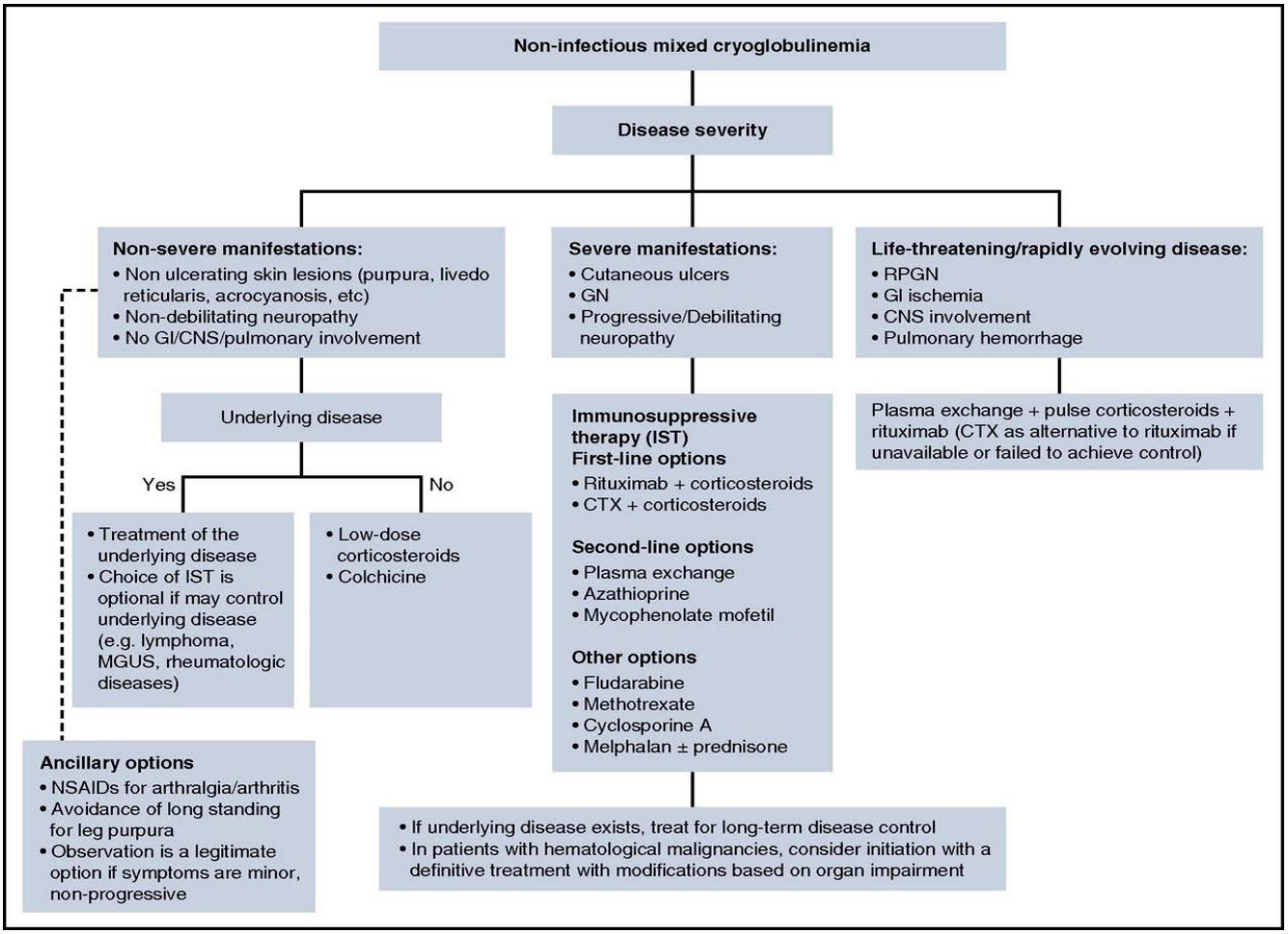

Figure 3: Management algorithm for non-infectious mixed cryoglobulinemia [6].

disease, 10% had acute and severe symptoms which necessitated emergency treatment with plasmapheresis and chemotherapy [7]. According to the recent guideline, TPE is listed as a Category II, grade 2A recommendation for the treatment of symptomatic cryoglobulinemia [8].

Treatment plans differ between infectious causes such as HCV versus noninfectious. Due to the rarity of noninfectious cryoglobulinemia, treatment data is limited. Treatment of symptomatic hyperviscosity does warrant TPE but should always parallel therapy targeting the underlying disease. It becomes difficult to design a treatment plan due to the heterogenic nature of the disease. The NCCN guidelines for patients with MM recommend induction therapy with Bortezomib, lenalidomide, and dexamethasone (category 1) regimen with the combination of bone-targeted treatment (bisphosphonates or denosumab). Patients with severe manifestations such as RPGN or GI ischemia need urgent intervention to suppress immune complex formation which is accomplished with Immunosuppressive Therapy (IST) as well. IST is primarily based on high-dose corticosteroids, cyclophosphamide, rituximab, and plasmapheresis (Figure 3).

It is also imperative to educate patients on avoiding exposure to cold temperatures by wearing warm clothes in air-conditioned facilities, gloves outside, and relocating to a warmer climate during the winter months. Foot and leg care is important to prevent wound complications. Checking the feet every day, wearing shoes and socks at all times, and trimming toenails with care should be incorporated [3].

Conclusion

In summary, type I cryoglobulinemia associated with MM is only rarely reported. Treatment recommendations include plasmapheresis and treatment of the underlying myeloma [3]. Prognosis will depend on the underlying disease. It is important to note that diagnostic delays can result in severe manifestations and multiple organ damage which would increase the mortality rate. Treatment approaches for severe type I cryoglobulinemia should involve plasmapheresis and include specific MM treatments to be introduced at an early stage to avoid cryoglobulinemia relapse [9]. Patient education on understanding their condition and the preventions they can take is vital to their success as well.

References

1. Adams BD, Baker R, Lopez JA, Spencer S. Myeloproliferative disorders and the hyperviscosity syndrome. Emerg Med Clin North Am. 2009;27(3):459-76.

2. Kwaan HC. Hyperviscosity in plasma cell dyscrasias. Clin Hemorheol Microcirc. 2013;55(1):75-83.

3. Muchtar E, Magen H, Gertz MA. How I treat cryoglobulinemia. Blood. 2017;129(3):289-98.

4. Néel A, Perrin F, Decaux O, Dejoie T, Tessoulin B, Halliez M, et al. Long-

term outcome of monoclonal (type 1) cryoglobulinemia. Am J Hematol. 2014;89(2):156-61.

5. Terrier B, Karras A, Kahn JE, Le Guenno G, Marie I, Benarous L, et al. The spectrum of type I cryoglobulinemia vasculitis: new insights based on 64 cases. Medicine (Baltimore). 2013;92(2):61-8.
6. Kaplan AA. Therapeutic plasma exchange: core curriculum 2008. Am J Kidney Dis. 2008;52:1180-96.
7. Brouet JC, Clauvel JP, Danon F, Klein M, Seligmann M. Biologic and clinical significance of cryoglobulins: A report of 86 cases. Am J Med. 1974;57:775-88.
8. Padmanabhan A, Connelly-Smith L, Aqui N, Balogun RA, Klingel R, Meyer E, et al. Guidelines on the use of therapeutic apheresis in clinical practice - evidence-based approach from the writing committee of the American Society for Apheresis: The Eighth Special Issue. J Clin Apher. 2019;34(3):171-354.
9. Judith P, Livartowski J, Kavian N, Chandesris O, Dupin N, Wallet N, et al. "Type I cryoglobulinemia in multiple myeloma, a rare entity: Analysis of clinical and biological characteristics of seven cases and review of the literature. Leuk Lymphoma 2012;54(4):767-77.