A Case of Type 1 Cryoglobulinemia with Waldenstrom's macroglobulinemia/Lymphoplasmocytic lymphoma and Dry Gangrene

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Background

Waldenström macroglobulinemia (WM) is a rare, indolent B-cell malignancy, characterized by the infiltration of plasma cells, plasmacytoid lymphocytes, and small lymphocytes to the bone marrow. (1-2) In rare cases, WM complicates by cryoglobulinemia, especially type I cryoglobulinemia, which usually presents with cutaneous and renal manifestations such as Raynaud's phenomenon, purpura, livedo reticularis, cutaneous ulcers, gangrene. **(2-5)** The following case report describes a patient with a long-standing history of Raynaud's phenomenon presenting with limb necrosis.

Case Report

This is a 68-year-old male with PMH of Raynaud's phenomenon, prior pulmonary embolism (taking Apixaban 2.5 BID), peripheral neuropathy, hypertension, asthma, and GERD who presented to an outside hospital with sudden onset of pain, skin pallor, decreased sensation, and swelling of the right hand, which was not associated to any recent trauma. Physical exam was significant for pallor of both hands however, the right hand was cooler compared to the left. The sensation of the dorsal aspect of the right hand was decreased. Bilateral radial and ulnar pulses were symmetric and bounding. His laboratory data was significant for normal white blood cell count (8.1 x 10^9/L), mild anemia (Hgb 12.7 g/dL), hyponatremia (130 mEq), abnormal coagulations (INR 1.59; PTT 62.2).

He was immediately placed on a heparin drip due to concern for acute limb ischemia. Unfortunately, during his hospital admission the patient developed similar skin changes to left foot (Image 4-5). A thromboembolic workup was conducted; ECHO revealed mild aortic stenosis but otherwise no abnormality. Upper and lower extremity duplex ultrasound revealed vessels patency with no evidence of thrombus. CTA confirmed right upper extremity arterial patency. T this point, a hypercoagulability workup was initiated. Skin biopsy was performed, revealing intraluminal vascular deposits of cryoglobulins. A bone marrow biopsy revealed >30% lymphoplasmacytic infiltration exhibiting MYD88 L265P mutation; findings consistent with Waldenstrom's Macroglobulinemia. Baseline serum IgM was 150 mg/dL with normal FLC and K/L ratio. HIV, HBV, and HCV were negative. He was treated with plasma exchange (PLEX) on presentation to reduce the circulating immune complex burden. After completing PLEX, he was treated with 1 cycle of Bendamustine/Rituximab (BR) and a rapid taper of corticosteroids.

One month later, he presented to our hospital with 2 days history of fatigue, fevers, and chills. His physical exam revealed extensive dry gangrene of his right fingers and left foot which was markedly worse from his prior hospitalization (Image 2), however without signs of infection. His laboratory data was unremarkable. Given the concern for systemic infection, the patient was started on broad spectrum antibiotics, in addition to therapeutic anticoagulation with Lovenox, as there was concern for worsening ischemia.

Case Report

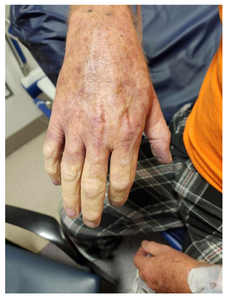

Image 1

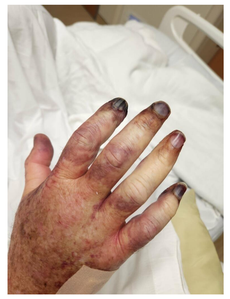

Image 2

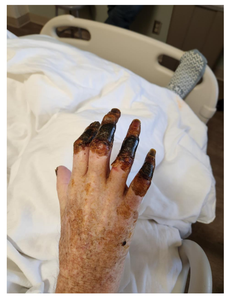

Image 3

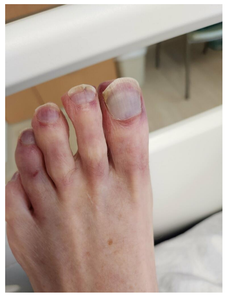

Image 4

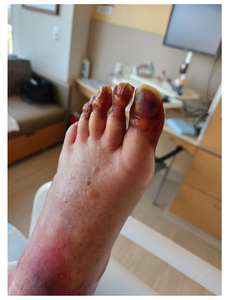

Image 5

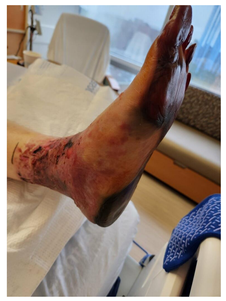

Image 6

Further work up showed his serum viscosity to be within normal limits (1.4). IgM was within upper limit of normal (171 mg /dL). A CTA of the right upper extremity with and without contrast was a somewhat limited study however showed normal-appearing arteries. CTA abdomen aorta with runoff revealed no significant peripheral artery disease. US ABI of the left foot was 1.37, while right foot was 1.36. Blood cultures obtained on admission were without growth after 48 hours.

Due to patent arterial vasculature of his extremities, vascular surgery elected not to intervene. Although the arterial flow to the foot was intact, this was not salvageable due to extensive necrosis (Image 6). Thus, general surgery offered a left below the knee amputation to provide the best functional outcome, which the patient was agreeable to. Surgical specimen of the left lower extremity showed ischemic gangrene of soft tissue and skin of the foot with no evidence of osteomyelitis, and severe atherosclerosis of the anterior and posterior tibial arteries, with viable resection margins. Due to gangrene in the right second, third, fourth, and fifth fingers (Image 3), hand surgery was consulted and recommended autoamputation of the R fingers to optimize wound healing. The patient was to continue Augmentin for duration to be determined until his fingers auto amputated and continue anticoagulation with Apixaban 2.5 mg BID. The patient was then discharged with the plan to undergo cycle 2 of his bendamustine/rituxan with his outpatient hematologist and oncologist.

Discussion

Waldenstrom's macroglobulinemia (WM) is rare case of non-Hodgkin lymphoma (incidence 2%). The clinical features of WM arise secondary to organ infiltration by clonal B cells and IgM, in addition to specific immunologic and physio-chemical properties of circulating pentameric IgM. The former may lead to anemia, lymphadenopathy, and hepatosplenomegaly while the latter may cause cryoglobulinemia with subsequent hyperviscosity and symptoms related to vascular occlusion (6,7). This patient had a history of Raynaud's phenomenon and arthralgia which could have been early manifestations of Type I cryoglobulinemia with eventual development of digital ischemia and gangrene likely from hyperviscosity syndrome.

There have been few cases of reported gangrenous necrosis associated with Waldenstrom's macroglobulinemia (8-10). This is one of few cases in which a patient had developed dry gangrene due to underlying Waldenstrom's Macroglobulinemia and type 1 cryoglobulinemia. His extensive limb gangrene warranted treatment for hyperviscosity with plasmapheresis during his prior hospitalization, which has been proven to be more effective in decreasing plasma viscosity and IgM levels in patients with WM (11).

To control malignant clonal cells, this patient underwent the standard treatment for symptomatic Waldenstrom's Macroglobulinemia, consisting of Bendamustine plus rituximab (BR), which is usually given for 4 to 6 cycles **(12)**, and a steroid taper.

Conclusion

We present here a rare case of dry gangrene in the setting of type 1 cryoglobulinemia with Waldenstrom's Macroglobulinemia. Though his limb ischemia was irreversible on presentation, prompt and appropriate treatment may help in preventing future episodes of limb ischemia in addition to prolonging median progression-free survival. The patient's preference in choosing to undergo L BKA may also reduce future sources of infection.

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This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.