

Multiple Myeloma with Gangrene of all Four Extremities

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Abstract

Introduction: Multiple myeloma represents a malignant proliferation of plasma cells derived from a single clone and it results in bone pain or fracture, renal failure, susceptibility to infections, anemia, and hypercalcemia. The hyperviscosity syndrome is rare. Cryoglobulins are immunoglobulins that precipitate in the cold temperature less than 37°C. Monoclonal cryoglobulins are associated with a significant hematologic disorder and are often asymptomatic. We reported the second case of multiple myeloma with gangrene of all four extremities.

Case: The Patient was a 77 year-old farmer who was referred due to 2-weeks history of blue, cold and painful fingers spread to middle of forearms and forelegs which was accompanied by feet skin erosions, dark points on auricle and discoloration of nose tip. In physical examination, quadrigangrene associated with auricle and tip of nose ischemia was seen. Serum proteins electrophoresis demonstrated monoclonal gammopathy and serum was positive for cryoglobulin. Bone marrow study showed neoplastic plasma cells infiltration. The patient with cryoglobulinemia, based on multiple myeloma was treated.

Keywords: Multiple myeloma, cryoglobulinemia, gangrene

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Introduction

Multiple myeloma represents a malignant proliferation of plasma cells derived from a single clone and it results in bone pain or fracture, renal failure, susceptibility to infections, anemia, hypercalcemia and occasionally clotting abnormalities, neurologic symptoms and hyperviscosity vascular manifestations.(1) Hyperviscosity is defined on the basis of the relative viscosity of serum as compared with water, Normal relative serum viscosity is 1.8, symptoms of hyperviscosity occur at a level of 5 to 6.(1) The hyperviscosity syndrome results from high levels of proteins capable of increasing the serum viscosity.(2-5) Cryoglobulinemia refers to the presence in serum of immunoglobulins that precipitate at a cold temperature.(6) Type I cryoglobulins are single monoclonal immunoglobulins usually associated with hematological disorders, Types II and III are mixed cryoglobulins, composed of monoclonal or polyclonal IgM respectively, having rheumatoid factor activity that bind to polyclonal immunoglobulins. (6) Type I cryoglobulins account for 10-15% of the total. (6) These are composed of a single monoclonal

immunoglobulin usually a IgM paraprotein, less frequently IgG Although overlap exists among the clinical features of types I, II and III cryoglobulinemia, in general type I rarely causes symptoms related to vasculitis and tends to be associated with signs of peripheral vessel occlusion and clinical manifestations related to hyperviscosity syndrome may be observed as well as purpura lesions, acrocyanosis, Raynaud phenomena, dystrophic manifestations until formation of torpid ulcers and gangrene.(2-5) Type I cryoglobulinemia is usually found associated to lymphoproliferative diseases and patients are clinically indistinguishable from those with Waldenström's macroglobulinemia, multiple myeloma, immunocytoma or chronic lymphocytic leukemia.(6) In many cases cryoglobulins and a high cryocrit may be only a casual finding.(6)

Case Report

The Patient was a 77- years old farmer who was referred with blue, painful and cold fingers of upper & lower extremities. These features have been since 2 weeks ago and developed gradually to middle of forearms and forelegs (figure 1). Simultaneously,



Fig. 1



Fig. 2

tip of nose discoloration & black points on auricle were established (figure 2). Multiple erosive lesions were developed till above the ankles. Patient's problems began 2 years ago, presenting blisters and cutaneous ulcer on lower extremities, which have been recovered and presented again on another point that have been treated by corticosteroid as pemphigus disease from 6 month ago, and a relative recovery have had.

Two weeks ago, he had an upper respiratory tract infection that was treated with penicillin and antihistamine. After 3 days large blisters appeared on lower extremities till above ankle and fingers discoloration developed to middle of forearms and forelegs.

In physical examination, the patient appeared toxic, febrile (38.5°C oral). The conjunctiva was pale. Tip of nose ischemia and necrosis, and auricle ischemia were seen. No lymphadenopathy was detected. Grade 2/6 systolic murmur was auscultated. Bilateral pulmonary fine crackles were found. On upper extremities fingers gangrene with indefinite border ischemia till middle of forearms was seen.

No radial pulsation was found. On lower extremities fingers gangrene and developed ischemia till middle of forelegs in association with no dorsal pedis pulsation were seen. No more positive point was detected in physical examination. Laboratory finding including WBC=34×10³/μl, Hb= 7.3 g/dl, Hct= 21.9 %, Plt= 468×10³/μl, ESR= 148 mm in 1h, PT= 20 sec, PTT= 73 sec, INR= 2.6, Ca= 7.5 mg/dl, P= 3.8 mg/dl, Urea= 107 mg/dl, Cr =1.6 mg/dl, Na= 144 mmol/l, K= 4.1 mmol/l, AST= 582 IU/l, ALT= 378 IU/l, Alk Ph= 206 IU/l, Total Bil= 0.4 mg/dl, Direct Bil= 0.1 mg/dl, Alb=3.6 g/dl, LDH= 404 IU/l, C₃= 54 mg/dl, C₄= 15 mg/dl, IgG= 7.3 g/dl, Anticardiolipin Ab= 3 GPL, positive RF, HbsAg and HCV Ab and VDRL and ANA and Direct & Indirect Coombs test and blood culture were negative. Chest x ray was normal. Serum proteins electrophoresis demonstrated monoclonal gammopathy (Fig. 3) with positive cryoglobulinemia (Fig. 4).

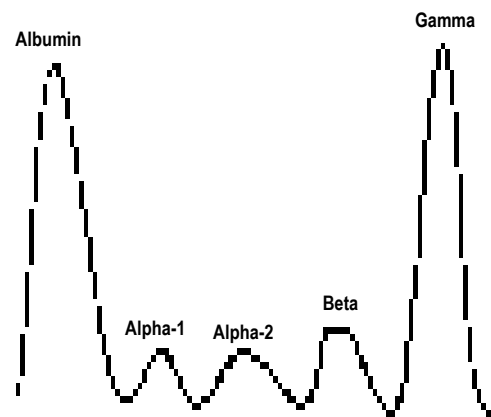


Fig 3- Serum proteins electrophoresis

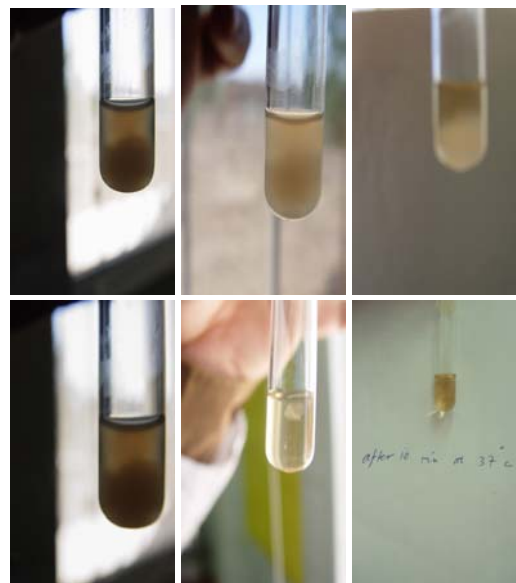


Fig. 4- Cryoglobulin precipitation and dissolving on 37°C

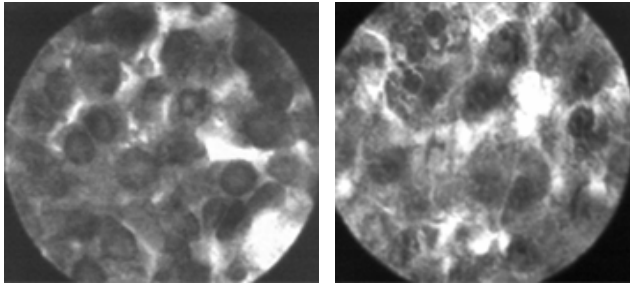


Fig. 5- Bone marrow sampling

In paraclinic: In ECG, RBBB was seen. No mass was seen within cardiac cavity in echocardiography. Bone marrow aspiration showed plasma cells (66%) and bone marrow biopsy had 60-80% cellularity with myeloid to erythroid ratio of 3 and bone marrow was infiltrated by neoplastic plasma cells (Fig. 5).

He was treated with plasmapheresis 3 lit/d and VAD combination chemotherapy (vincristine, 4 mg/d in a 4-day continuous infusion, doxorubicin 12 mg/d in a 4-day continuous infusion, dexamethasone 40 mg/d for 4 day). This choice of chemotherapy was selected because of its rapid response. His extremities should be amputated but he didn't accept. He died after several days.

Discussion

Cryoglobulins are found in wide spectrum of diseases such as malignancies, infections and systemic autoimmune diseases which include three different types as monoclonal, polyclonal and essential mixed cryoglobulinemia.(7)

In our patient, monoclonal cryoglobulin was detected which is typically seen in myeloproliferative disorders such as multiple myeloma. Several case-reports have been presented about cryoglobulinemia presentations in multiple myeloma which have reported fingers gangrene, diffuse livedoreticularis (8), vasculitis, cutaneous

ulcers(9) and gall bladder gangrene(10) but only one diffuse and extensive gangrene in form of quadrigangrene till middle of forearm and forelegs due to cryoglobulinemia has been reported(11) so with this point of view, current presented case is the second one.

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