
Blood Hyperviscosity Syndrome Revealing Multiple Myeloma in Emergency Department: Report of a New Case

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Abstract

Introduction: Blood hyperviscosity syndrome is a rare and serious complication of multiple myeloma. It is an unusual mode of presentation of multiple myeloma.

Case presentation: A 60-year-old man admitted to the emergency department for hemorrhagic syndrome. Two days before his admission, he presented epistaxis with neurosensory signs. Blood count showed platelets at 139000/mm³, normochromic normocytic anemia. Peripheric blood smear showed erythrocytes in rolls. Serum protein electrophoresis showed monoclonal gammapathies and immunonephelometric assay showed an IgG Kappa. The myelogram showed a plasmocyte infiltration at 55%. There was no bone lytic lesion visible on standard X-ray. The diagnosis of IgG Kappa stage III multiple myeloma was retained.

Discussion: Blood hyperviscosity syndrome is a therapeutic emergency; it is defined by all the manifestations related to the elevation of blood viscosity. Raising the concentration of plasma proteins increases the plasma viscosity in a variable, inter-individual and multi-elemental manner, including molecular weight, structure, concentration, and ability to form aggregates which could explain the rarity of IgG involvement in the genesis of blood hyperviscosity (low molecular weight, isomeric structure). This IgG is secreted by a plasmocytic clone invading the bone marrow characterizing multiple myeloma.

Key words: Blood hyperviscosity syndrome, multiple myeloma, IgG monoclonal gammapathy
Introduction

Blood Hyperviscosity Syndrome (BHVS) is a medical therapeutic emergency. It is defined as the set of clinical manifestations secondary to the elevation of the blood or plasma viscosity, leading to a lack of tissue oxygenation. The viscosity of a fluid is defined as a resistance to flow. It depends on several parameters that allow to classify it into cellular and plasma viscosity. This last one can be increased by changing its composition in water and in macromolecules (globulins, albumin, fibrinogen). Thus, monoclonal gammapathy (MG) may be a cause of plasma hyperviscosity, especially in multiple myeloma (MM), which is a malignant hemopathy characterized by a monoclonal plasmocytic proliferation invading the hematopoietic bone marrow.

Case presentation

A 60-year-old patient having a medical history of high blood pressure treated with beta blockers, chronic smoking at the rate of 15 year packs, recent hospitalization for pulmonary sepsis treated with antibiotic therapy with good evolution, was admitted to emergency department for hemorrhagic syndrome. Two days before his admission, he presented a hemorrhagic syndrome consisting of spontaneous epistaxis of average abundance, neurosensory signs such as headache, tinnitus and buzzing ear, associated with general signs made of fatigability and myalgia. He did not report bone pain or infectious signs. All this evolved in a context of apyrexia and deterioration of the general state with weight loss quantified at 10 kilograms in four months.

Clinical examination found a patient in good general condition, apyretic, conscious and well oriented in time and space. The hemodynamic status was stable. Cutaneous examination found bruising at the injection sites without associated purpuric lesions, with nasal bleeding requiring emergency anterior packing. Cardiovascular examination did not show signs of heart failure. Abdominal exam did not find hepatomegaly or splenomegaly.

The blood count test showed: platelets at 139000 element/mm$^3$, normochromic normocytic anemia (Hemoglobin = 6.2 g / dl, Mean corpuscular volume = 88%, mean corpuscular hemoglobin concentration = 31.5%). Peripheric blood smear showed erythrocytes in rolls, with no abnormality of the white cell morphology. Inflammation markers were elevated with prolonged erythrocyte sedimentation rate (ESR) at 136 mm per hour.

Biochemical assessment showed hyperproteinemia at 158 g/l, a normal renal function (creatinine at 8 mg/l), normal electrolytes without hypercalcemia.

Serum protein electrophoresis (SPEP) showed a monoclonal peak migrating into the gamma globulin zone (Figure 1). The immunoelectrophoresis-serum test (IEP-serum) showed IgG Kappa monoclonal immunoglobulin (Figure 2).

The bone marrow study showed 55% medullary plasmocytosis with dystrophic plasma cells. There was no bone lytic lesion visible on standard X-ray. The diagnosis of IgG Kappa MM was considered according to the following criteria: IgG monoclonal gammapathy (MG) and bone marrow plasmocytosis > 10%.

It was classified as symptomatic MM because of anemia, history of infections and BHVS and MM stage III according to the Durie-Salmon classification and the international staging system (ISS) {beta 2-microglobulin at 21.94mg/l (> 5, 5mg/l)}.

In the emergency department, an anterior nasal packing was performed for epistaxis to stop bleeding, a careful hydration and transfusion of 2 packed red blood cells. The patient was then transferred to the internal medicine department.
Discussion

The rheological properties of blood are complex and depend on its components: cellular or plasmatic [1]. Thus, the main determinants of blood viscosity are: cell volume, red blood cell's mechanical properties, plasma viscosity which is depending on the concentration and the nature of proteins, applied strain deformation [2].

Changes in plasma viscosity caused by a protein depend on several elements: the molecular weight (IgG: 160 000 Da, IgM: 1 million Da), the structure (IgG: isomeric, IgM: pentameric) and the ability to form aggregates. From these characteristics, we understand why it is so rare to induce a BHVS by an IgG MG compared to IgM MG, excepting the IgG3 subtype whose ability to form unstable complexes at moderate concentrations explains the most frequent occurrence of BHVS [1].

The BHVS is clinically characterized by the classic triad of Waldenstrom: mucosal bleeding (epistaxis, gum bleed etc), visual disturbances (visual acuity decline, diplopia) and neurological manifestations (headache, tinnitus, dizziness, ataxia, chorea, motor deficit, but also disturbances of consciousness up to coma with seizures) [3]. Other manifestations that may be encountered include nonspecific general signs, dyspnea, signs of heart failure, pulmonary hypertension, and signs of
microcirculatory dysregulation with livedo reticularis and necrosis of the extremities [4,5].

Hematologically, there are non-specific findings such as hemodilution anemia, the blood film showed rouleaux, prolonged ESR, disorders of coagulation tests by interaction of Ig with coagulation proteins, sometimes hypercalcemia, pseudo-hyponatremia or acute renal failure due to tubular necrosis [6]. Viscosity measurement is not done in current practice, it is carried out using a viscometer, it is expressed in milipascal.second or more commonly in centipoise, the usual values at 37°C vary between 1.4 and 1.8 cP, clinical manifestations generally appear for values exceeding 4 or 5 cP, but there are very important variations in terms of symptoms onset defining the concept of "individual threshold" [1].

The fundus examination performed in emergency usually shows a retinal microcirculation involvement with dilated tortuous vessels, secondary to blood stasis.

The causes of BHVS are dominated by MG with Waldenström's disease at the top of the list, due to the properties of IgM and its predominant intravascular distribution. MM is a rare cause of BHVS, observed in 2 to 6% of cases, and is mainly associated with IgA myeloma [1]. The other etiologies are: cryoglobulinemia, especially type I, hypergammaglobulinaemia during connective tissue diseases and certain rare causes (during HIV infection, hepatitis, or Castelman's disease, dyslipidemic myeloma, cryofibrinogenemias, some cancers especially breast cancer in its mucinous type). Myeloproliferative syndromes and abnormalities of the erythrocyte (hemoglobinopathies, abnormalities of the membrane) can also increase blood viscosity [2]. In front of evocative symptoms it is necessary to think of BHVS whose management presents certain peculiarities. Indeed, management of BHVS must be urgent, with the aim of reducing rapidly the hyperviscosity in order to control symptoms. The measures applied are divided into nonspecific: hydration, oxygenation, anemia must be considered as a protective element; however, a transfusion will be necessary in case of intolerance of anemia. And specific measures: plasmapheresis, which must be urgent at the onset of clinical signs or prophylactic, when the patient's protein levels approaches the usual "threshold" of symptoms, followed by etiological treatment [1].

References


