A rare case of multiple myeloma with several atypical manifestations

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ABSTRACT

A 75-year-old woman presented asthenia and anemia after recurrent intestinal bleeding. Colonoscopy showed the presence of blood clots in the ascending colon, without active bleeding. During hospitalization, right toe cyanosis progressed to ischemic necrosis and was resistant to analgesics and vasodilators. The positron emission tomography-computed tomography scan showed a nodular thickening in the midfield of the right lung. Blood chemistry evidenced an Immunoglobulin (Ig) G-λ monoclonal peak. Multiple myeloma (MM) was diagnosed by bone marrow biopsy and serum/urine Ig-free chain dosage. The patient no longer had intestinal bleeding after the first MM chemotherapy (CHT). After 6 months of CHT, a partial hematological response and peripheral vascular improvement occurred. Extremely rare conditions may result in MM. In this case report, seemingly unrelated atypical manifestations co-existed and responded to hematological CHT for MM, confirming their association with the disease.

Introduction

Multiple myeloma (MM) is the second most common hematological malignancy in high-income countries, characterized by a monoclonal proliferation of plasma cells resulting in the production of monoclonal antibodies.[1] An asymptomatic precursor condition, termed monoclonal gammopathy of undetermined significance (MGUS), typically precedes the disease for several years.

The main clinical features of MM are bone pain or fracture, renal failure, hypercalcemia, anemia, susceptibility to infections and occasionally clotting abnormalities, neurologic symptoms, and vascular manifestation of hyperviscosity.

There is a male predominance, and it is rare under 40 years of age. The annual age-adjusted incidence in the world is 2.1 per 100,000 and it is more common in males and black Africans.[2,3]

The etiology is unknown. However, frequent alterations in promoter genes of chromosome 14 play a role in disease development. In addition, other oncogenes such as NRAS, KRAS, and BRAF may participate in plasma cell proliferation. Other factors contributing to disease occurrence include obesity, alcohol consumption, environmental causes such as insecticides, organic solvents, Agent Orange, and radiation exposure.[4]

Extramedullary disease (EMD) is a rare but recognized manifestation of MM characterized by the involvement of several organs including skin, liver, lymphatic system, pleura, and central nervous system. The incidence is about 3-5% in newly diagnosed MM patients but it has been reported in up to 20% of patients in the relapsed MM setting. The presence of EMD has been associated with more aggressive phenotypes of MM, elevated serum lactate dehydrogenase enzyme, and altered genes.[5]

Case Report

A 75-year-old woman was hospitalized for anemia, asthenia, and weight loss (15 kgs in eight months). She had already been hospitalized more than once, elsewhere for intestinal bleeding with acute anemia and the need for blood transfusions.

Medical history included chronic ischemic heart disease treated with two coronary stentings, aortic biological valve

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replacement for valvular stenosis, hypertension, hepatic steatosis, diverticulosis of the descending sigma, breast cancer treated with surgery and radiotherapy (about 7 years before), and MGUS. No alcohol but a previous smoking habit (approximately 30 cigarettes a day).

Her current medications included Pantoprazole 40 mg, Bisoprolol 5 mg, Rifaximin 200 mg three times a day for seven days each month, Ferrous Sulfate 105 mg, and Allopurinol 300 mg.

On clinical exam, she was apyretic, with arterial blood pressure 160/90 mmHg, regular heart rate 90/min, and 98% blood O_2 saturation. Cardiovascular and respiratory examinations were unremarkable; there were neither edema nor lymphadenopathies. A diffuse soreness was elicited by deep palpation in the lower abdominal quadrants. Murphy, Blumberg, and Giordano signs were negative. Peristalsis was valid. The digital rectal examination showed red blood on gloves, no fissures.

At admission, hemoglobin values were 8.2 g/dL, with normal white cell and platelet count. Laboratory biochemistry was normal with absence of liver or renal failure and electrolyte disorders. Serum protein electrophoresis revealed a monoclonal peak of immunoglobulin (Ig) G-λ (1.56 g/dL, 19.5%) with an inverted kappa/λ ratio (0.07). The Bence-Jones proteinuria was negative. Serum oncological markers were negative, except for β_2-microglobulin. Fecal calprotectin was slightly increased by 152 mg/kg (n.v.: 120 mg/kg) (Table 1).

Due to the recurrent episodes of intestinal bleeding, serum hemoglobin level reduction, and multiple transfusion needs, a colonoscopy was performed: blood clots and residues were found in all the explored tracts, mostly in the right colon but no active source of bleeding was identified.

Video capsule endoscopic examination identified blood residues in the ascending colon but, once again, failed to identify an active source of bleeding.

At the computed tomography (CT) angiography scan, the absence of active bleeding in the whole colic frame and hyperemia of the last ileal loops' mucosa were evidenced.

For the persisting intestinal bleeding, a further colonoscopy was performed, showing the presence of clots and partially oxidized blood, mainly in the right segments, with no evidence of bleeding sources. Due to the high risk of bleeding, mucosal biopsies were not performed.

Due to the recurring anemic state, during hospitalization, the patient received in total, six concentrated red blood cell transfusions and intravenous infusion of ferric carboxymaltose; hemoglobin varied in the range of 8.0-11.2 g/dL.

Mielobiopsy confirmed the diagnosis of IgG-λ MM.

The hematology consultant requested a positron emission tomography (PET)-CT scan which showed increased tracer uptake by all the bone marrow compartment and by retromandibular, lateral, cervical, axillary, and inguinal lymph nodes. In addition, in the right mid-lung field, a nodular thickening (SUV max 5.1) was found.

The biopsy of the peri-umbilical fat performed in the suspicion of amyloidosis resulted negative.

On the 10th day of hospitalization, the patient presented pain and intermittent cyanosis of her right big toe, with a Raynaud's like symptomatology (Figure 1). Lower limb arterial Doppler ultrasound examination revealed delayed flow of the anterior and posterior tibial arteries with reduced speed on the right, normal to the left. Autoimmunity screening was negative for lupus anticoagulants, anti-cardiolipin, and anti-β_2-glycoprotein-1 antibodies. Amlodipine 5 mg first, then Nifedipine 10 drops three times a day were prescribed for vasodilation, without significant improvement. Tramadole was prescribed for pain.

Table 1. Patient's parameters at entry main serum and urinary biochemical.

Analyte	Assessed value	Normal range
Hemoglobin (g/dL)	8.2	12.0-15.5
IgG (g/L)	22.00	7.37-16.07
IgA (g/L)	1.46	0.7-4.00
IgM (g/L)	0.39	0.4-2.30
Serum protein electrophoresis		
Albumin (%)	47.5	55.8-66.1
α 1 (%)	6.7	2.9-4.9
α 2 (%)	9.5	7.1-11.8
β 1 (%)	6.8	4.7-7.2
β 2 (%)	2.1	3.2-6.5
γ (%)	27.4	11.1-18.8
Monoclonal peak (g/dL) (%)	1.56 g/dL (19.5%)	
A/G ratio (%)	0.9	1.10-2.40
Serum kappa chains (mg/L)	26.5	6.7-22.4
Serum λ chains (mg/L)	356	8.3-27
Serum K/L ratio	0.07	0.31-1.56
Urinary kappa chains (mg/L)	<7.44	<10
Urinary λ chains (mg/L)	<4.09	<5
β2-microglobulin (ng/mL)	4344	609-2366
Fecal calprotectin (mg/kg)	152	120

Table 2. Patient's laboratory values at six-month follow-up.

Analyte	Assessed value	Normal range
Hemoglobin (g/dL)	11.9	12.0-15.5
Urinary kappa chains (mg/L)	<7.28	<10
Urinary λ chains (mg/L)	4.5	<5
Serum protein electrophoresis		
Albumin (%)	57	55.8-66.1
α 1 (%)	5.9	2.9-4.9
α 2 (%)	13.2	7.1-11.8
β 1 (%)	6.2	4.7-7.2
β 2 (%)	4.5	3.2-6.5
γ (%)	13.2	11.1-18.8
Monoclonalpeak (%)	8	-
A/G ratio (%)	1.32	1.10-2.40
Serum kappa chains (mg/L)	9.2	6.7-22.4
Serum lamdba chains (mg/L)	243	8.3-27
K/L ratio	0.04	0.31-1.56

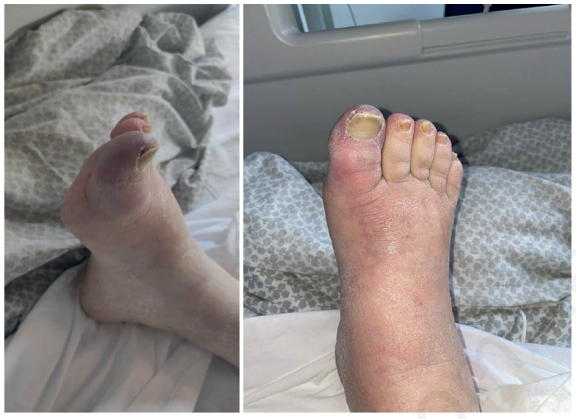

Figure 1. Right toe.

Discussion

Rare cases of bleeding of the ascending colon for amyloidosis in a patient with MM,[6,7] rare cases of hypoperfusion of extremities with toe ischemia due to hyperviscosity,[8] and rare cases of pulmonary plasmacytoma in patients with MM were separately described in the literature.[4,9,10]

After the diagnosis of MM, the patient started chemotherapy (CHT) with daratumumab – lenalidomide – dexamethasone; since the first CHT administrations, the patient had no longer presented intestinal bleeding; six months after the start of hematological therapy, the patient obtained a good partial response of the disease – according to the International Myeloma Working Group (IMWG) criteria – and the peripheral vascular symptoms partially reverted. A PET-CT scan will be scheduled for pulmonary follow-up.

The documentation reported in the literature and the response to the CHT allowed us to confirm the relationship between MM and the different atypical manifestations which initially seemed to be individual comorbidities.

Conclusions

Since the first administration, the patient has no longer presented intestinal bleeding; six months after the start of hematological therapy the patient obtained a good partial response to the disease (according to the IMWG criteria) and peripheral vascular symptoms partially regressed.

After a year of CHT, PET-CT scan repeated to investigate the pulmonary thickening revealed the complete absence of the tracer uptake.

Laboratory biochemistry showed an improvement in general values, a reduction of serum light chains, and the monoclonal peak (Table 2).

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