Non-traumatic splenic rupture in amyloidosis as a rare evolution of multiple myeloma

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Abstract

We report the case of a 64-year-old man with a diagnosis of IgG lambda multiple myeloma (MM) symptomatic for bone lesions for which he received autologous stem cell transplant after induction treatment and high-dose melphalan, thalidomide and lenalidomide therapy. Twelve years after the diagnosis, he had an unexpected and acute onset of abdominal pain with signs of hypovolemic shock. A computed tomography scan was immediately performed and demonstrated a splenic rupture. A splenectomy was performed but, a week after, the patient developed an acute respiratory distress syndrome and died. After histological exam of the spleen, non-traumatic spleen rupture due to amyloidosis was our final diagnosis. This event is potentially fatal and rare in patients with MM; clinicians should be aware of this potential course of the disease and monitor patients also for amyloid induced organ damages.

Introduction

Non-traumatic splenic rupture (NSR) is a rare event and occurs in neoplastic patients due to infiltration of the spleen with changes in its histologic structure, splenic infarcts, and coagulation disorders leading to intrasplenic and subcapsular bleeding and eventually to capsular rupture.1 NSR is a potentially fatal emergency and patients’ survival depends on both an immediate diagnosis and surgical treatment, as well as on the underlying causes. The most common ones are severe infections, malignancies, metabolic disorders, vascular, and haematological diseases. It is an unusual event in multiple myeloma (MM); otherwise amyloid light-chain (AL) amyloidosis is an established risk factor of NSR. This condition is characterized by the widespread deposits of amyloid and consequent organ damage. About 10% to 15% of patients with MM may develop AL amyloidosis while approximately 10% of patients with MM have coexistent AL amyloidosis at diagnosis. We here report the peculiar case of a patient who developed NSR due to splenic amyloidosis as evolution of his IgG lambda MM.

Case Report

The patient is a 64-year-old male with a diagnosis in 2005 of IgG lambda MM. International Staging System II, symptomatic for bone lesions. His past medical history includes atrial fibrillation, treated with amiodarone and apixaban, and colonic diverticulosis.

He underwent induction chemotherapy (CT) with thalidomide and dexamethasone, followed by peripheral stem cells mobilization with cyclophosphamide, conditioning CT with melphalan and autologous peripheral blood stem cells transplant, obtaining a complete remission (CR). He then received maintenance therapy with thalidomide and antiirassorbitive treatment with pamidronate until bone disease progression in April 2011. Therefore, first line therapy with lenalidomide plus weekly dexamethasone was performed, achieving a biochemi- cal CR. After two years, due to grade 3 neurotoxicity according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE version 4.02) and a left mandibular osteonecrosis, he discontinued the treatment; however, CR was maintained up to March 2015 when, due to bone relapse and anemia, he resumed lenalidomide at a lower dose (10 mg) plus weekly dexamethasone. Abdomen and heart ultrasounds were periodically performed and resulted normal. The treatment was continued till April 2018, when the patient, due to worsening of paresthesia, performed an electromyography that showed a severe axonal and demyelinating polyneuropathy, involving both motor and sensitive fibers of upper and lower arms. A subsequent computed tomography scan of the chest showed also a large osteolytic lesion at the VI left rib. Laboratory tests revealed an increase of serum free lambda chains with a pathological kappa/lambda ratio, anemia (haemoglobin 10.3 g/dL), an increase of beta 2 microglobulin (3500 mg/L) and a stable renal function (serum creatinine 1.47 mg/dL). Abdominal ultrasound was performed, without evidence of spleen or liver enlargements. Due to the worsening of bone pain at the hemithorax, a radiotherapy of the left rib lytic lesion was started in May 2018 with 3D conformational technique (3 Gy/day in 10 fractions). Seven day after, the patient started to complain abdominal pain; at physical examination, cold extremities and hypotension were evident. A computed tomography scan without contrast medium was urgently done and revealed a large abdominal bleeding due to splenic rupture (Figure 1). The patient didn’t report any trauma or trigger events and the spleen wasn’t involved in the radiation field (it received only a total of 0.6 Gy).

An exploratory lapatomomy with splenectomy was immediately performed. The patient was then started on fluid replacement therapy, wide spectrum antibiotics, and dopamine infusion for hypotension. Seven days after the intervention, acute respiratory distress syndrome occurred and the patient died (Figure 2).

The histological exam from surgical specimen described splenic parenchyma of 198 grams, 12×10×3 cm of diameter, with interruption of the capsule, focal areas of arterial layers dissection and eosinophilic material deposition within them, presenting green birefringence on polarized light Congo red method and configuring a diagnosis of amyloidosis.
Discussion

NSR is a rare condition that may occur in up to 0.1%-0.5% of patients with no associated trauma. A main distinction should be made between non-traumatic rupture in a pathological spleen with increased fragility, or a rupture triggered by a minor physical event, such as sneezing, coughing, vomiting, straining during defaecation or muscular exertion and defined atraumatic-idiopathic splenic rupture. This condition is extremely rare and the diagnosis should be made after exclusion of other more frequent events, following Orloff and Peksin criteria (Table 1).5,6

A systematic review regarding 845 patients with pathologic NSR evidenced that only a minority of them has no aetiological factors (7%), but the majority shows at least one causal event. They described a NSR-mortality rate of 12.2%, being splenomegaly (OR 2.34, P=0.040), age >40 years (OR 1.94, P=0.007), and neoplastic diseases (OR 2.63, P=0.008) the main factors associated with an increased NSR-related mortality. In particular hematologic malignancies, such as acute lymphatic leukemia, acute myeloid leukemia and non-Hodgkin lymphoma, were recognized as the major causes.

Another work by Renzulli et al. identifies 31 patients with NSR in amyloidosis (AL in 25/31 patients, amyloid A in 4/31, not specified in 2/31).7 Interestingly, among patients affected by AL amyloidosis, 79% (n=19) had NSR as initial manifestation of disease. In a retrospective analysis by Munford et al., 337 patients with systemic AL-amyloidosis were evaluated, with particular reference to coagulation abnormalities.5 Prolongation of prothrombin time was also recognized by mixed axonal-demyelinating peripheral neuropathy. It occurs in almost 17% of patients and it is caused by amyloid deposition in the vasa nervorum.

New oral anticoagulant treatment can also be related to NSR and a single case of NRS imputed to apixaban has been reported.8 Furthermore, coagulation cascade alterations are also common features of amyloidosis. In a retrospective analysis by Munford et al., 337 patients with systemic AL-amyloidosis were evaluated, with particular reference to coagulation abnormalities. In the reported case, the concurrence of AL amyloidosis and the ongoing anticoagulant therapy could have increased the risk of NSR.

Conclusions

AL amyloidosis can be an evolution of MM. Survival improvement in the treatment of MM due to new available therapies increased the patients’ probability to develop MM-associated amyloidosis. Clinicians

![Figure 1. Computed tomography scan of the abdomen showing splenic rupture and haemoperitoneum.](image1)

![Figure 2. Graphic summary of the evolution of patient’s disease. MM, multiple myeloma; ISS, international staging system; CT, chemotherapy; APBSC, autologous peripheral blood stem cells; CR, complete response; PD, progressive disease; NRS, non-traumatic splenic rupture; ARDS, acute respiratory distress syndrome.](image2)

Table 1. Orloff and Peksin criteria5 for the diagnosis of atraumatic-idiopathic splenic rupture.

| Criteria | Description |
|----------|-------------|
| a. | No history of trauma prior to operation or retrospectively after operation |
| b. | No evidence of disease that can affect spleen |
| c. | No evidence of perisplenic adhesions or scarring of spleen |
| d. | Spleen is normal on gross and histological examination |
| e. | Full viral studies of acute phase and convalescent sera show no significant rise in viral antibody titers (fifth criterion added by Crate and Payne) |

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should be aware of this possibility and control patients for amyloid-induced organ damage. In this context, NRS is a rare event and, in our case, the unusual and fatal course was due to a rapid disease progression and multiorgan failure.

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