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CASE REPORT

Pathologic rupture of the spleen during induction with ATRA in a patient with acute promyelocytic leukemia

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Pathological rupture of the spleen is a rare but well recognized complication in hematological malignancies. Early clinical recognition of this life-threatening complication is necessary for rapid intervention. Here, we report on the case of a 26-year-old woman with acute promyelocytic leukemia who presented rupture of the spleen on day +2 of treatment with ATRA plus idarrubicin. In patients with acute leukemia, the presence of a painful abdomen and a sudden drop in hemoglobin levels, should alert of a possible splenic rupture, even without additional symptoms. This would facilitate an early treatment intervention with no modification to the chemotherapy schedule. *Medical Oncology* (2000) **17**, 337–339.

Keywords: ATRA; leukemia; spleen rupture

Introduction

Rupture of the spleen without previous trauma is a well recognized but serious complication appearing with relative frequency in infectious or parasitic diseases with large splenomegaly, but is not frequent in hematological malignancies.[1]

The most important pathophysiological factors that lead to the rupture in hematological diseases are splenic involvement, splenic infartation and coagulation disorders.[2–7] Other factors such as male sex, adulthood, large splenomegaly, rapid growth of the spleen or splenic abscesses, Valsalva's manoeuvre and cytoreductive chemotherapy may be contributory factors.[1,4]

Case report

A 26-year-old woman was admited to our hospital on 15 December 1998, complaining of fatigue over the previous 4–5 months which had intensified during the last week, with frequent menstruation, and spontaneous hematomas. Two days prior to admittance she presented dry cough and pleuritic pain on the left side, with fever >38°C twelve hours earlier. Physical examination showed the woman to be very pale with fever of 39°C. Abdomen was not painful, without masses or enlarged spleen or liver. Several hematomas of less than 5 cm were observed.

Laboratory analyses showed hemoglobin 9 gr/dl; white blood cell count 7.7×10^9/l (2% neutrophils,

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18% lymphocytes, 1% eosinophils, 79% blast cells) and platelets 8×10^9/l. PT: 45%, APTT: 47 s (control: 32 s), fibrinogen: 89 mg/dl, AT-III: 86%; D-dimers: 3360 μg/ml; FDP >20 μg/ml. Serum lactate dehydrogenase level was 1086 units/l (normal < 460 units/l). Other laboratory tests were normal.

Bone marrow aspiration showed 93% of blast cells with reniform or bilobed nuclei, 10% hypergranulars, some of them containing Auer rods. Immunophenotype analysis showed that bone marrow blasts were positive for CD13, CD15, CD33 and negative for HLA/DR. Bone marrow cytogenetics revealed the following pattern: 46XX, t(15;17) (q21,q21) and the presence of PML/RARα fusion genes was confirmed by RT-PCR.

Abdominal ultrasound at diagnosis showed a normal liver and only moderate splenomegaly with a normal structure.

She began treatment according to the Spanish PETHEMA protocol LPA-96: ATRA: 45 mg/m2/d; dexamethasone: 10 mg/12 h for 7 d if leukocytes >5× 10^9/l; and idarrubicin: 12 mg/m^2 on days 2, 4, 6 and 8.

On day +2 of treatment, the patient showed a progressively distended and painful abdomen, without peritoneal irritation signs. The hemoglobin dropped below 7 g/dl without adequate rise after blood transfusions. The temperature reached up to 39°C, and broad spectrum antibiotics were administered. Pulse rate and blood pressure were maintained.

Abdominal X-ray showed diffuse opacification of the abdomen and central situation of the loops of intestine, suggestive of free fluid in the abdominal cavity. Abdominal ultrasound was then performed and splenic enlargement was observed with massive liquid in the abdominal cavity. Computed tomography scan of the abdomen showed an enlarged spleen of hypodense predominance in its upper half and with active captation areas of contrast and massive fluid hemorrhagic liquid in the peritoneal cavity compatible with probable splenic rupture.

An emergency splenectomy was performed. The patient received red blood cell concentrates, fresh frozen plasma, cryoprecipitates and transfusion of platelets. She remained hemodynamically stable throughout the intervention period. Spleen showed a laceration of 5 cm.

Pathological examination showed a spleen of 710 g, congestive aspect with partial absence of capsule.

The splenic parenchyma itself was infiltrated by myeloid tumor cells compatible with promyelocytic leukemia.

After intervention the patient was admitted to the intensive care unit. Chemotherapeutic treatment and ATRA were maintained according to the above mentioned protocol. The patient achieved complete remission on day 30. Currently, she is receiving consolidation therapy without additional problems.

Discussion

Spontaneous rupture of the spleen is a rare complication of hematological malignancies. In 1861, Rokitansky[8] described the first spontaneous rupture of the spleen in a patient with leukemia. Recently it has been reported that between 0.72 and 3.5% of spontaneous splenic ruptures can be associated with leukemia.[6,9]

Giagounidis *et al*,[4] in a review from 1861, identified 136 cases of pathological rupture of the spleen but only 21 cases of spontaneous rupture in acute myelogeneous leukemia. Moreover, this complication is apparently even rarer in APL. In fact as far as we know, only one other AML-M3 case has been published[10] and the present case is the first one reported receiving induction with ATRA plus chemotherapy.

The clinical symptoms of splenic rupture (hypotension, tachycardia, abdominal pain, nausea and vomiting, fever and the rare Kehr's sign) are generally due to intra-abdominal hemorrhage.[1,3,4,9,11] In our case, symptomatology was less important because adequate perfusion and expansion of the plasma by hydration and transfusions were maintained.

Ultrasound and computed tomography are non-invasive techniques with high sensibility and specificity and are currently the methods of choice for the diagnosis of splenic rupture.[1] In our patient both of them suggested such a diagnosis.

Guth *et al*,[12] in a prospective study including 11 patients, one of them with acute leukemia, demonstrated that the pathological spleen rupture can heal after parenchymal disruption and proposed that a subset of hemodynamically stable patients can be successfully managed without surgery using CT diagnosis, closed clinical monitoring and minimal transfusions. However, until now, the splenectomy has been considered the most desirable therapy.[3,4] Moreover, following surgery, patients usually show a rapid complete

recovery and can receive chemotherapy without delay, which is critical in order not to reduce the possibilities of achieving complete remission,[11] as has been shown in our patient.

The mortality increases (about 60%) in cases with a late diagnosis or additional complications caused by the underlying disease.[1,3] Since survival from this serious complication is closely related to its early management, the diagnosis of splenic rupture must be considered in all patients with hematological malignancies who experience mild clinical symptoms and excessive transfusion requirements.

In summary, the present case shows that splenectomy after spontaneous rupture of spleen can be safely performed in AML-M3 patients maintaining the ATRA and chemotherapy schedule.

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