Open Journal of
Clinical & Medical
Case Reports

Volume 6 (2020)
Issue 7

ISSN: 2379-1039

An eighty eight years old man with spontaneous splenic rupture after granulocyte colony stimulating factor (G-CSF) administration

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Abstract

Background: The mainly use of Granulocyte colony stimulating factor (G-CSF) is stem cell mobilization in neutropenic patients and healthy donors as well as for engraftment. Most of their secondary effects are mild and temporary; however there is a relation between spontaneus splenic rupture and G-CSF treatment.

Case presentation: We report a case of an 88 years old man, who presented with an spontaneus splenic rupture after use of G-CSF.

Conclusion: Although it is an uncommon side effect, the mortality is very high, so clinicians should be aware of the importance about maintaining a high index of suspicion for this condition.

Keywords

Spleen; hemoperitoneum; shock; neutropenia

Abbreviations

G-CSF: Granulocyte colony stimulating factor; AIDS: Acquired immune deficiency syndrome; MDS: Myelodysplastic syndrome; NV: Normal value; CRP: C-reactive protein; PCT: Procalcitonin; SSR: Spontaneus splenic rupture

Background

Granulocyte colony stimulating factor (G-CSF) was discovered in 1980 and it has been used for acceleration of neutrophil recovery after chemotherapy (in solid and hematologic malignancies), mobilization of peripheral blood progenitor cells from healthy donors, bone marrow/peripheral stem

cell transplantation, and management of neutropenia due to other causes including acquired immune deficiency syndrome (AIDS) and genetic disorders of granulocyte production. The most common adverse events are bone pain, headache and fatigue, but it has been described important complications such as stroke, myocardial infarction and splenic rupture. These infrequent situations could be severe and lethal [1].

Case Report

We report a case of an 88 years old man with medical history of lower extremity peripheral artery disease, myelodysplastic syndrome (MDS) with pancytopenia (without specific treatment) and cronic ferropenic anemia secondary to angiodysplasias of the gastrointestinal tract. Endoscopic treatment for the gastrointestinal angiodysplasias was unsuccessful, so treatment with octreotide was started as compassionate use. He was treated with intravenous iron and periodic blood transfusion. His diary medications included: lorazepam 1mg/day, cinitaprida 20mg (oral antihistamine) and clopidogrel 75mg/day. He had no known allergies.

The patient had been well until approximately one day before of admission, when general discomfort and high temperature of 38,6ºC developed. One month before, the patient was admitted in the hospital because of celulitis in his right hand after management of a periferic intravascular catheter needed for blood transfusion.

On examination, the patient was alert and cooperative. The temperature was 38ºC, the blood pressure 110/65 mm Hg, the pulse 110 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 89% while he was breathing ambient air. He presented normal cardiac auscultation, but crackles at left lower lung. There was no other signs on examination. In blood tests, we observed normocytic-normochromic anemia (hemoglobin 9.1 g/dl, prior 9.7 g/dl, Normal Value (NV): 13-16.8 g/dl), leukopenia 2.4 x 1000/mcl (prior 2.2 x 1000/mcl; NV: 4-11.3 x 1000/mcl), neutropenia 1.4 x 1000/mcl (prior 1 x 1000/mcl; NV: 4-11.3 x 1000/mcl), lymphopenia 0.4 x 1000/mcl (prior 0.56 x 1000/mcl; NV: 1.2-5 x 1000/mcl) and C-reactive protein (CRP) 13mg/dl (NV < 1mg/dl) with normal procalcitonin (PCT) 0.25ng/ml (NV < 0.5 ng/ml). The other biochemistry coagulation and urine tests were normal. The chest radiography was normal too.

Because of his immunodeficient state and a recent history of hospital admission; we assumed the diagnosis of nosocomial pneumonia and began antibiotic treatment with piperacilin-tazobactam. The patient had a good response and recovered from his prior state. Blood and urine cultures were negative. Antibiotic treatment was stopped at 7th day of treatment.

However, his cytopenias worsened: hemoglobin 7 g/dl and neutrophils 0.3 x1000/mcl. A peripheric blood smear was normal, so we dismissed the possibility of leukaemia. Hematologist evaluated the patient and reactive neutropenia was assumed because of the recent acute infectious process in a patient with MDS. Because of that, treatment with G-CSF 300 mcg/24h s.c. and red blood cells transfusion was started. One day after, the patient developed a syncope without trauma. On examination, he was alert but his general

condition was bad: He showed pale skin, significant sweating, hypotension and tachycardia. However, he presented normal cardiac and pulmonary auscultation. The abdomen was painful and no soft; the remainder of the examination was normal (rectal examination included). In blood test, we observed: hemoglobin 7.7 g/dl, leukocytes 45.3 x 1000/mcl, neutrophils 40.7 x 1000/mcl, LDH 361 U/l (NV: 135-225 U/l), bilirubin 1.9 mg/dl (NV: 0.2-1mg/dl), lactic acid 12.3 mmol/l (NV: 0.5-2.2 mmol/l). Supportive care was started with intensive fluid therapy and blood transfusión. Thoraco-abdmino-pelvic computerized tomography (CT) scan showed spontaneus splenic rupture with arterial bleeding and a big hemoperitoneum (Figure 1).

The patient had a high surgical risk, so we tried to avoid the splenectomy doing an arteriography. However, it was impossible because of his significant arteriosclerosis, and we had to perform the surgery. The post-operative period was complicated with multiple organ dysfunction and he died at second day after G-CSF administration.

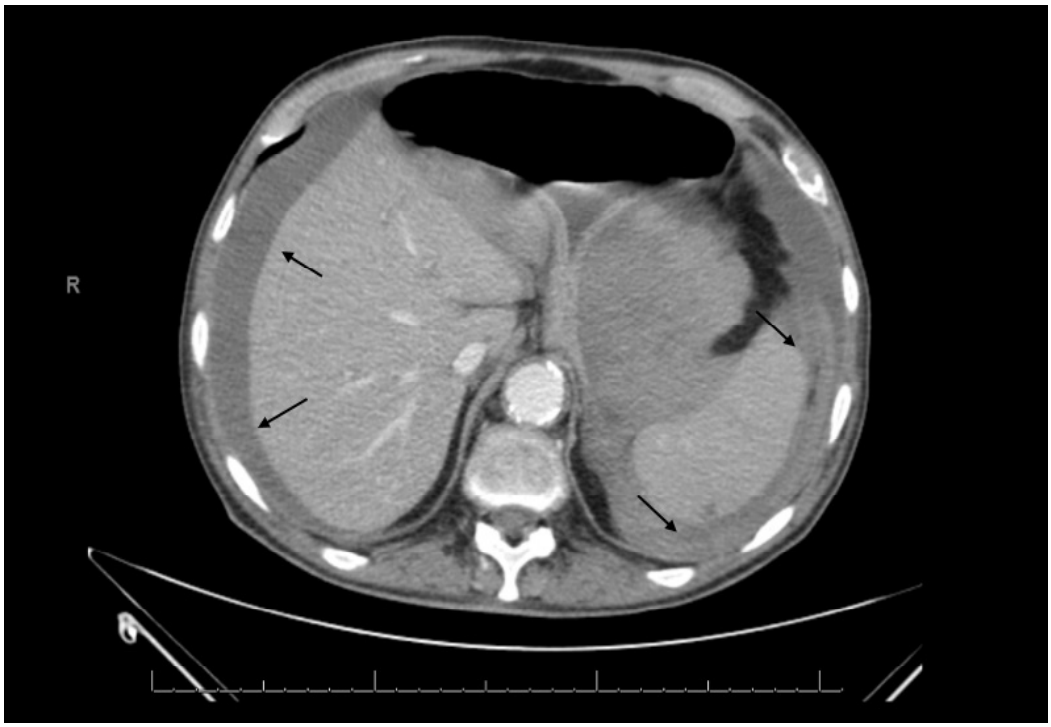

Figure 1: CT- Scan with splenic hematoma (right arrows) and hemoperitoneum (left arrows).

Discussion

Splenic ruptur is a potential lethal condition with a very high mortality and it is most often associated with trauma. If we find an spontaneus splenic rupture (SSR) we have to look for an underlaying splenic disease.

The case describes a patient with MDS, disease that is rarely associated with SSR; however, there have been previous reports of splenic enlargement and rupture in association with G-CSF administration [2,3,4]. G-CSF treatment is related with bone pain, headache, asthenia, fever, stroke, heart attack, splenic hematoma or splenic rupture [5]. Although the mechanism is not well known, it has been suggested that it could be secondary to a rapid spleen enlargement, because of the extramedullary hematopoiesis [6,7].

In clinical trials with mice, expression levels of the DNA-synthesizing enzymes thymidylate synthase (TS) and thymidine kinase (TK) mRNA in the splenic cells were significantly increased 6 hours after G-CSF treatment [7]. This seems to be as a result of an increasing in replication of hematopoietic cells. Likewise, another clinical trial was performed with healthy donors and splenic enlargement was 1.47 cm (median). Seven days after apheresis plasma, spleen recovered the previous size without any splenic rupture [9]. In the literature review, most of the cases occurred between the third and sixth days after G-CSF injection and most of patients referred with abdominal pain [6,10].

Risk factors for splenic rupture are not well known, but it seems that splenomegaly could be a determining factor for SSR after G-CSF administration [5,8]. Because of that, it could be useful to monitorize the splenic size in patients who need G-CSF administration [11,12]; however, in most of the cases reported splenomegaly was not described [1,10]. On the other hand, there is no relationship between the splenic enlargement and G-CSF dose or neutrophil blood count, so it could be an idiosyncratic effect [1].

In our case, the patient had mild splenomegaly (maximum diameter 13 cm in the last ultrasound examination which was performed two years ago), and he had received previously G-CSF without secondary effects. The splenic rupture in this case would have happened as a result of the splenic hematopoiesis commonly seen in MDS [13], enhanced after G-CSF administration [8,14] with secondary splenic congestion and splenic rupture.

The management of SSR include supportive treatment, G-CSF discontinuation, and emergent splenectomy if needed. A conservative approach could also be preferred in selected patients that are hemodinamically stable [1,5,11].

Conclusion

Although SSR is an uncommon condition, it is serious and potentially fatal; clinicians should be aware of SSR associated with G-CSF administration and maintain a high index of suspicion.

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Manuscript Information: Received: December 16, 2020; Accepted: April 07, 2020; Published: April 15, 2020

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Citation: Castro-Martínez, Castillo Maza C. An eighty eight years old man with spontaneous splenic rupture after granulocyte colony stimulating factor (G-CSF) administration. Open J Clin Med Case Rep. 2020; 1650.