An 88-year old man with spontaneous splenic rupture after granulocyte colony stimulating factor administration

Marta De Castro Martinez[1*], Cristina Castillo Maza[1]

European Journal of Medical Case Reports
Volume 4(9):285–287

https://doi.org/10.24911/ejmcr/173-1567102492

ABSTRACT

Background: The main 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 spontaneous splenic rupture and G-CSF treatment.

Case Presentation: We report a case of an 88-year old man, who presented with a spontaneous 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: Case report, spleen, hemoperitoneum, shock, neutropenia.

Received: 02 October 2019 **Accepted:** 06 May 2020

Type of Article: CASE REPORT **Specialty:** Hepatology

Funding: None.

Declaration of conflicting interests: The authors declare that there is no conflict of interest regarding the publication of this case report.

Correspondence to: Marta De Castro Martinez
*Internal Medicine Service, Hospital Universitario 12 de Octubre, Madrid, Spain.
Email: mailto:martadecastro84@gmail.com; martadecastro84@gmail.com
Full list of author information is available at the end of the article.

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 Presentation

We report a case of an 88-year old man with medical history of lower extremity peripheral artery disease, myelodysplastic syndrome (MDS) with pancytopenia (without specific treatment), and chronic 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 1 mg/day, cinitaprida 20 mg (oral antihistamine), and clopidogrel 75 mg/days. He had no known allergies.

The patient had been well until approximately 1 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 cellulitis in his right hand after the management of a peripheric intravascular catheter 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 were 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 × 1,000/mcl (prior 2.2 × 1,000/mcl; NV: 4-11.3 × 1,000/mcl), neutropenia 1.4 × 1,000/mcl (prior 1 × 1,000/mcl; NV: 4-11.3 × 1,000/mcl), lymphopenia 0.4 × 1,000/mcl (prior 0.56 × 1,000/mcl; NV: 1.2-5 × 1,000/mcl) and C-reactive protein 13 mg/dl (NV < 1 mg/dl) with normal procalcitonin 0.25 ng/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 piperacillin-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 cytopenia worsened hemoglobin 7 g/dl and neutrophils 0.3 ×1,000/mcl. A peripheric blood smear was normal, so we dismissed the possibility of leukemia. Hematologist evaluated the patient and reactive neutropenia was assumed because of the recent acute infectious process in a patient with MDS. Because of that, we began treatment with G-CSF 300 mcg/24 hour s.c. and red blood cells transfusion. One day after starting this treatment, the patient developed a syncope without trauma. On examination, he was alert but his general condition was bad, with pale skin and significant sweating. He also had hypotension and tachycardia. 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 × 1,000/mcl, neutrophils 40.7 × 1,000/mcl, Lactate dehydrogenase (LDH) 361 U/l (NV: 135-225 U/l), bilirubin 1.9 mg/dl (NV: 0.2-1 mg/dl), lactic acid 12.3 mmol/l (NV: 0.5-2.2 mmol/l). Supportive care was started with intensive fluid therapy and blood transfusion. Thoraco-abdmino-pelvic computerized tomography (CT) scan showed spontaneous splenic rupture (SSR) with arterial bleeding and a big hemoperitoneum (Figure 1).

Because of the high surgical risk, we made an urgent arteriography for splenic artery embolization, however it was impossible because of the significant arteriosclerosis. Finally, an urgent splenectomy was performed but the patient had a complicated process with multiple organ dysfunction and he died at second day after G-CSF administration.

Discussion

Splenic rupture is a potential lethal condition with a very high mortality; the main etiology is traumatic. In general, a normal spleen needs a big trauma for breaking, so if we find an SSR we have to look for an underlaying splenic disease.

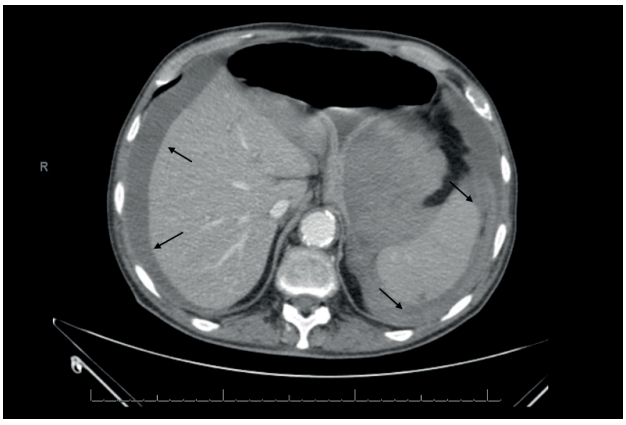

Figure 1. *CT- Scan with splenic hematoma (right arrows) and hemoperitoneum (left arrows).*

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 [2-4]. 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 and thymidine kinase mRNA in the splenic cells were significantly increased 6 hours after G-CSF treatment [7]. This seems to be as a result of an increase 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 [8]. In the literature review, most of the cases occurred between the third and 6th days after G-CSF injection and most of patients referred with abdominal pain [6,9].

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 [5,10]. Because of that, it could be useful to monitorize the splenic size in patients who need G-CSF [11,12]; although in most of the cases reported splenomegaly was not described [1,9]. On the other hand, there is no relationship between the splenic enlargement and G-CSF dose or neutrophil blood count [1]. Hence, it could be an idiosyncratic effect.

In our case, the patient had mild splenomegaly (maximum diameter 13 cm in the last ultrasound examination which was performed 2 years ago) although the patient had received previously G-CSF without secondary effects. Maybe one reason to explain splenic rupture in our case was the splenic hematopoiesis commonly seen in MDS [13], that could be dramatically increased after G-CSF administration [10,14], with secondary splenic congestion and splenic rupture.

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

Conclusion

Despite it is rarity and potential severity, clinicians should be aware of SSR associated with the administration of G-CSF and maintain a high index of suspicion.

What is new?

Spontaneous splenic rupture after granulocyte colony stimulating factor (G-CSF) administration is not a common situation. This is an interesting case because it is uncommon and idiosyncratic side effect with a high mortality.

List of Abbreviations

AIDS	Acquired immune deficiency syndrome
G-CSF	Granulocyte colony stimulating factor
MDS	Myelodysplastic syndrome REVERSE
NV	Normal value
SSR	Spontaneous splenic rupture

Consent for publication

Written informed consent was obtained from the next kin of the deceased patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author details

Marta De Castro Martinez[1], Cristina Castillo Maza[1]

1. Internal Medicine Service, Hospital Universitario 12 de Octubre. Madrid, Spain.

References

1. Akyol G, Pala C, Yildirim A, Keklika M, Demir K, Dortdudak S et al. A rare but severe complication of filgrastim in a healthy donor: splenic rupture. Transfus Apher Sci. 2014;50(1):53–5. https://doi.org/10.1016/j.transci.2013.07.036
2. Goddard S, Chesney A, Reis M, Ghorab Z, Brzozowski M, Wright F et al. Pathological splenic rupture: a rare complication of chronic myelomonocytic leukemia. Am J Hematol. 2007;82(5):405–8. https://doi.org/10.1002/ajh.20812
3. Arshad M, Seiter K, Bilaniuk J, Qureshi A, Patil A, Ramaswamy G et al. Side effects related to cancer treatment. J Clin Oncol. 2005;23(33):8533–4. https://doi.org/10.1200/JCO.2005.04.1012
4. O'Malley DP, Whalen M, Banks PM. Spontaneus Splenic ruptura with fatal outcome following G-CSF administration for myelodysplstic syndrome. Am J Hematol. 2003;73(4):294–5. https://doi.org/10.1002/ajh.10317
5. Dincer A, Gottschall J, Margolis D. Splenic rupture in a parental donor undergoing peripheral blood progenitor cell mobilization. J Pediatr Hematol Oncol. 2004;26(11):761–3. https://doi.org/10.1097/00043426-200411000-00015
6. Funes C, Garcia-Candel F, Majado M, González-García C, Bas A, Salido E et al. Splenic rupture in a plasma cell leukemia, mobilized with G-CSF for autologous stem cell transplant. J Clin Apher. 2010;25(4):223–5. https://doi.org/10.1002/jca.20233
7. De Larrea C, Cibeira M, Rovira M, Rosiñol L, Esteve J, Bladé J. Spontaneous rupture of the spleen as immediate complication in autologous transplantation for primary systemic amyloidosis. Eur J Haematol. 2008;80(2):182–4. https://doi.org/10.1111/j.1600-0609.2007.01005.x
8. Stroncek D, Shawker T, Follmann D, Leitman S. G-CSF-induced spleen size changes in peripheral blood progenitor cell donors. Transfusion. 2003 May;43(5):609-13. https://doi.org/10.1046/j.1537-2995.2003.00384.x
9. Ganetsky A, Kucharczuk C, Percio S, Frey N, Gill S. Spontaneous subcapsular splenic hematoma associated with filgrastim in a patient undergoing allogeneic hematopoietic stem cell transplantation. Ann Pharmacother. 2013;47(5):e22.
10. Nakayama T, Kudo H, Suzuki S, Sassa S, Mano Y, Sakamoto S. Splenomegaly induced by recombinant human granulocyte-colony stimulating factor in rats. Life Sci. 2001;69(13):1521–9. https://doi.org/10.1016/S0024-3205(01)01244-9
11. Nabil M, Goker H, Kilic Y, Dagmoura H, Cakmak A. Spontaneous splenic rupture in a healthy allogeneic donor of peripheral-blood stem cell following the administration of granulocyte colony-stimulating factor (g-csf). A case report and review of the literature. Haematologica. 2006;91(2):26–8.
12. Hatzimichael E, Benetatos L, Stebbing J, Kapsali E, Panayiotopoulou S, Bourantas K. Spontaneous splenic haematoma in a multiple myeloma patient receiving peg-filgrastim support. Clin Lab Haematol. 2006;28(6):416–8. https://doi.org/10.1111/j.1365-2257.2006.00819.x
13. Yamamoto K, Miwa Y, Abe-Suzuki S, Abe S, Kirimura S, Onishi I, et al. Extramedullary hematopoiesis: elucidating the function of the hematopoietic stem cell niche (Review). Mol Med Rep. 2016;13(1):587–91. https://doi.org/10.3892/mmr.2015.4621
14. Masood N, Shaikh A, Memon W, Idress R. Splenic rupture, secondary to G-CSF use for chemotherapy induced neutropenia: a case report and review of literature. Cases J. 2008;1(1):418. https://doi.org/10.1186/1757-1626-1-418

Summary of the case

1	**Patient (gender, age)**	Eighty 8 years old man
2	**Final diagnosis**	Spontaneous splenic rupture
3	**Symptoms**	Hypotension and tachycardia
4	**Medications**	Intensive fluid therapy and blood transfusion
5	**Clinical procedure**	Urgent splenectomy
6	**Specialty**	Hematology