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CAUGHT IN THE CROSSFIRE: A CASE OF SPLENIC INFARCTION AMID G-CSF THERAPY IN CHRONIC MYELOMONOCYTIC LEUKAEMIA

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ABSTRACT

This report highlights a rare but significant complication associated with the use of granulocyte-colony stimulating factor (G-CSF) therapy, specifically splenic infarction, in a 67-year-old male with chronic myelomonocytic leukaemia (CMML) undergoing chemotherapy. G-CSFs, such as pegfilgrastim, are frequently used to prevent febrile neutropenia in cancer patients undergoing myelotoxic chemotherapy. While G-CSF is effective in reducing the risk of neutropenia, its administration has been linked to uncommon but severe complications such as splenic infarction and rupture. Our patient, receiving dose-dense chemotherapy with G-CSF support, developed severe abdominal pain midway through treatment. A computed tomography (CT) scan revealed multiple splenic hypodensities consistent with splenic infarction, but no active bleeding. Conservative management was successfully employed, avoiding surgical intervention. This case underscores the need for vigilance when administering G-CSF, particularly in patients at high risk for complications, and contributes to the limited body of literature on G-CSF-induced splenic infarction.

KEYWORDS

Splenic infarction, G-CSF, chronic myelomonocytic leukaemia

LEARNING POINTS

- *Clinical vigilance in G-CSF therapy:* This report highlights the need for heightened awareness of rare but severe complications, such as splenic infarction, associated with granulocyte-colony stimulating factor (G-CSF) therapy. Internists managing patients on chemotherapy must recognise early signs of such complications to optimise patient outcomes.
- *Risk-benefit assessment:* It emphasises the importance of individualised treatment strategies, balancing the lifesaving benefits of G-CSF in preventing febrile neutropenia with the potential risks, particularly in patients with predisposing conditions such as chronic myelomonocytic leukaemia (CMML).
- *Conservative management insights:* The successful non-surgical management of splenic infarction in this case underscores the potential for conservative approaches, providing valuable guidance for internists in similar clinical scenarios.

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INTRODUCTION

Granulocyte-colony stimulating factors (G-CSFs) play a crucial role in the mobilisation of peripheral blood stem cells and the apheresis process. Additionally, these pharmaceutical agents are employed in the management of chemotherapy-induced neutropenia among patients with non-myeloid malignancies undergoing myelotoxic chemotherapy, as they enhance the proliferation, maturation and functional capacity of white blood cells[1]. Febrile neutropenia (FN) is a common complication associated with chemotherapeutic treatment, underscoring its significance as a critical oncologic emergency. This condition is closely associated with a marked increase in both morbidity and mortality rates, elevated utilisation of healthcare resources and a considerable reduction in the efficacy of chemotherapy regimens[2]. G-CSF has demonstrated effectiveness in reducing both the duration and severity of neutropenia, thereby decreasing the likelihood of FN. Furthermore, it facilitates the administration of full-dose-dense chemotherapy when clinically indicated[3-5]. G-CSF serves as a viable option for primary prophylaxis when the risk of neutropenic fever exceeds 20% with any chemotherapy regimen. Additionally, it may be utilised for secondary prophylaxis or for the management of established neutropenic fever[2-5].

Moreover, a limited number of case reports have documented severe complications such as splenic rupture, splenic infarction, myocardial infarction and stroke, which are associated with the administration of colony-stimulating factors in both haematologic and solid tumours. Among individuals experiencing splenic complications, some cases were managed conservatively, while others with more severe complications required splenectomy[6-9].

This case presents a 67-year-old male diagnosed with chronic myelomonocytic leukaemia (CMML), who underwent dose-dense chemotherapy accompanied by a colony-stimulating factor as a primary prophylactic measure to prevent FN. Midway through treatment, the patient developed splenic infarction, as confirmed by a computed tomography (CT) scan. The management of this complication was conducted conservatively, thereby eliminating the need for surgical intervention.

CASE DESCRIPTION

We present the case of a 67-year-old male diagnosed with high-risk CMML in October 2023. The patient presented to the haematology/oncology clinic exhibiting symptoms of malaise, dizziness, chills, tachycardia and hypotension, which raised concerns about sepsis. Following the administration of 1 litre of intravenous fluids and cefepime, he was subsequently referred to the emergency department. Upon admission to the medicine floor, he underwent evaluation and management for sepsis and lactic acidosis. However, due to persistent hypotension necessitating vasopressor support and elevated lactic acid levels greater than 5 mmol/l, he was transferred to the medical intensive care unit. This admission marked the patient's fourth instance of neutropenic fever since the initial diagnosis of CMML. His condition was further complicated by a peripheral blast crisis, prompting treatment with azacitidine and venetoclax, as well as the presence of pancytopenia accompanied by leukocytosis (now showing a downtrend) and severe thrombocytopenia, placing him at risk for tumour lysis syndrome. The patient had received chemotherapy on 5 April 2024, as well as pegfilgrastim on 8 April 2024, for neutropenic support. He reported experiencing severe abdominal pain, rated at 8 out of 10. A CT scan conducted on 10 April 2024 discounted the existence of an infectious focus and indicated hepatosplenomegaly, alongside diffuse low-density lesions in the spleen suggestive of a developing splenic infarct and minimal perisplenic fluid accumulation; however, no active bleeding was detected *(Fig. 1 and 2)*. The critical illness of the patient appeared to be associated with the underlying CMML, recent chemotherapy and complications from treatment, including splenic infarction, potentially attributable to the use of filgrastim.

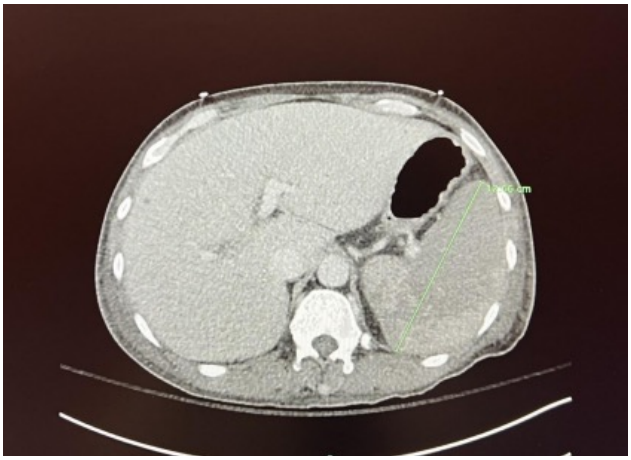

Figure 1. Hepatosplenomegaly with multiple splenic hypodensities consistent with splenic infarction (green arrow) after using G-CSF.

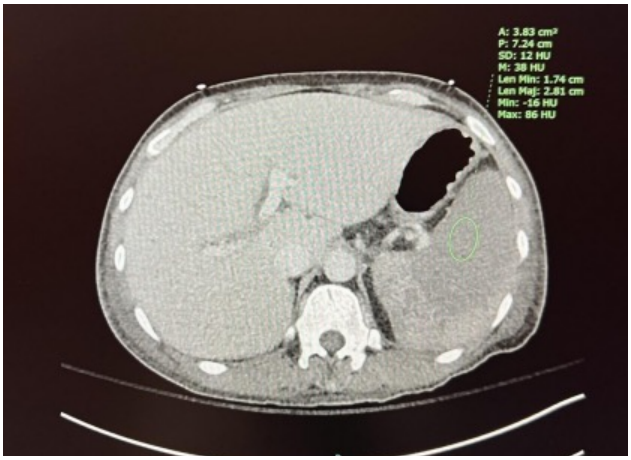

Figure 2. Diffuse low-density lesions in the spleen consistent with a developing splenic infarct.

DISCUSSION

Granulocyte-colony stimulating factor (G-CSF) therapy is frequently prescribed to cancer patients for the prevention

and management of FN caused by myelosuppressive chemotherapy. Prophylactic administration of G-CSF is recommended when the risk of chemotherapy-induced FN exceeds 20%, as it aids in maintaining dose density and intensity, which has been shown to confer a significant survival benefit[1-4].

Dose-dense and dose-intensified chemotherapy regimens, particularly in high-risk cancer patients, rely heavily on G-CSF support to ensure adherence to treatment schedules and optimal therapeutic outcomes[3-5]. Pegfilgrastim, a long-acting formulation of filgrastim, is one of the key agents used for this purpose. Its unique polyethylene glycol (PEG) formulation extends its duration of action, allowing for once-per-cycle dosing. Pegfilgrastim prevents FN by increasing neutrophil levels through the promotion of proliferation, differentiation and maturation, as well as enhancing the survival of mature neutrophils[10]. Phase III clinical trials have demonstrated the efficacy of pegfilgrastim in significantly reducing the risk of FN in patients undergoing chemotherapy[11].

Beyond its use in cancer patients, G-CSF also plays a crucial role in healthy donors during peripheral blood stem cell transplant (PBSCT) mobilisation. Despite its well-established safety profile, G-CSF is associated with adverse effects, including bone pain and localised skin reactions at the injection site[2]. Rare but severe complications have also been reported, including splenic infarction and life-threatening splenic rupture. Case reports highlight these risks in both cancer patients and healthy donors receiving G-CSF, suggesting a possible correlation between G-CSF administration and splenic complications[6-8,12]. Splenic rupture secondary to pegfilgrastim has also been observed in patients with underlying malignancies, emphasizing the importance of monitoring spleen size and function during treatment[9,12].

Given the mechanism of action of pegfilgrastim, careful monitoring of complete blood counts, with particular attention to the white blood cell count, is imperative to avoid complications such as leukocytosis[11]. The maximum safe dosage of pegfilgrastim remains undefined, although clinical trials have permitted doses up to 300 µg/kg[13]. Overdose cases, while rare, have been documented. For example, a 79-year-old patient self-administered pegfilgrastim over eight consecutive days without immediate adverse effects, while another case involving a 36 mg overdose resulted in leukocytosis, bone pain and rhinorrhoea[12]. These cases underscore the necessity for preventive measures, such as patient education and vigilant monitoring for signs and symptoms of toxicity, as there is no specific treatment for pegfilgrastim overdose.

While G-CSF remains an indispensable tool in cancer treatment and PBSCT mobilization, clinicians must weigh its benefits against potential risks. Adherence to established guidelines and comprehensive patient monitoring ensures the safe and effective use of G-CSF in diverse clinical scenarios.

CONCLUSION

Granulocyte-colony stimulating factors (G-CSFs) have revolutionised the management of chemotherapy-induced neutropenia, playing an indispensable role in reducing the risk of FN and enabling patients to maintain dose-dense chemotherapy regimens. This case highlights the therapeutic benefits of G-CSF, particularly in high-risk patients such as those with CMML. However, it also underscores the potential for severe complications such as splenic infarction which, though rare, can occur as a consequence of G-CSF administration. In conclusion, while G-CSF remains a cornerstone in preventing chemotherapy-induced neutropenia and FN, clinicians must remain cautious of its rare but serious side effects. This case serves as a reminder of the delicate balance between therapeutic benefit and risk, reinforcing the need for thorough patient monitoring and an individualised approach to cancer treatment.

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