Case Report

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Filgrastim-induced cutaneous vasculitis in a patient undergoing stem cell mobilization

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Abstract:

Neupogen (filgrastim), a granulocyte colony-stimulating factor, is widely utilized for the management of chemotherapy-induced neutropenia and as part of mobilization regimens for hematopoietic stem cell transplantation. Filgrastim-induced cutaneous vasculitis (CV) is a rare adverse event. This case report details a patient at a bone marrow transplantation center diagnosed with Hodgkin lymphoma who received gemcitabine, dexamethasone, and cisplatin (GDP) chemotherapy as a mobilization regimen. The course of chemotherapy was uneventful. On day 9 postchemotherapy, filgrastim was initiated to mobilize stem cells. By day 2 of filgrastim administration, the patient developed a severe rash and pruritus. After thorough evaluation and exclusion of other potential causes, the rash was attributed to filgrastim-induced CV, as the patient was not receiving any other medications that could account for this reaction. While low-dose systemic corticosteroids are typically recommended for treating this condition, filgrastim was continued for an additional 3 days to complete stem cell mobilization. The patient was managed with diphenhydramine (1 ampoule three times daily) for symptomatic relief, and the rash resolved gradually following the discontinuation of filgrastim, without the need for corticosteroid therapy. Filgrastim is generally well tolerated, with common side effects including bone pain, nausea, vomiting, diarrhea, fever, and headache. However, rare but serious adverse effects, such as splenic rupture, pulmonary toxicity (particularly in combination with other drugs causing similar effects), arterial thrombosis, and CV, have been reported postmarketing. This case highlights the importance of recognizing and managing rare adverse events associated with filgrastim.

Keywords:

Filgrastim, granulocyte colony-stimulating factor, hematopoietic transplant, Hodgkin lymphoma, vasculitis

Introduction

Filgrastim is a recombinant short-acting granulocyte colony-stimulating factor (G-CSF) that mimics the biological functions of endogenous G-CSF. It is widely used to manage neutropenia induced by chemotherapy, which suppresses the immune system and reduces white blood cell (WBC) counts. In addition, filgrastim is employed as a mobilization regimen in hematopoietic stem cell transplantation, particularly in protocols for multiple myeloma. Other indications include neutropenia associated with HIV infection, postbone marrow transplantation, and various other conditions.[1,2]

Cutaneous vasculitis (CV) is an autoimmune disorder characterized by inflammation of the blood vessels. It can present as either idiopathic or secondary to various triggers, including drugs, which are implicated in up to 30% of CV cases. Drug-induced vasculitis (DIV), often classified as hypersensitivity vasculitis, involves inflammation and

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necrosis of small blood vessels secondary to drug exposure. Clinically, it primarily presents with cutaneous manifestations, with or without systemic symptoms.[3]

In most cases of drug-induced CV, discontinuation of the offending agent is sufficient to achieve remission, resulting in a favorable prognosis.[4]

This report describes a rare case of CV induced by filgrastim (Neupogen) in a neutropenic patient following chemotherapy.

Case Report

A 30-year-old male diagnosed with Hodgkin's lymphoma was admitted to a bone marrow transplant center for autologous stem cell transplantation. As part of the stem cell mobilization protocol, the patient received a chemomobilization regimen consisting of gemcitabine, dexamethasone, and cisplatin (GDP) on day +1. Following the initiation of this regimen, his WBC count progressively declined from 11.3 × 10^9/L to 2.5 × 10^9/L by day +8. Hemoglobin levels were recorded at 10.7 g/dL, neutrophil counts at 1.5 × 10^9/L, and platelet counts at 171 × 10^9/L on the same day. Renal, hepatic, and electrolyte profiles remained within normal ranges throughout.

On day +8, the patient received an additional dose of gemcitabine. The following day, filgrastim was initiated at a dose of 600 µg in the morning and 300 µg in the evening to enhance stem cell mobilization. Paracetamol was prescribed as needed to manage any associated bone pain or fever.

Three days after initiating filgrastim, the patient developed tender, erythematous plaques on the anterior abdominal region, lower limbs, and bilateral arms. These skin lesions were not associated with fever. Furthermore, they were not faded by pressure as shown in Figure 1. After ruling out alternative causes of the dermatological manifestation and confirming that no other concurrent medications were associated with this presentation, the patient was diagnosed with G-CSF-induced CV.

The clinical team considered two management options: discontinuing filgrastim and initiating systemic corticosteroid therapy or continuing filgrastim until the completion of stem cell collection. Given the urgency of stem cell mobilization, filgrastim was continued, and the patient was treated with diphenhydramine (administered intravenously three times daily) to manage the rash and associated pruritus.

The cutaneous lesions began to resolve gradually with diphenhydramine treatment and completely resolved after 4 days. Following the successful collection of stem cells, filgrastim was discontinued, and no recurrence of vasculitis was observed.

Discussion

DIV is an uncommon condition, representing approximately 30% of all cases of CV. The clinical presentation of DIV is often limited to cutaneous manifestations, although systemic involvement can occasionally occur. The underlying pathogenic mechanisms of DIV remain incompletely understood. Proposed mechanisms include the formation and deposition of immune complexes, direct activation of the complement system by the causative drug, direct damage to neutrophils, induction of neutrophil apoptosis, formation of neoantigens between the drug and host proteins, and modulation of the immune response.[5]

Management of drug-induced CV begins with the discontinuation of the suspected offending agent, which is often sufficient to achieve complete resolution of symptoms in many cases. However, the therapeutic approach should be tailored to the severity of the presentation and the extent of systemic involvement.[6]

For patients with isolated cutaneous involvement, a short course of topical or systemic corticosteroids is typically effective in resolving symptoms. Conversely, cases with systemic manifestations may require more intensive treatment, including systemic corticosteroids and immunosuppressive agents such as mycophenolate mofetil, azathioprine, or cyclophosphamide, to prevent disease progression and restore organ function.[7]

In this case, the patient's vasculitis was limited to the skin and presented as tender, erythematous plaques. Systemic corticosteroids were not deemed necessary, and the symptoms were successfully managed with antihistamine therapy (diphenhydramine). Upon cessation of the causative drug, filgrastim, the vasculitis resolved completely without further intervention, demonstrating that supportive care and drug withdrawal can be sufficient for managing mild, cutaneous forms of DIV.[8,9]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

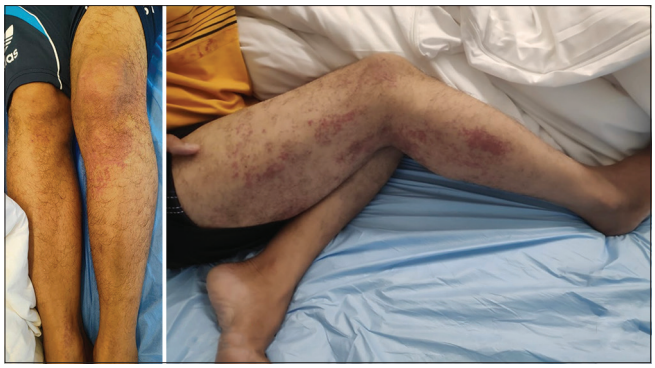

Figure 1: Showing the extensive rash on patients body

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Conflicts of interest

There are no conflicts of interest.

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