

Case Report

Granulocyte colony-stimulating factor associated arteritis in a patient with castration-resistant prostate cancer

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Abbreviations & Acronyms

CRP = C-reactive protein
CRPC = castration-resistant prostate cancer
CT = computed tomography
G-CSF = granulocyte colony-stimulating factor
PSL = prednisolone

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Introduction: Granulocyte colony-stimulating factor-associated arteritis is a rare adverse event of granulocyte colony-stimulating factor, with an incidence of 0.47% among all patients who receive granulocyte colony-stimulating factor. We herein present a case of granulocyte colony-stimulating factor-associated arteritis.

Case presentation: A 72-year-old man with castration-resistant prostate cancer and multiple bone metastases was treated with docetaxel and pegfilgrastim. He developed a high fever on day 12 without other symptoms. His white blood cell count and C-reactive protein levels were high. Antibiotic therapy was ineffective, and contrast-enhanced computed tomography showed thickened subclavian and brachiocephalic artery walls. He was diagnosed with granulocyte colony-stimulating factor-associated arteritis.

Conclusion: When patients receiving chemotherapy with granulocyte colony-stimulating factor develop an unexplained fever, granulocyte colony-stimulating factor associated arteritis should be considered.

Key words: arteritis, castration-resistant prostate cancer, docetaxel, granulocyte colony-stimulating factor, prednisolone.

Keynote message

Arteritis is a rare adverse event associated with G-CSF. However, it is essential to consider G-CSF-associated arteritis when patients receiving chemotherapy with G-CSF develop an unexplained fever.

Introduction

In prostate cancer chemotherapy, the G-CSF is commonly used as a preventive and supportive therapy for neutropenia. Bone pain and injection-site reactions are common adverse events of G-CSF, but G-CSF-associated arteritis has rarely been reported. Here, we report a case of arteritis induced by G-CSF.

Case report

A 72-year-old man was admitted to our hospital with CRPC and multiple bone metastases. He received docetaxel (75 mg/m²) with oral PSL at a dose of 10 mg/day, followed by pegfilgrastim, a supportive long-acting G-CSF. Pegfilgrastim is uncommonly used with the docetaxel regimen. However, he opted to receive pegfilgrastim to avoid frequent hospital visits. Pegfilgrastim was administered subcutaneously on day 2. He visited our hospital on day 12, complaining of a high fever without other symptoms. Physical examination results were unremarkable. Laboratory tests revealed a slightly elevated white blood cell count (11 100/μL) and a high CRP level (10.83 mg/dL). Blood culture results were negative, but infectious disease was suspected. Subsequent antibiotic therapy was ineffective. Contrast-enhanced CT was performed to detect the cause of the high fever on day 15. CT showed thickening of the walls of the subclavian and brachiocephalic arteries (Fig. 1). Autoimmune disease was excluded because of the etiology, subjective symptoms, and normal levels of anti-nuclear antibody,

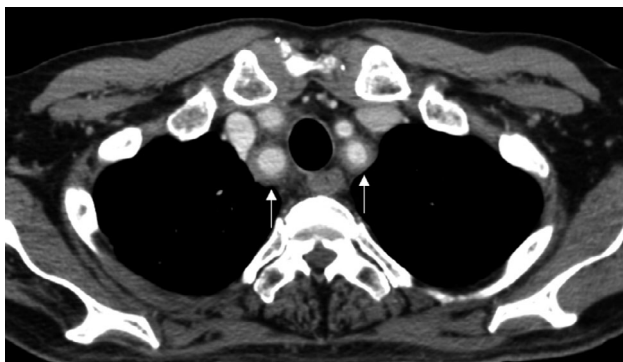


Fig. 1 Contrast-enhanced CT at diagnosis showing the thickened wall of the subclavian and brachiocephalic artery (arrow).

myeloperoxidase-anti-neutrophil cytoplasmic antibody, and serine proteinase 3 anti-neutrophil cytoplasmic antibody. The patient was diagnosed with G-CSF-associated arteritis. While antibiotic therapy was discontinued, the patient continued receiving oral PSL (10 mg/day). On day 20, the white blood cell count and CRP level were almost normal. Follow-up CT performed 3 months after diagnosis revealed the disappearance of arterial wall thickening (Fig. 2). PSL was continued for 3 months, and there was no relapse after its discontinuation. Androgen deprivation therapy was continued for the treatment of CRPC.

Discussion

G-CSF-associated arteritis is rare, with only a few reported cases. To the best of our knowledge, this is the first reported case of G-CSF-associated arteritis in a patient with urological cancer.

Based on the data from the Japanese Adverse Drug Event database, G-CSF-associated arteritis occurs in 0.47% of all cases of G-CSF administration.¹ According to a recent systematic review of 16 cases with G-CSF-associated arteritis,² the most prevalent cancer type was breast cancer (56%), followed by hematological malignancies (19%) and lung cancer (19%). Fever (94%) and neck pain (38%) were common clinical symptoms, and the average interval from G-CSF administration to the appearance of these G-CSF-associated arteritis



Fig. 2 Contrast-enhanced CT 3 months after diagnosis shows improvement of the subclavian and brachiocephalic arteries (arrow).

symptoms was 15 (range: 1–62) days. The incidence of arteritis induced by long-acting G-CSF and regular G-CSF was 43.8% and 37.5%, respectively. The remaining cases were not classified due to insufficient data. The most prevalent vascular sites of arteritis were the thoracic aorta and supra-aortic vessels (88%), including the carotid, subclavian, and brachiocephalic arteries, followed by the carotid artery (12%). Docetaxel was the most commonly used single chemotherapy (63%), which was also administered to our patient. Taimen *et al.*² observed that G-CSF synergized with docetaxel in promoting vascular inflammation via neutrophil proliferation. However, the relationship between docetaxel and G-CSF-associated arteritis remains unclear.

Arteritis may be caused by both infectious or non-infectious reasons.^{3,4} Most non-infectious arteritis cases were caused by autoimmune diseases (giant cell arteritis and Takayasu arteritis) and were less frequently caused by drugs.⁵ G-CSF is reportedly strongly associated with the occurrence of arteritis.^{5–7} However, arteritis is a rare adverse event of G-CSF. Therefore, it is difficult to suspect G-CSF-associated arteritis. In our case, infectious arteritis was ruled out because of the negative blood culture and poor responsiveness to antibiotic therapy. Autoimmune disease was excluded because of the absence of temporal artery tenderness and the patient's age. G-CSF-associated arteritis should be considered when patients receiving chemotherapy with G-CSF develop an unexplained fever.

G-CSF-associated arteritis is treated by discontinuing G-CSF. Steroid therapy is required in cases with severe or active organ involvement associated with arteritis, and the dose depends on severity.^{8–11} A standard dose of steroid therapy in patients with G-CSF-associated arteritis is not yet established. However, in previous reports, the dose of steroid therapy for patients with G-CSF-associated arteritis was 20–80 mg/day of oral PSL, or 1 g/day of methylprednisolone depending on the severity.^{12–19} In our case, the original PSL dosing at 10 mg/day was continued because there was no organ involvement. Based on a systematic review,² several cases went into remission without steroid therapy after G-CSF discontinuation. However, one case progressed to aortic dissection despite steroid therapy.¹² Since the individual course of the disease is not predictable, it is essential to monitor each patient carefully. The re-administration of G-CSF should be avoided in patients with G-CSF-associated arteritis,² and alternative therapy with a lower rate of neutropenia should be considered.

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Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent was obtained from the patient for the publication of this report and associated images.

Registry and the Registration No. of the study/trial

Not applicable.

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