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Case Report

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography revealed the course of granulocyte-colony stimulating factor-associated aortitis: A case report ☆

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ABSTRACT

A 72-year-old man with diffuse large B-cell lymphoma underwent fluorine-18 fluorodeoxyglucose (FDG) PET/CT, revealing lymphoma lesions and no evidence of aortitis. The patient received chemotherapy and was treated with granulocyte colony-stimulating factor (G-CSF) for neutropenia. During chemotherapy, the patient underwent PET/CT again, revealing FDG accumulation and wall thickening at the aortic arch, which suggested aortitis. The patient was only experiencing fatigue. G-CSF-associated aortitis was suspected, and the original G-CSF was switched to another G-CSF while continuing chemotherapy. Three months later, the third round of PET/CT showed that FDG accumulation and wall thickening of the aortic arch vanished. PET/CT may be useful for not only the diagnosis but follow-up of G-CSF-associated aortitis. Radiologists should recognize incidental aortitis on PET/CT in patients receiving G-CSF administration.

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Introduction

In the Individual Case Safety Report (ICSR) database, established by the World Health Organization (WHO), granulocyte colony-stimulating factor (G-CSF) drugs (e.g., lipegfilgrastim, lenograstim, filgrastim, and pegfilgrastim) were reported as one of the most common types of drugs associated with large-vessel vasculitis [1]. Nevertheless, G-CSF is commonly used for treating chemotherapy-associated neutropenia in patients with malignancies such as breast cancer, prostate cancer, and lymphoma [2]. G-CSF-associated aortitis is a rare

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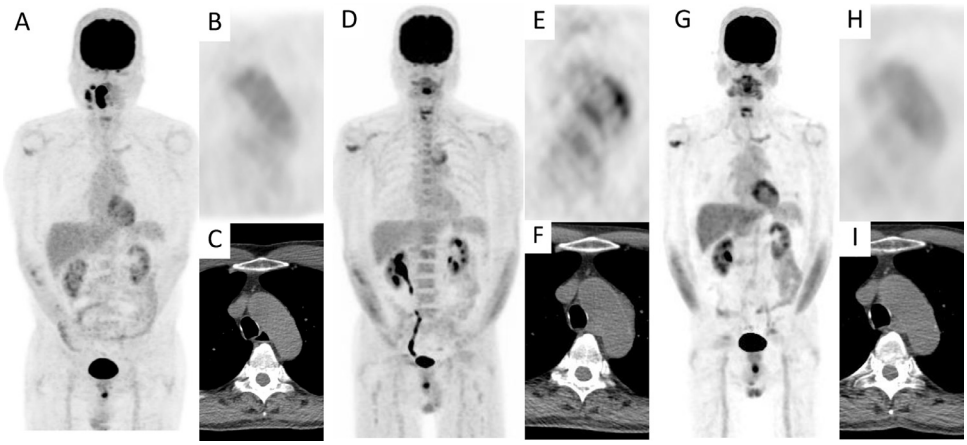

Figure – (A-C) Results from the first round of ^{18}F-FDG PET/CT. The lymphoma lesions (right tonsil and enlarged right cervical lymph node) showed FDG accumulation, and there were no signs of aortitis. (D-F) Results from the second round of ^{18}F-FDG PET/CT, performed after chemotherapy. Fourteen days after the last administration of G-CSF (pegfilgrastim), wall thickening of the aortic arch and FDG accumulation were observed, as well as physiological diffuse FDG accumulation in the bone marrow. (G-I) Results from the third round of ^{18}F-FDG PET/CT, performed after chemotherapy. The wall thickening improved and FDG accumulation decreased.

adverse event, and it has been observed by CT, MRI, and FDG PET/CT as nonspecific findings. There are reports on PET/CT that captured the onset of the disease as an increased accumulation of FDG at the wall of aorta, but no reports that followed the course until the remission. This disease may show only mild nonspecific symptoms clinically [2], which requires radiologists' careful reading not to miss the findings on PET/CT. Herein, we report the onset and the remission of G-CSF-associated aortitis that was detected on PET/CT.

Case presentation

A 72-year-old man was suspected of having a mesopharyngeal tumor and an enlarged right cervical lymph node. The patient underwent FDG PET/CT for the evaluation of lesions (Fig. A, MIP PET image; Fig. B, axial PET image; Fig. C, axial CT image). The right tonsil and enlarged right cervical lymph node showed FDG accumulation (SUVmax values of 30.0 and 13.4, respectively). There were no signs of aortitis at that time. The biopsy of the right tonsil revealed diffuse large B-cell lymphoma (DLBCL). The patient received one course of chemotherapy with rituximab, pirarubicin, cyclophosphamide, vincristine, and prednisolone (R-THP-COP therapy) and three courses of chemotherapy with rituximab, doxorubicin hydrochloride, cyclophosphamide, vincristine, and prednisolone (R-CHOP therapy). For neutropenia, the patient first received a granulocyte-colony-stimulating factor (G-CSF) drug, namely filgrastim, at a dose of 75 μg, and then received pegfilgrastim at a dose of 3.6 mg. Fourteen days after the last pegfilgrastim administration, the patient underwent PET/CT because of malaise (Figs. D-F). The DLBCL lesions became smaller, showing a reduction in FDG accumulation. However, the bone marrow showed diffuse FDG accumulation due to the G-CSF. Additionally, the wall of the aortic arch became thicker and exhibited increased FDG accumulation (SUVmax of 4.6), which suggested aortitis. Laboratory tests revealed subtle inflammation (C-reactive protein of 1.81 mg/dL, IL-6 of 9.8 pg/dL), but the laboratory results were negative for bacterial infections, tuberculosis, syphilis, and human immunodeficiency virus (HIV), as well as IgG4, anti-Ro/SS-A, antineutrophil cytoplasmic, and anti-nuclear antibodies. As a result, G-CSF-associated aortitis was suspected. Pegfilgrastim was switched to filgrastim and chemotherapy was continued. Laboratory tests showed improvement, and 3 months later, PET/CT was performed again (Figs. G-I). FDG accumulation of the DLBCL lesions and aortitis disappeared, and wall thickening vanished. Afterward, the patient progressed without relapse.

Discussion

G-CSF-associated aortitis is a rare adverse event, but the occurrence may be underestimated. The symptoms are similar to Takayasu arteritis (TAK) and may be nonspecific, including malaise, fever, and chest or abdominal pain as well as laboratory findings suggestive of inflammation, and some cases may be asymptomatic [2,3]. Pegfilgrastim has been used since the early 2000s and is frequently reported as the causative agent, whereas other drugs, such as filgrastim, have been used since the 20th century and have not been well investigated [2]. Aortitis can occur 2–15 days after G-CSF administration [3–5]. Neutrophil mobilization, activation of T cells, and release of inflammation cytokines, such as IL-6 and TNF-α, may be the cause, but the mechanism remains unclear [6,7]. Some cases improved with the change or discontinuation of the G-CSF drug, and some cases required steroid administration [8,9]. Aortitis occurs at the aorta and major branches, and the ascending aorta and descending thoracic aorta are the most common sites [6]. Aortitis is more common in females, similar to other forms of large-vessel vasculitis such as TAK and giant

cell arteritis (GCA) [1,2]. However, G-CSF-associated aortitis is more common in people over 50 years of age who undergo chemotherapy, unlike TAK and GCA [2,5,6].

Radiological features are not specific, whereas CT and MRI can reveal the thickened walls [2,4]. Moreover, there was a report of G-CSF-associated aortitis that showed 'double ring sign', which is considered specific to TAK [10]. PET/CT has been used to observe FDG accumulation at thickened walls, and in severe cases, aneurysms, dissections, and ruptures can occur [2,4,8,11–13]. Aortitis is classified into two categories depending on the cause: inflammatory (e.g., drug-induced vasculitis, rheumatoid arthritis, IgG4-related diseases, GCA, TAK) and infectious (e.g., syphilis, tuberculosis, Salmonella) [5]. According to the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides, vasculitis is categorized based on its features such as age and site [14]. There are several limitations. Firstly, we did not have a pathological confirmation because the biopsy was risky. There was possibility of other diseases like lymphoma. Secondly, there is no standard diagnostic method for G-CSF-associated aortitis. Despite the limitations, we diagnosed the present case as G-CSF-associated aortitis because 1) the period after G-CSF administration was consistent with previous reports, 2) it was atypical of GCA because it improved without steroids, 3) taxanes, which often induce vasculitis, were not used, and 4) there were no findings suggestive of other diseases.

There are no reports that captured the onset to the remission of aortitis on PET/CT. Moreover, the course of the disease was clarified by PET/CT, suggesting that the technique is useful not only for diagnosis but also for post-treatment follow-up.

Conclusion

G-CSF-associated aortitis is a rare adverse event that can cause complications. Radiologists should recognize incidental aortitis on PET/CT in patients receiving G-CSF administration.

Patient consent

Written and informed consent was obtained from the patient.

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