CASE REPORT

Pegfilgrastim-induced vasculitis of the subclavian and basilar artery complicated by subarachnoid hemorrhage in a breast cancer patient: a case report and review of the literature

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Abstract

Background: Pegfilgrastim (PEG) is a sustained-duration pegylated form of filgrastim, a granulocyte-colony stimulating factor agent that is widely used as prophylaxis against febrile neutropenia during chemotherapy. We report the case of a breast cancer patient who developed PEG-induced vasculitis complicated by subarachnoid hemorrhage (SAH) and review the relevant literature.

Case presentation: A 48-year-old woman had undergone surgery for breast cancer and was receiving docetaxel and cyclophosphamide as adjuvant chemotherapy (docetaxel 75 mg/m2, cyclophosphamide 600 mg/m2); on day 4 of treatment, PEG had been administered. On day 14, she was admitted to hospital with fever, general malaise, and neck pain, and her C-reactive protein level was found to be high (12.65 mg/dL). Although infection was initially suspected, antimicrobial treatment was ineffective and other laboratory test results were negative for this. Contrast-enhanced computed tomography on day 22 showed thickened vessel walls in the left subclavian artery, the origin of the common carotid artery, and the thoracoabdominal aorta. On day 26, magnetic resonance imaging of the head to investigate possible causes of headache showed signs consistent with SAH, and magnetic resonance angiography images showed irregularity in the basilar artery wall; the findings of both studies were considered to be due to PEG-induced vasculitis. Once treatment with prednisolone 40 mg/day had started, the wall thickening and irregularity improved.

Conclusion: Although an uncommon adverse effect, vasculitis affecting vessels of various sizes may be caused by PEG. To the best of our knowledge, this report is the first to describe a case of G-CSF-induced vasculitis complicated by SAH. In cases of persistent high fever and elevated inflammatory response after PEG administration and in the absence of infection, clinicians should consider the possibility of drug-induced vasculitis.

Keywords: Breast cancer, Granulocyte-colony stimulating factor, Pegfilgrastim, Subarachnoid hemorrhage, Vasculitis

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in the blood [1]. PEG is recommended for the prevention and management of febrile neutropenia (FN) during chemotherapy and is widely used in the treatment of various cancers. In the field of breast cancer, PEG is generally administered during adjuvant chemotherapy with dose-dense AC (doxorubicin plus cyclophosphamide) and TC (docetaxel plus cyclophosphamide) regimens.

Adverse events commonly associated with PEG include bone pain, back pain, and fever; however, these rarely lead to treatment discontinuation. Of greater concern is drug-induced vasculitis in blood vessels of various sizes, which is a known adverse effect of G-CSF agents; although their incidence is rare, capillary leak syndrome, cutaneous vasculitis, and large-vessel vasculitis have been reported [2].

According to a report by Oshima et al. in the Japanese Adverse Drug Event Report database, the frequency of G-CSF-induced large-vessel vasculitis in Japan is 0.47%, which is much higher than the 0.0014% reported for the USA [3]. Since 2015, the number of reported cases of G-CSF-induced vasculitis has been increasing, especially in Japan [4]. This may be partly due to increased awareness among clinicians, because in June 2018, the Japanese Ministry of Health, Labour and Welfare (MHLW) added large-vessel vasculitis to the list of serious adverse effects in the package insert for G-CSF preparations.

We report the case of a patient with PEG-induced vasculitis complicated by subarachnoid hemorrhage (SAH) and provide a review of the relevant literature. We also discuss the implications of the present case for clinical practice.

**Case presentation**

A 48-year-old woman visited our hospital complaining chiefly of fever, general malaise, and left cervical pain. The patient had previously undergone unilateral mastectomy, axillary sentinel node biopsy, and axillary dissection. After surgery, she was taking loxoprofen, acetaminophen, mirogabalin, and mexiletine, in addition to using Chinese herbal medicine. She had started on TC (docetaxel 75 mg/m², cyclophosphamide 600 mg/m²) as adjuvant chemotherapy. On day 4 of treatment, PEG had been administered for prevention of FN. On day 5, the patient had developed fever and arthralgia, and on day 7, a skin rash and pruritus had appeared on her neck and back. Although the symptom of itching had been relieved by treatment with an anti-allergic drug, she continued to have a fever of ≥38 °C and was admitted to hospital on day 14 for examination, investigations, and treatment.

On admission, the patient’s body height was recorded as 162 cm; body weight, 48.3 kg; body temperature, 37.6 °C; blood pressure, 91/47 mmHg; heart rate, 71 beats/min; and SpO₂, 99% (in room air). She had clear consciousness, general malaise, and spontaneous pain and tenderness on the left side of the neck. There was no redness or swelling in the neck, and the cervical lymph nodes were not enlarged. Table 1 summarizes the laboratory values on admission; an elevated neutrophil-pre-dominant white blood cell count of 14.11 × 10³/μL and an elevated C-reactive protein (CRP) level of 12.65 mg/dL were observed, but procalcitonin level was normal and the results of blood and urine culture were negative. Plain computed tomography (CT) images of the chest and abdomen showed no obvious evidence of infection.

Figure 1 shows the course of the patient’s condition after admission. Because of the possibility of infection, intravenous drip infusion of tazobactam–piperacillin (TAZ/PIPC 4.5 g, four times a day), a broad-spectrum antibacterial medication, was started on the day after admission. However, the patient continued to have fever ≥38 °C and left cervical pain, and right cervical pain newly appeared. Despite the administration of TAZ/PIPC, blood test results showed no reduction in inflammatory response, and therefore infection was considered unlikely to be the cause of the patient’s symptoms.

On the 8th day after admission (day 22 of treatment), contrast-enhanced CT (Fig. 2) and carotid artery ultrasonography (Fig. 3) were performed to investigate the possibility of vasculitis, based on the persistent high fever and neck pain. The CT images showed thickened

| Variable | Laboratory value |
|----------|------------------|
| Blood | |
| White blood cells, /μL | 14.11 × 10³ |
| Neutrophils, /μL | 12.43 × 10³ |
| Hemoglobin, g/dL | 10 |
| Platelets, /μL | 172 × 10³ |
| Biochemistry | |
| CRP, mg/dL | 12.65 |
| Procalcitonin, ng/mL | 0.04 |
| D-dimer, μg/mL | 1.3 |
| Total bilirubin, mg/dL | 0.7 |
| AST, U/L | 36 |
| ALT, U/L | 25 |
| Autoimmune antibodies | |
| MPO–ANCA, IU/mL | <0.5 |
| PR3–ANCA, IU/mL | <0.5 |
| C3, mg/dL | 125 |
| C4, mg/dL | 27 |
| Anti-DNA | <2.0 |

**Table 1** Laboratory values on the patient’s admission to hospital

**ALT** alanine aminotransferase, **AST** aspartate aminotransferase, **C3** complement 3, **C4** complement 4, **CRP** C-reactive protein, **DNA** deoxyribonucleic acid, **MPO–ANCA** myeloperoxidase–anti-neutrophil cytoplasmic antibody, **PR3–ANCA** serine proteinase 3–anti-neutrophil cytoplasmic antibody
vessel walls in the left subclavian artery, the origin of the common carotid artery, and the thoracoabdominal aorta (Fig. 2B), suggesting vasculitis. The carotid artery ultrasonography revealed hypoechoic or isoechoic wall thickening around the vessels from the bilateral common carotid bifurcation to the bilateral internal carotid arteries (Fig. 3A), thus providing further evidence of vasculitis. Levels of myeloperoxidase–anti-neutrophil cytoplasmic antibody (MPO–ANCA), serine proteinase 3–anti-neutrophil cytoplasmic antibody (PR3–ANCA), and complements C3 and C4 were all normal, and the test result for anti-deoxyribonucleic acid (DNA) antibodies was negative, excluding the possibility of autoimmune disease.

Because the patient’s symptoms appeared immediately after PEG administration, we diagnosed PEG-induced vasculitis and started treatment with prednisolone (PSL) 40 mg/day on the same day. After administration of PSL, her fever rapidly resolved, CRP level decreased, and the cervical pain gradually eased until resolving completely by the 20th day of hospitalization (day 34). Images of the neck obtained by CT (Fig. 2C) and ultrasonography (Fig. 3B) on the 22nd day of hospitalization (day 36) showed clear improvement in the thickening of the vessel walls.

On the fourth day of hospitalization (day 18), the patient developed headache, but this fluctuated from day to day. On the 24th day of hospitalization (day 38), magnetic resonance imaging (MRI) of the head revealed SAH and vascular irregularity in the basilar artery. After contrast-enhanced CT and cervical US showed improvement in the vascular wall thickening, and the head MRI scan showed a trend toward improvement in the vascular irregularity, the patient was discharged on the 44th day. CRP C-reactive protein, CT computed tomography, MRI magnetic resonance imaging, PSL prednisolone, SAH subarachnoid hemorrhage, TAZ/PIPC tazobactam–piperacillin; US ultrasonography
While the patient was followed up as an outpatient, the dose of PSL was gradually tapered until the treatment was discontinued, and the MRA image obtained at 5 months after discharge shows that the vascular irregularity has improved (Fig. 4D), with no sign of SAH recurrence. Since her discharge from the hospital, she has been receiving tamoxifen as adjuvant therapy, but TC therapy has not been resumed.

**Discussion**

We have described a case of PEG-induced vasculitis of the subclavian and basilar artery complicated by SAH. To the best of our knowledge, this is the first report of a case of G-CSF-induced vasculitis complicated by SAH. The patient developed skin rash, fatigue, and neck pain after PEG administration; left cervical pain was her chief complaint during hospitalization. Although the skin rash
Fig. 3 Carotid artery US images before and after treatment. A US image of the right internal carotid artery on day 8 of hospitalization, revealing hypoechoic or isoechoic wall thickening around the vessels from the bilateral common carotid bifurcation to the bilateral internal carotid arteries (white arrowheads). B US image of the right internal carotid artery on day 22 of hospitalization, showing improvement in the vessel wall thickening after treatment. US ultrasonography

Fig. 4 MRI images of the head. A Fluid-attenuated inversion recovery image on day 24 of hospitalization. The high-signal area along the sulcus suggested SAH (white arrows). B MRA image on day 24 of hospitalization, showing wall irregularity in the basilar artery (white arrowheads). C Cerebral angiography on day 26 of hospitalization. No signs of cerebral aneurysm were observed. Wall irregularities are visible in the left vertebral artery, basilar artery, and bilateral posterior cerebral arteries (white arrowheads). D MRA image 5 months after discharge. The irregularities in the wall of the basilar artery had completely disappeared. MRA magnetic resonance angiography, MRI magnetic resonance imaging, SAH subarachnoid hemorrhage
and fatigue were likely to have been adverse effects of TC therapy, left cervical pain is not a typical adverse effect of TC. The patient reported, through a detailed interview, that her physical condition started to feel abnormal after taking PEG, which led us to strongly suspect the possibility of a PEG-induced adverse effect. Furthermore, the imaging findings excluded the possibility of infection or autoimmune disease as the cause, and no local skin changes or enlarged lymph nodes were observed. Consequently, we concluded that PEG-induced vasculitis was the most probable cause.

Table 2 summarizes details of the present case in addition to all 25 cases of vasculitis associated with PEG administration identified through our literature search for G-CSF-associated vasculitis, from the first, published in 2017, to the present. Although PEG was approved by the US Food and Drug Administration and by the European Medicines Agency in 2002, and has been marketed in Japan since 2014, it was not until 2017 that the first of these cases reports was published. Of the cases identified, 88% (23/26) of the patients were women, median age was 66 (43–76) years, and 58% (15/26) of patients had breast cancer as the primary disease. Median time to onset of symptoms after PEG administration was 8 (1–17) days; and most patients were hospitalized within 2 weeks of PEG administration. In 7 cases, including the present case, large-vessel vasculitis was observed not only in the aorta, but also in the common carotid artery, which is a major branch of the carotid artery.

Most patients received corticosteroid treatment; prednisolone was administered at a dose of 0.5–1.0 mg/kg/day (absolute dose, 30–60 mg/day). In the present case, the patient also received prednisolone 40 mg/day. Symptoms were found to improve rapidly in all patients who received corticosteroid treatment. In addition to the case of SAH described in this report, G-CSF-associated vasculitis complicated by aneurysm [5] and aortic dissection [6] have also been reported, and thus, early diagnosis and therapeutic interventions, such as corticosteroid treatment for vasculitis, may be needed to prevent serious complications.

In a systematic review of data from 57 patients with G-CSF-induced vasculitis [4], 91% (52/57) were found to be women, median age was 60 (40–77) years, and 47% (27/57) had breast cancer as the primary disease. Although any G-CSF preparation can cause vasculitis, 67% (38/57) of the cases were reported to have been caused by a sustained-duration form of G-CSF. This is consistent with the trend observed in cases listed in Table 2, including the present case.

Regarding concomitant chemotherapy, in 40% of the identified cases of vasculitis (including the present case), the patients had been treated with a taxane-based regimen; however, other anticancer agents had been used in another 10% of cases. This suggests that vasculitis can be caused by G-CSF agents used in combination with any types of chemotherapy, although there may be synergic effects between taxane agents and G-CSF agents [7, 8]. Because vasculitis has been reported to have improved in all cases after restarting treatment with chemotherapy alone after discontinuing G-CSF, and there have been no reports of vasculitis caused by taxanes alone, we can conclude that G-CSF was the main cause of the patient’s condition, while perhaps also bearing in mind that vasculitis is especially likely to occur when G-CSF is used in combination with taxanes. G-CSF-induced vasculitis may tend to occur in middle-aged women with breast cancer, who are likely to be treated with a taxane-based regimen; however, we were unable to identify any specific risk factors through our literature search.

Although restarting G-CSF is not recommended, the TC regimen may be restarted in cases in which the vasculitis has fully resolved. However, in the present case, although the vasculitis had improved, a serious complication (i.e. SAH) had occurred, therefore we decided not to restart the TC regimen.

Although the mechanism underlying G-CSF-induced large-vessel vasculitis has not been fully clarified, it has been suggested to involve induction of immune mediators such as interleukin (IL)-2 and IL-6, leading to generation of pathological Th17 cells [6]. Sato et al. reported a case in which IL-6 was elevated at the onset of aortitis, but decreased during its improvement, suggesting that activation of antigen-specific CD4+ T cells, as stimulated by IL-6, may promote autoimmunity [6]. Furthermore, it has been suggested that phagocytosis and/or enzymatic activity resulting from activation of neutrophil precursors may be the cause of wall damage [5].

Takayasu arteritis (TAK) and giant cell arteritis (GCA) are diseases known to cause large-vessel vasculitis [9]. In TAK, vasculitic pain is experienced at the site of vasculitis, and stenosis and dilation of the vessels are observed on imaging. Both conditions have many similarities to G-CSF-induced vasculitis: elevated CPR in the blood test results, more frequent occurrence in middle-aged women, and higher prevalence in East Asia [3, 7]. As in G-CSF-induced vasculitis, inflammatory mediators (e.g. IL-6) and Th17 are known to be involved in the pathogenesis of TAK and GCA [10], and a similar genetic predisposition (e.g. Th17 pathway) may explain the high prevalence in East Asia. Moreover, there have been reports of G-CSF-induced vasculitis leading to aortic dissection [6], and of GCA being triggered by G-CSF administration [11], suggesting that G-CSF-induced large-vessel vasculitis may be caused by the same mechanism underlying TAK and GCA.
Table 2: Previously reported cases of PEG-associated vasculitis

| Reference | Year | Age (years) | Sex | Primary disease     | Symptoms                  | CRP (mg/dL) | Time between PEG administration and symptoms (days) | Location of vasculitis | Diagnostic modality | Steroid |
|-----------|------|-------------|-----|---------------------|---------------------------|-------------|------------------------------------------------------|------------------------|--------------------|---------|
| Koyama et al. [19] | 2021 | 43          | F   | Breast cancer       | + Back pain               | 27.1        | 5                                                    | Arch/TA               | CT                 | PSL 60 mg |
| Fujiiwara et al. [20] | 2021 | 66          | F   | Colon cancer        | + Back pain               | 20.2        | 2                                                    | Arch/TA, SCA          | CT                 | PSL 30 mg |
| Kametani et al. [21] | 2021 | 56          | M   | Mucinous chondrosarcoma | + General fatigue, rash with pain | 38.8        | 4                                                    | Arch/TA               | CT                 | PSL 60 mg |
| Saito et al. [22] | 2021 | 71          | F   | Intrahepatic cholangiocarcinoma | + Back pain, chest pain | 18.9        | 7                                                    | Arch/TA               | CT                 | PSL 30 mg |
| Jimbo et al. [1] | 2021 | 58          | F   | Breast cancer       | + Myalgia, chills, nausea | 13.7        | 8                                                    | SCA                   | CT                 | None      |
| Lee et al. [7] | 2020 | 66          | F   | Breast cancer       | + Myalgia, chest discomfort, dyspepsia | 21.8        | 15                                                   | Arch/TA, CCA          | CT, PET/CT         | PSL 0.5 mg/kg |
| 49          | F   | Breast cancer | + | Myalgia, chills, headache | 29.6        | 12                                                   | Arch/TA, CCA, SCA, innominate artery | CT                  | PSL 0.5 mg/kg |
| 50          | F   | Breast cancer | + | Myalgia, chills    | 32.9        | 17                                                   | Arch/TA, AA, CCA, innominate artery | CT                  | PSL 0.5 mg/kg |
| 59          | F   | Breast cancer | + | Myalgia, chills, headache | 10.9        | 14                                                   | Arch/TA, CCA          | CT                 | PSL 0.5 mg/kg |
| 53          | F   | Breast cancer | + | Left anterior neck pain | 8.2         | 11                                                   | CCA                   | CT                 | None      |
| Nakamura et al. [23] | 2020 | 66          | F   | Breast cancer       | + Malaise, abdominal discomfort | 20.4        | 10                                                   | Arch/TA, AA          | CT, MRI            | PSL 55 mg |
| Taimen et al. [8] | 2020 | 53          | F   | Breast cancer       | + Chest pain, sore throat, earache, dyspnea | Unknown | 1                                                     | Arch/TA               | CT, MRI            | Corticosteroid |
| Miyazaki et al. [25] | 2020 | 65          | F   | Pancreatic cancer   | +                        | 46.4        | 4                                                    | Arch/TA               | CT                 | None      |
| Hoshina et al. [26] | 2019 | 72          | F   | Breast cancer       | +                        | 27.9        | 4                                                    | Arch/TA               | CT                 | PSL 60 mg |
| Yukawa et al. [27] | 2019 | 71          | F   | Endometrial cancer  | +                        | 21.4        | 13                                                   | SCA                   | CT                 | None      |
| Sasaki et al. [28] | 2019 | 69          | M   | Non-Hodgkin lymphoma | +                        | 30.1        | 13                                                   | Aorta                  | CT                 | None      |
| Lardieri et al. [29] | 2018 | 72          | F   | Uterine cancer      | + Cough, lumbar and back pain | 30.1        | 13                                                   | Aorta                  | CT                 | None      |
| 76          | F   | Breast cancer | + | Precordial pain | 35.9        | 7                                                    | Aorta                  | CT                 | None      |
| 61          | F   | Breast cancer | + | Left neck pain      | 25.4        | 7                                                    | Aorta                  | CT, MRI            | None      |
| 65          | F   | Breast cancer | + | Chest tightness, cough | 30.8        | 9                                                    | Aorta                  | CT                 | Steroid   |
| 66          | M   | Prostate cancer | + |                        | 33.3        | 8                                                    | Aorta                  | CT                 | None      |
| 69          | F   | Esophageal cancer | + |                        | 11          |                                                       | Aorta                  | CT, US             | None      |
| Reference       | Year | Age (years) | Sex | Primary disease   | Symptoms                          | CRP (mg/dL) | Time between PEG administration and symptoms (days) | Location of vasculitis | Diagnostic modality | Steroid               |
|-----------------|------|-------------|-----|-------------------|-----------------------------------|-------------|----------------------------------------------------|------------------------|---------------------|----------------------|
| Sato et al. [6] | 2017 | 67          | F   | Lung cancer       | Malaise                           | 202         | 8                                                  | Arch/TA, CCA           | CT, US              | mPSL 80 mg           |
| Present case    | 2022 | 48          | F   | Breast cancer     | Malaise, left neck pain           | 1265        | 14                                                 | Arch/TA, AA, CCA       | CT, US              | PSL 40 mg            |

AA abdominal aorta, Arch aortic arch, CCA common carotid artery, CRP C-reactive protein, CT computed tomography, F female, M male, mPSL methylprednisolone, MRI magnetic resonance imaging, PEG pegfilgrastim, PET positron emission tomography, PSL prednisolone, SCA subclavian artery, TA thoracic aorta, US ultrasonography.
It has been reported that 15% of cases of non-traumatic SAH do not originate from an aneurysm (e.g. ruptured cerebral aneurysm), and that of these non-aneurysmal cases, two-thirds are due to perimesencephalic hemorrhage and one-third due to rare conditions including hemorrhage associated with inflammatory lesions of cerebral arteries, non-inflammatory lesions of intracerebral vessels, vascular lesions in the spinal cord, sickle cell disease, and the use of certain drugs [12]. In cases of inflammatory lesions of cerebral arteries, the possibilities of primary angitis and angiitis secondary to autoimmune diseases (e.g. Behcet’s disease and polyarteritis nodosa) can be considered [13–15]. In the present case, the patient had no notable history of disease or injury other than breast cancer, and no cerebral aneurysm was detected on cerebral angiography, which together suggest that she had non-traumatic non-aneurysmal SAH. MRA images obtained several months after treatment for PEG-induced vasculitis showed improvement in the irregularities of the cerebral vessel wall, and no evidence of recurrence. Because the condition was reversible, the wall irregularities were unlikely to have been caused by underlying disease, so we considered it to be a case of G-CSF-induced vasculitis. Autoimmune vasculitis can be classified according to the size of the vessels affected (i.e. large-, medium- or small-vessel vasculitis) [16]. By contrast, G-CSF-induced vasculitis can cause vasculitis in vessels of any size [2].

Mechanisms suggested for development of non-aneurysmal SAH associated with vasculitis include small-vessel vasculitis as well as chronic hypoperfusion and hypoxia following cerebral vascular stenosis, leading to angiogenesis with formation of abnormal, and therefore rupture-prone, collateral vessels [17, 18]. In the present case, the localized nature of the SAH suggests that the hemorrhage originated from peripheral vessels of the posterior cerebral artery or from the neovascular vessels. In summary, PEG caused large-vessel vasculitis of the thoracoabdominal aorta and common carotid artery, which triggered small-vessel vasculitis in the brain, resulting in SAH as a complication.

Conclusions
Vasculitis associated with PEG is under-recognized in clinical practice; however, cases involving cerebrovascular vessels can be fatal, so clinicians should be alert to this possibility. Drug-induced vasculitis should be considered in patients experiencing persistent fever and elevated inflammatory response after PEG administration, and when infection has been excluded as a cause. In such cases, early diagnosis and therapeutic intervention may prevent serious complications.

Abbreviations
AA: Abdominal aorta; AC: Doxorubicin plus cyclophosphamide; ALT: Alanine aminotransferase; Arch: Aortic arch; AST: Aspartate aminotransferase; CCA: Common carotid artery; CT: Computed tomography; CS: Complement 3; C4: Complement 4; CRP: C-reactive protein; DNA: Deoxyribonucleic acid; F: Female; FN: Febrile neutropenia; G-CSF: Granulocyte-colony stimulating factor; GCA: Giant cell arteritis; IL: Interleukin; M: Male; MRA: Magnetic resonance angiography; MRI: Magnetic resonance imaging; MPO–ANCA: Myeloperoxidase–anti-neutrophil cytoplasmic antibody; PEG: Pegfilgrastim; PET: Positron emission tomography; PSL: Prednisolone; PR3–ANCA: Serine proteinase 3–anti-neutrophil cytoplasmic antibody; SAH: Subarachnoid hemorrhage; SCA: Subclavian artery; TA: Thoracic aorta; TAK: Takayasu arteritis; TAZ/PIPC: Tazobactam/piperacillin; TC: Docetaxel plus cyclophosphamide; US: Ultrasonography.

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Competing interests
TN has received honoraria from Chugai Pharmaceutical, Eli Lilly, Pfizer, Novartis Pharma, AstraZeneca, and Daiichi Sankyo. The other authors have no conflict of interest to declare.

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References
1. Jimbo H, Horimoto Y, Okazaki M, Ishizuka Y, Kido H, Saito M. Drug-induced aortitis of the subclavian artery caused by pegfilgrastim: a case report. Surg Case Rep. 2021;7(1):197.
2. D’Souza A, Jaiyesimi I, Trainor L, Venuturumili P. Granulocyte colony-stimulating factor administration: adverse events. Transfus Med Rev. 2008;22(4):280–90.
3. Oshima Y, Takahashi S, Tani K, Tojo A. Granulocyte colony-stimulating factor–associated aortitis in the Japanese Adverse Drug Event Report database. Cytokine. 2019;119:47–51.
4. Muzzana M, Pedrazzoli P, Lasagna A. G-CSF and G-CSF–related vasculitis: a systematic review of the literature and intriguing future research perspectives. Future Oncol. 2021;17(33):4619–34.
5. Miller EB, Grosu R, Landau Z. Isolated abdominal aortitis following administration of granulocyte colony stimulating factor (G-CSF). Clin Rheumatol. 2016;35(6):1655–7.

6. Sato Y, Kaji S, Ueda H, Torni K. Thoracic aortitis and aortic dissection following pegfilgrastim administration. Eur J Cardiothorac Surg. 2017;52(3):993–4.

7. Lee SY, Kim K, Kim JY, Park TK, Choi SH, Im YH, Kim MY, Park YH, Kim DK. The incidence and clinical features of PEGylated filgrastim–induced acute aortitis in patients with breast cancer. Sci Rep. 2020;10(1):18647.

8. Taimen K, Heino S, Kohonen I, Relas H, Huovinen R, Hanninen A, Pirila L. Granulocyte colony-stimulating factor– and chemotherapy-induced large-vessel vasculitis: six patient cases and a systematic literature review. Rheumatol Adv Pract. 2020;4(1):kkaa004.

9. Parodis I, Dani L, Notarnicola A, Martenhed G, Fernstrom P, Matikas A, Wiklander OP. G-CSF–induced aortitis: two cases and review of the literature. Autoimmun Rev. 2019;18(6):615–20.

10. Yoshifuji H. Pathophysiology of large vessel vasculitis and utility of inter-leukin-6 inhibition therapy. Mod Rheumatol. 2019;29(2):287–93.

11. Umeda M, Ikenaga J, Koga T, Michitsui T, Shimu T, Fukui S, Nishino A, Nakasima Y, Kawashiri SY, Iwamoto N, Ichinose K, Hiro Yamai, Tama M, Nakamura H, Oruchi T, Kawai T. Giant cell arteritis which developed after the administration of granulocyte-colony stimulating factor for cyclic neutropenia. Intern Med. 2016;55(16):2291–4.

12. van Ginj J, Rinkel GJ. Subarachnoid haemorrhage: diagnosis, causes and management. Brain. 2001;124(2):249–78.

13. Spitzer C, Mull M, Rohde V, Kosinski CM. Non-traumatic cortical subarachnoid haemorrhage: diagnostic work-up and aetiological background. Neuroradiology. 2005;47(7):525–31.

14. Jayasurya R, Murugesan N, Kumar R, Dubey AK, Priyamvada PS, Swaminathan RP, Parameswaran S. Spontaneous non-traumatic subarachnoid hemorrhage without cerebrovascular malformations in a maintenance hemodialysis patient. Indian J Nephrol. 2015;25(5):310–4.

15. Cuvinicu V, Viguier A, Caliviere L, Roposo N, Larrue V, Cognard C, Bonneville F. Isolated acute nontraumatic cortical subarachnoid hemorrhom. AJNR Am J Neuroradiol. 2010;31(8):1355–62.

16. Jennette JC, Falk RJ, Bacon PA, Baez N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillemin L, Hagen EC, Hoffman GS, Jayne DR, Kallenberg CG, Lamprecht P, Langford CA, Matteson EL, Merkel PA, Ozen S, Pusey CD, Rasmussen N, Rees AJ, Scott DG, Specks U, Stone JH, Takahashi K, Watts RA. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1–11.

17. Shuaib UA, Kate M, Hornik J, Jenakathil T. Recurrent non-aneurysmal subarachnoid haemorrhage in Takayasu arteritis: is the cause immunological or mechanical? BMJ Case Rep. 2013;2013:bcr2013008825.

18. Joshi H, Allen J, Qiu D, Wu J, Nahab F, Law K, Hu R. Spontaneous non-aneurysmal subarachnoid hemorrhage in Takayasu arteritis: a case implicating hyperperfusion and cerebral dysautoregulation. BJR Case Rep. 2019;5(2):20180131.

19. Koyama Y, Adachi K, Yagi M, Go Y, Orimoto K, Kawai S, Uenaka N, Okazaki K, Watadani T, Abe O, Kurokawa M. Arteritis following administration of granulocyte colony--stimulating factor: a case series. Int J Hematol. 2019;110(3):370–4.

20. Lardieri A, McCulley L, Christopher Jones S, Wronnow D. Granulocyte colony-stimulating factors and aortitis: a rare adverse event. Am J Hema. 2018;93(10):E333–6.

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