Unexpected outcome (positive or negative) including adverse drug reactions

Unilateral lymphadenopathy due to the use of granulocyte colony stimulating factor

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Summary

A 36-year-old woman was admitted to our hospital after modified radical mastectomy operation. Adjuvant chemotherapy was administered using TAC regimen. Severe neutropenia occurred after chemotherapy. Granulocyte colony stimulating factor (G-CSF) was given to treat neutropenia. On the second day of G-CSF use, the patient complained of swelling of her neck on the left side, which subsided spontaneously after discontinuation of G-CSF medication. However, the same symptom recurred following G-CSF use on the second cycle of chemotherapy. B-mode ultrasound showed swollen lymph nodes and biopsy revealed no evidence of metastasis. Therefore, the unilateral lymphadenopathy is considered to be the side effect of G-CSF, which is very rare.

BACKGROUND

Chemotherapy induced neutropenia is a frequent and serious complication of cytotoxic cancer treatment. Granulocyte colony stimulating factors (G-CSFs) are commonly used to treat neutropenia, to achieve rapid recovery of patients and allow for continuation of chemotherapy without adjustment of doses. Severe side effects of G-CSFs are very rare, and G-CSFs are considered very safe. Herein, we report a case of unilateral lymphadenopathy related to G-CSF use in a 36-year-old woman, who suffered from chemotherapy-induced neutropenia after modified radical mastectomy.

CASE PRESENTATION

A 36-year-old Chinese woman was admitted in December 2010. She was diagnosed of breast cancer of pT2N3M0, IIIB, estrogen receptor (ER) (–), progesterone receptor (PR) (–), Her-2 neu (++) and had undergone modified radical mastectomy surgery before admission. Physical examination was normal upon admission. TAC regimen (docetaxel/epirubicin/cyclophosphamide) was given to the patient for adjuvant chemotherapy. After one cycle of chemotherapy, the patient developed severe neutropenia with an absolute neutrophil count of 200 cells/microl on the 7th day. Then G-CSF was administered at a dose of 5 ug/kg/day for 9 days to as a rescue treatment. On the second day of the use of G-CSF, she complained of swelling of her neck on the left side. Physical examination identified a soft mass with tenderness, about 40×50 mm in size (figure 1). B-mode ultrasound suggested that the mass was swollen lymph nodes (figure 2). The mass regressed to 20×20 mm after discontinuation of G-CSF. However, the mass increased in size again after prophylactic use of G-CSF after second cycle of chemotherapy. To rule out lymph node metastasis, paracentesis was performed. Biopsy showed no evidence of metastasis in the lymph nodes (figures 3 and 4). Lymphadenopathy spontaneously disappeared after the cessation of G-CSF.

OUTCOME AND FOLLOW-UP

Chemotherapy and radiotherapy have been completed in the patients. She visits our clinic every 2 months. All the physical examinations and laboratory tests have been normal ever since.

DISCUSSION

Human G-CSF is a haematopoietic hormone promoting the growth, proliferation, differentiation and maturation of myeloid and leukocytic lineages. G-CSFs have been used to increase granulocyte count in neutropenic patients, reducing the incidence and duration of neutropenia in patients receiving cytotoxic chemotherapy. Prophylactic G-CSFs use is recommended for patients undergoing chemotherapy regimen associated with a risk of febrile neutropenia in more than 20% patients, as is, its use in situations where dose-dense or dose-intense chemotherapy strategies have survival benefit.¹

G-CSF is generally considered safe and effective. Benefits of G-CSF treatment include less infection, less antibiotic use and shorter hospital stay. Some minor self-limited side effects have been reported, including muscle pain, headache, fever, rhinitis, rashes, fatigue, thrombocytopenia and injection site reactions.^{2–3} These side effects are generally mild to moderate. Life-threatening complications such as stroke, myocardial infarction and splenic rupture are very rare.^{4–5}

In this case, we reported another side effect of G-CSF therapy, lymphadenopathy, which is extremely rare. Kawachi *et al.*⁶ reported a case of a patient with Richter's syndrome who developed pronounced lymphadenopathy in response to administration of G-CSF in 1994. Enlargement of lymph nodes was generalised in that case. Postmortem microscopic examination of the lymph nodes discovered features of small lymphocytic lymphoma. Presence of G-CSF receptor on the neoplastic cells was demonstrated by Northern blot.⁶ In our case, a 36-year-old woman received daily subcutaneous injections of

Figure 1 The left side of the patient's neck swelled after the use of granulocyte colony stimulating factor G-CSF.

Figure 2 B-mode ultrasound showed the swelling lymph nodes (a, b).

Figure 3 B-mode ultrasound showed the swelling lymph nodes and biopsy needle (red arrow) (a, b).

Figure 4 Specimen of the swelling lymph node showed plasma cells and neutrophilic granulocytes (a, b).

G-CSF to treat severe neutropenia induced by adjuvant chemotherapy. Lymphadenopathy was identified on the second day of the treatment, regressed after discontinuation of G-CSF and recurred upon reuse of G-CSF. Biopsy of the swollen lymph nodes suggested 'plasma cells and neutrophilic granulocytes' in the lesion site. Expression of G-CSF receptors on T-cells and neutrophils has been well known⁷ and may explain lymphadenopathy induced by G-CSF therapy. Though no evidence of malignancy was found by biopsy, the possibility of lymph node metastasis of cancer could not be completely ruled out. Notably, the lesion was unilateral and many risk factors were present in this patient such as extensive lymph metastases (as many as 20 lymph nodes), negative for both ER and PR and positive for Her-2 neu (++) . More and more studies have shown that G-CSF is expressed by cancer cells.^{8,9} It is possible that cancer cells may interact with exogenous G-CSF through surface G-CSF receptors, which in turn causes inflammatory infiltration and is manifested as unilateral lymph node enlargement.

Side effect of G-CSF or metastasis, lymphadenopathy caused extra psychological burden for the patient. Close follow-up is warranted and undergoing.

Learning points

- ▶ Human G-CSFs have been widely used to improve granulocyte count in neutropenia. It is generally considered safe and effective.
- ▶ As we know, lymphadenopathy with the use of G-CSF is rare.
- ▶ The result of biopsy is very important, and further follow-up is needed.

Competing interests None.

Patient consent Obtained.

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