

cancer or relapsed ovarian carcinoma must be viewed as purely speculative, and randomized trials are required.

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Anaphylactoid Reaction in a Normal Donor Given Granulocyte Colony-Stimulating Factor

To the Editor: Colony-stimulating factors, such as granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF), are increasingly used to mobilize blood stem cells in normal donors for collection by apheresis and infusion into allogeneic transplant recipients.¹ G-CSF also has been given to normal donors to mobilize granulocytes for subsequent apheresis collection and transfusion into neutropenic recipients.² Side effects of G-CSF administered to normal donors generally have been mild and reversible, and include bone pain, headache, fatigue, and nausea.^{3,4} Serious and potentially life-threatening toxicity of G-CSF has been reported in only one normal donor, who developed spontaneous splenic rupture.⁵ This report describes the first case of an anaphylactoid reaction that occurred in a normal donor after subcutaneous (SQ) injection of G-CSF given to mobilize neutrophils for granulocyte collection.

A 16-year-old female patient agreed to donate G-CSF-mobilized granulocyte components on a protocol approved by the University Institutional Review Board. Evaluation and screening for blood-product donation were performed using a modification of criteria established by the American Association of Blood Banks.² The donor felt well the morning of G-CSF administration and denied any recent illness. Vital signs just before G-CSF were blood pressure 110/70 (mmHg) and heart rate 88 beats per minute (bpm). G-CSF (Filgrastim; Neupogen, Amgen, Thousand Oaks, CA) 590 µg (10 µg/kg) was given SQ. Fifty minutes later, the patient complained of acute onset of shortness of breath and severe crampy lower abdominal pain. Physical examination showed blood pressure 80/50 (mmHg), heart rate 140 bpm, respiratory rate of 28 per minute, clear lungs by auscultation, a diffusely tender abdomen without rebound tenderness, and no rash. Oxygen saturation was 100%. An intravenous fluid bolus was administered, along with H₁ and H₂ receptor blockers and corticosteroids. Subsequently, the systolic blood pressure increased and the respiratory distress resolved; however, the

intensity of the abdominal pain persisted. The severity of the pain decreased after administration of meperidine (50 mg). Epinephrine (0.2 mg) was given SQ and within 10 minutes, the patient's abdominal pain resolved. Two hours after the G-CSF injection, the patient also developed bladder spasms and passed small blood clots in the urine. The following day, the patient complained only of weakness. The abdominal pain and hematuria did not recur, and the blood pressure remained normal.

In normal donors, there have been no published reports of anaphylactoid reactions to G-CSF. Within one hour of G-CSF injection, the patient reported developed signs and symptoms consistent with an anaphylactoid drug reaction, which rapidly responded to therapy directed to that diagnosis. The immediate temporal relationship to cytokine administration and the failure to identify any other cause suggested that the adverse event was caused by G-CSF. Filgrastim is a recombinant protein produced by *Escherichia coli*, which differs from endogenous G-CSF by addition of an N-terminal methionine and by being nonglycosylated.⁴ It is possible that either Filgrastim itself or another component of the product was responsible for the anaphylactoid drug reaction observed in this patient. Acute urticarial and delayed-type hypersensitivity reactions have been associated with polysorbate 80 (Tween® 80), a component of Filgrastim.^{6,7}

G-CSF frequently is prescribed for cancer patients given myelosuppressive chemotherapy. Only two reports of anaphylactoid reactions possibly associated with G-CSF have been described, one in an allogeneic transplant recipient, and the other in a patient with Felty's syndrome and infection.^{8,9} In both cases, the association between G-CSF and the anaphylactoid reaction was uncertain because of the possibility that the reaction observed could have been caused by either concurrent medications or the patients' serious illnesses. However, based on the reason for this uncertainty, it is possible that the frequency of this adverse event in cancer patients is underreported because many patients with cancer have complex illnesses and take other medications while receiving G-CSF. Thus, rare but serious adverse events caused by G-CSF may be attributed to other causes. These confounding issues less likely would be factors in recognition of this adverse drug event in healthy normal donors. Recognizing these concerns, and that far fewer normal donors than cancer patients have been given Filgrastim, physicians should be cognizant that the adverse event profile of Filgrastim given to normal donors may not be exactly the same as that observed in cancer patients. The author recommends that all normal donors given G-CSF be carefully monitored after drug administration, and that they be informed that although G-CSF has a good safety profile, rare but potentially serious adverse events can occur.

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