

LETTER TO THE EDITOR

Severe allergic reaction with anaphylaxis to G-CSF (lenograstim) in a healthy donor

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Haemopoietic growth factors such as G-CSF have been widely used to stimulate granulocyte production in neutropenic patients. Various studies have looked at the potential side effects of G-CSF and found it to have a good safety profile.^{1,2} Most commonly, G-CSF is used to prevent or shorten the period of neutropenia secondary to chemotherapy. It acts by supporting the proliferation, differentiation and activation of committed progenitor cells of the granulocyte series. G-CSF is also extensively used to mobilize into the peripheral blood haemopoietic stem cells from healthy sibling or volunteer unrelated donors. Currently, two forms of recombinant human G-CSF are available for this purpose: both of these are licensed in the UK for use in healthy donors. Lenograstim is a Chinese hamster ovary-derived G-CSF consisting of 174 amino acids with 4% carbohydrate, indistinguishable from native G-CSF. Filgrastim is an *Escherichia coli*-derived G-CSF, differing from lenograstim in being non-glycosylated and in having an extra methionine group at the N-terminal end of the peptide chain.

We describe a case of a severe allergic reaction with anaphylaxis to lenograstim (Granocyte, Chugai Pharma, London, UK) in a healthy volunteer unrelated donor. The donor was a 26-year-old man, with a history of mild asthma but no known drug allergies. He was not taking any regular medications for his asthma. He was physically active, with no other medical history. After being selected as an HLA match for a patient in need of an unrelated donor haemopoietic stem cell transplant, the volunteer donor underwent a full medical assessment including a chest X-ray, and was deemed medically fit to undergo the PBSC collection.

In accordance with The Anthony Nolan Trust policy, the G-CSF injections were given by a fully qualified nurse from 'Healthcare at Home', which is an independent company that provides healthcare services to individuals within their own homes in the UK. Under normal circumstances, the nurse remains with the donor for 1 h after each injection to ensure that no adverse events have occurred. This is done for a total of 3 days. The fourth injection is given at the blood stem cell collection centre. The Healthcare at Home nurse is fully trained to manage adverse reactions, should they occur, and carries the appropriate emergency kit to deal with any allergic response to the drug.

The donor received his first dose (10 mcg/kg) of lenograstim s.c. Forty minutes after the injection, he began to feel dizzy and developed redness and puffiness of his

eyes. Over the next few minutes, his clinical state deteriorated rapidly with shortness of breath and he developed severe chest tightness with bronchospasm, hypotension and tachycardia. A clinical diagnosis of severe allergic reaction with anaphylaxis was made. The nurse immediately administered epinephrine i.m. and oxygen. The donor responded well to the treatment and improved clinically within minutes of the epinephrine injection. He was transferred by ambulance to a local accident and emergency department. On arrival, he was found to have stable observations-T 36.8, pulse-103/min regular, BP 123/67 mm Hg, RR 16/min and O₂ saturation of 99% on air. He was given 200 mg of hydrocortisone i.v. along with chlorpheniramine. He was kept under observation for a few hours and then discharged home with anti-histaminics.

As the donor was well on the day of the injection and had not received or taken anything apart from the lenograstim, we believe it had a causal role in his reaction. This donor had been assessed in accordance with Anthony Nolan policy and fully satisfied the medical and physical criteria required for PBSC mobilization. All protocols were followed strictly. He had been assessed medically with a full history, examination and blood tests and had been deemed fit. We believe that we could not have predicted this reaction. The nurse from 'Healthcare at Home' reacted swiftly and decisively, with a good outcome. This highlights the importance of having staff trained in dealing with emergencies on administering the injection, and then observing the donor for an hour after the injection.

The donor was followed up by the Anthony Nolan Donor Welfare Officer and the Medical Officer. The donor remained well and, despite having gone through a severe reaction to G-CSF, was quite committed and went on to donate his BM.

Given the life-threatening nature of the incident and the fact that G-CSF is used extensively, we felt it necessary to report this case. Allergic reactions to G-CSF have been documented earlier but there are very few reports of anaphylaxis. Khoury *et al.*³ reported a high incidence (10/20 patients) of side effects including anaphylaxis (2/10) in chronic myelogenous leukaemia (CML) patients who had received sibling donor transplants and then G-CSF. No predictive factors could be identified and the underlying mechanism remained unknown. Batel-Copel *et al.*⁴ reported an anaphylactic reaction following an i.v. dose of G-CSF. This patient had chemotherapy for an unknown primary adenocarcinoma. Similarly, Jaiyesmi *et al.*⁵ have reported acute anaphylaxis following subcutaneous.c. administration of G-CSF.

In conclusion, it is clearly important that clinicians remember that G-CSF can cause severe anaphylactic

reactions even in normal persons and ensure that staff are fully trained to deal with such emergencies if they do arise.

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