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Allogeneic peripheral blood stem cell collection as of 2008

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Abstract

The rapid growth of the use of recombinant human granulocyte colony-stimulating factor (rhG-CSF) to mobilize and collect allogeneic peripheral blood stem cells (PBSCs) for transplantation has made it a new international standard. While the procedure remains safe, older donors, donors with significant comorbidities and pediatric donors are now often employed. This brings a new set of challenges in the donor evaluation, medical clearance, informed consent and collection process. Rare and unexpected severe adverse events related to rhG-CSF administration and PBSC apheresis have been described. Proper PBSC donor counseling, evaluation and care have become even more important.

Keywords: Normal donors; Granulocyte colony-stimulating factor; G-CSF; Filgrastim; Allogeneic stem cell transplantation

1. Introduction

The last decade has witnessed the rapid growth of the use of recombinant human granulocyte colony-stimulating factor (rhG-CSF) in allogeneic peripheral blood stem cell (PBSC) donors. Over 15,000 stem cell donors are harvested every year, and rhG-CSF mobilized PBSCs accounted for 75% of related and 50% of unrelated donor donations in North America alone in 2003 [1]. This manuscript provides a concise outline of the key features of PBSC collection as performed in most transplant or apheresis units worldwide as of 2008. As the non-glycosylated rhG-CSF form (filgrastim) is the product most often administered (at least in North America), the terms rhG-CSF and filgrastim will be used interchangeably in the text.

2. Normal PBSC donor evaluation and informed consent

Table 1 outlines the key diagnostic elements of normal PBSC donor evaluation. In general, these tests should reflect current Foundation for the Accreditation of Cellular Therapy (FACT; www.factwebsite.org) standards for donor evaluation. They should also reflect current FDA regulatory requirements (www.fda.gov) for the United States or, for other countries, local regulatory requirements. The evaluation is primarily aimed at (1) identifying factors that could jeopardize donor safety and well-being during donation and (2) detecting infectious agents or diseases that could potentially be transmitted to the recipient.

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Table 1
Normal PBSC donor work-up

1. Physical assessment, medical history
2. EKG, CXR
3. Hematology, chemistry profile, coagulation profile, electrolytes, serum protein electrophoresis
4. Infectious disease screening panel (Hepatitis A, B, C, HIV, HTLVI/II, syphilis, West Nile virus, CMV)
5. ABO, Rh typing
6. Urinalysis
7. Serum or urine pregnancy tests (for women of childbearing age)
8. Peripheral venous access assessment
9. Marrow aspiration/biopsy (if abnormal blood counts or otherwise clinically indicated)
10. Additional testing as clinically indicated

While there is no clear-cut upper age limit in the related donor setting, older related donors deserve more attention, as they are far more likely to carry significant comorbidities (hypertension, diabetes, atherosclerotic vascular disease, degenerative joint disease, etc.). Appropriate subspecialty consultations should be requested in these cases. This is likely to become a more pressing issue in the years ahead, as an increasing number of older recipients, whose siblings are of similar age, are now considered candidates for allogeneic stem cell transplantation [2,3]. Younger donors (i.e. pediatric) present an entirely different set of challenges, primarily related to venous access as well as donor consent (frequently requiring the involvement of a third party to minimize the potential for a conflict of interest) [4]. There is also more hesitation in administering growth factors to healthy pediatric donors, in view of the possible potential for long-term adverse events (see below). In the unrelated donor setting, the age range is between 18 and 55–60 years, depending on the national registry in question.

Normal donors with positive testing for hepatitis B and C can still be employed as donors if no suitable alternative donor can be identified. Under these circumstances the recipient needs to be counseled about the long-term risk for acute and chronic hepatitis transmission. Likewise, normal donors with a past history of treated malignancy may still be considered as donors, although a five-year cancer-free period is usually advised and appropriate recipient counseling is indicated. These two categories of donors should be told that they will also be deferred from regular blood donation. All donors should be notified about their test results, and appropriate follow-up with their personal physician(s) should be arranged as clinically indicated.

An emerging issue is the potential conflict of interest related to donor work-up, medical evaluation and ultimately informed consent in the related donor setting. It has become clear that in many cases, at least in the US, physicians directly or indirectly involved in the care of the recipient are also involved in the PBSC donor evaluation and clearance process (Anderlini P & O'Donnell P; personal communication, 2007). Ideally, at least some degree of separation between donor and recipient care should be implemented in the related donor setting, as it is accomplished effectively through unrelated donor registries.

3. Cytokine administration to normal donors

RhG-CSF (primarily filgrastim, but also lenograstim) is ordinarily employed for this purpose, although occasionally recombinant human granulocyte-macrophage colony-stimulating factor (rhGM-CSF) and other agents such as AMD3100 (a CXCR4 antagonist) have been used [5,6]. The filgrastim dose usually ranges from 5–16 mcg/kg subcutaneously daily, given once or in two divided doses for 4–7 days [7,8].

There is evidence supporting a dose–response effect with regard to CD34+ cell mobilization [9]. Most allogeneic donors are mobilized with 10 mcg/kg for 5 days [10–14]. Doses as high as 20 mcg/kg daily have been employed. There is some evidence suggesting that a twice-daily rhG-CSF (lenograstim, filgrastim) administration schedule may be more effective than a once-daily schedule. It has also been suggested that the glycosylated form of rhG-CSF (lenograstim) may be biologically more active than the non-glycosylated form (filgrastim) for PBSC mobilization [15]. The pegylated form of G-CSF is currently being investigated for allogeneic PBSC mobilization [16].

Filgrastim-related adverse events can be divided into common "expected" ones (usually mild-to-moderately severe) and uncommon "unexpected"