Bone Marrow Transplantation for Fanconi Anaemia Using a Fludarabine-based Preparative Regimen with CD34+ Cell Selection

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Abstract

Fanconi anaemia (FA) is an important cause of inherited aplastic anaemia in childhood because of its relatively high frequency of occurrence, the implication for different management, and the need for genetic counselling. The common manifestations are congenital physical abnormalities, marrow failure, and predisposition to development of cancers. Bone marrow transplantation has been used to treat marrow failure for FA patients but they are at increased risks of transplant related toxicities and graft versus host disease. We report two children with FA who were treated successfully with matched sibling bone marrow transplantation using a new fludarabine-based conditioning regimen without irradiation. The stem cell source was from marrow which was infused after positive selection of CD34+ cells. Both patients had haematological recovery and no major post-transplant complications occurred. One achieved full donor chimerism and stable mixed chimerism was present in another. This regimen appears to be effective and can prevent FA patients from major transplant related complications.

Key words Aplastic anaemia; Bone marrow transplantation; Fanconi anaemia

Introduction

Inherited marrow failure syndromes comprise 30-35% of cases of paediatric marrow failure while Fanconi anaemia (FA) represents about two-third of the total. Other than Fanconi anaemia, the inherited marrow failure syndromes also include rare conditions such as Shwachman-Diamond syndrome, dyskeratosis congenita, Diamond-Blackfan anaemia, Kostmann’s syndrome etc. FA is an autosomal recessive disorder and there are currently at least 11 known FA genes with diverse mutations. The manifestations in FA are heterogeneous with variable phenotypic expression. These include various congenital physical abnormalities such as skin hyper-pigmentation, café au lait spots, short stature, abnormal thumbs and radii, and organ malformations. Marrow failure occurs in most FA patients and approximately 3 quarters of them develop evidence of marrow failure within the first decade of life. FA patients are also predisposed to develop haemic malignancies and solid tumours. It should be noted that 25% or more of the known FA patients have few or none of the physical abnormalities. The diagnosis of FA therefore relies on alertness of clinicians and should then be confirmed by demonstration of cellular hypersensitivity to DNA clastrogenic (cross-linking) agent, such as the diepoxybutane (DEB) test which should induce excessive chromosome breakage or aberrations in FA lymphocytes.

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