



Engraftment, Graft Failure, and Rejection

13

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Abstract

Engraftment following HSCT is an essential goal for sustained long-term and effective hematopoiesis. It's the most important criteria for a better overall survival. However, stem cell engraftment may be accompanied with a clinical condition known as engraftment syndrome (ES) that could have a devastating outcome. Nurses caring for HSCT recipients must be aware of ES symptoms in order to intervene quickly and appropriately. On the other hand, graft failure (GF) is a major complication and is associated with a dismal prognosis. It is classically divided into primary or secondary graft failure. The risk factors associated with GF may be related to characteristics of the graft, the patient, the donor, or the transplant procedure. The conditions that are associated with an increased occurrence of GF and the available treatment options will be thoroughly discussed in the chapter along with the nursing considerations.

Keywords

Engraftment • Engraftment syndrome • Graft failure • Graft rejection
Pediatrics • Nursing

13.1 Engraftment

Engraftment is the process by which hematopoietic stem cells (HSC) make their way (homing) to free bone marrow (BM) niches where they can find optimal conditions to survive and proliferate. Once they have reached the BM microenvironment, HSC have to proliferate to generate all hematopoietic cell subsets (Servais et al. 2013). A fundamental goal for successful engraftment is that the transplanted HSC are capable of

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sustaining long-term effective hematopoiesis; production of red blood cells, white blood cells, and platelets; and their release to peripheral blood (Locatelli et al. 2014). Engraftment is the most important variable for a better overall survival after stem cell transplant (Cluzeau et al. 2016).

13.2 Engraftment Definition

Various definitions of engraftment exist in the literature. Engraftment is most commonly defined as the first of three consecutive days of achieving a sustained peripheral blood neutrophil count of $>500 \times 10^6/L$ (Wolff 2002). Platelet engraftment is usually defined as independence from platelet transfusion for at least 7 days with a platelet count of more than $>20 \times 10^9/L$ (Teltschik et al. 2016). The two major factors affecting engraftment are the graft source and the hematopoietic stem cell transplant (HSCT) conditioning regimen. Generally, there are three common sources of HSCT grafts: bone marrow (BM), harvested from the iliac crest; peripheral blood stem cells (PBSC), following G-CSF mobilization of HSC to the peripheral circulation with later collection of these cells by leukapheresis; and cord blood (CB). Champlin et al. (2000) published a large retrospective multivariate analysis which compared results of 288 HLA-identical sibling PBSC transplantations with results of 536 HLA-identical sibling BM transplantations. Patients who received PBSC had significantly faster recovery of neutrophils and platelets compared to BM transplants. Neutrophils exceed the threshold of $500 \times 10^6/L$ between 2 and 6 days earlier with PBSC than after BM. In an EBMT study, the time interval for engraftment was 12 days for PBSC and 15 days for BM. Platelet recovery is also faster by approximately 6 days, i.e., platelet recovery of $20 \times 10^9/L$ was reached at day +15 for PBSC patients and day +20 for patients receiving BM (Schmitz et al. 2002). CB transplant is associated with delayed engraftment. A large study of 1268 patients (73% children) with acute leukemia (64% acute lymphoblastic leukemia (ALL), 36% acute myeloid leukemia) in remission analyzed engraftment kinetics and outcomes after a single-unit CB transplantation with

myeloablative conditioning regimen. The median time to neutrophil engraftment was 25 days (range 11–108) for children and 23 days (range 11–116) for adult recipients ($P = 0.6$) (Ruggeri et al. 2014). Furthermore, when comparing intensity of conditioning regimens, Slavin et al. (1998) described for the first time that allogeneic non-myeloablative HSCT was better tolerated than any standard myeloablative conditioning, with a shorter period of neutropenia and a shorter period of platelet dependence.

Methods of determining donor engraftment rely on the assessment of donor and recipient cell components in the recipient BM or PB, termed as chimerism analysis (see Chap. 12).

13.3 Engraftment Syndrome

Engraftment syndrome (ES) is a clinical condition that is characterized by fever, rash, pulmonary edema, weight gain, liver and renal dysfunction, and/or encephalopathy. It occurs at the time of neutrophil recovery after stem cell transplantation (SCT) (Chang et al. 2014). Most data suggest that ES results from a pro-inflammatory state caused by the release of diverse cytokines and other mediators of inflammation. Clinical features of ES are similar in children and adults. Criteria for the diagnosis of ES typically include fever (thought to be not from infection) and features of systemic vascular leak, as ES was previously referred to as capillary leak syndrome. ES can resemble acute or hyperacute GvHD giving rise to the question of whether ES is an early manifestation of GvHD.

13.4 Management of ES

ES may be self-limited and require no therapy. Indications for treatment include a temperature of $>39^\circ C$ without an identifiable infectious etiology and clinically significant manifestations of vascular leak, especially pulmonary edema. ES is corticosteroid responsive, and treatment is given only as long as symptoms persist, usually for 1 week (Spitzer 2015).

13.5 Nursing Considerations

Due to the potentially devastating outcomes associated with ES, nurses caring for SCT recipients must be aware of ES and its symptoms in order to intervene quickly and appropriately (Thoele 2014). Nursing assessment, in order to identify changes, should include the assessment of the clinical manifestation of ES, with anticipated presentation 9–13 days posttransplantation:

- Frequent temperature monitoring.
- Routine skin assessment for rashes or abnormalities.
- Respiratory rate, oxygen saturation, and breath sounds (for signs of pulmonary edema).
- Weight changes.
- Appropriate investigations are undertaken to rule out infection such as blood cultures, complete blood count (CBC), and chest X-ray.

Nursing care should include symptom relief by administration of antipyretics; oxygen for hypoxia; diuretics for weight/fluid gain, edema, ascites, and effusions; and a renal dose of dopamine if needed. Nurses should educate patients and caregivers about the signs and symptoms of ES as well as the treatment and management.

13.6 Graft Failure

Although incidence is relatively low, graft failure (GF), when it does occur, is a major complication associated with a dismal prognosis, particularly in recipients of alternative donor HSCT (Ayas et al. 2015). It remains an important contributor to morbidity and mortality after allogeneic SCT. Recent studies indicate that patients experiencing GF have a lower probability of survival in comparison to those with sustained engraftment of donor cells (Olsson et al. 2013; Locatelli et al. 2014).

GF is defined as the lack of hematopoietic cell engraftment following autologous or allogeneic SCT (Lowsky and Messner 2016). It is classically divided into primary or secondary graft failure.

Primary graft failure is defined as no evidence of engraftment or hematological recovery of donor cells, within the first month after transplant, without evidence of disease relapse.

Secondary graft failure refers to the loss of a previously functioning graft, resulting in cytopenia involving at least two blood cell lineages.

Primary graft failure is usually associated with a more significant risk of morbidity and mortality in comparison with secondary graft failure (Olsson et al. 2013; Kato et al. 2013).

13.7 Graft Rejection

The term graft rejection refers to immune-mediated rejection of the donor cells by residual host cells because of genetic disparity between the recipient and the donor. Therefore, this term is only relevant to allogeneic transplants (Lowsky and Messner 2016). Immunological rejection of the hematopoietic stem cell graft is a major cause of graft failure (Olsson et al. 2013). Marrow graft rejection is usually defined by the absence of donor cells in a patient with pancytopenia and reduced marrow cellularity (Martin 2016). Chimerism studies performed by methods of FISH (in sex-mismatched transplant) or by microsatellites enable early diagnosis of GF, and it could be crucial of optimizing the chance of rescuing patients with graft failure (Locatelli et al. 2014). They should be carried out routinely especially in patients who have inadequate marrow function and might be candidates for donor lymphocyte infusion (DLI) or a second transplant (Martin 2016).

The incidence of GF varies between different transplant modalities, studies, and reports. In autologous transplants, a reasonable estimate of GF is between 1 and 3%. The incidence of GF is higher in allogeneic transplant recipients especially if the patient receives an HLA-mismatched or T-cell-depleted graft or a single-unit CB transplant (Lowsky and Messner 2016). Olsson et al. (2013) reported a large retrospective study of 967 transplants performed between 1995 and 2010 and an overall GF rate of 5.6%, with a higher incidence of GF in recipients of SCT for

nonmalignant disorders. Analysis of 23,272 patients from the CIBMTR database produced a similar incidence of primary GF (5.5%) in patients with hematological malignancies after myeloablative conditioning (Olsson et al. 2015). Recently, a retrospective study of a large cohort of 4684 unrelated donor HSCT in the period (2006–2012) confirmed a low rate of graft failure (3.8%) (Cluzeau et al. 2016).

13.8 Risk Factors Associated with Graft Failure

Several risk factors that are associated with GF have been identified over the years (Fig. 13.1). They may be related to characteristics of the graft, the patient, the donor, or the transplant procedure (Olsson et al. 2015). The conditions that are associated with an increased occurrence of graft failure include:

1. HLA disparity – Earlier studies reported that an increase in the degree of HLA mismatch was associated with a higher risk for GF for siblings and unrelated grafts (Anasetti et al. 1989). In particular, HLA class I mismatches are important determinants for graft failure (Petersdorf et al. 2001). Donor selection criteria regarding HLA matching have changed over the years, and it is difficult to compare the results of previous to current studies. HLA disparity is not a consistent finding in more recent studies. Passweg et al. (2011) reported

- HLA disparity
- ABO-mismatching in the donor/recipient pair
- Reduced-intensity conditioning
- Primary diagnosis
- Graft source
- Cell dose
- Graft manipulation
- Others

Fig. 13.1 Risk factors for graft failure include

in a study of 709 participants with hematological malignancies who received unrelated donor reduced-intensity conditioning (RIC) transplants that the risk of GF was comparable between the HLA-matched and HLA-mismatched donors. However, immunological T-cell-mediated responses toward HLA contribute to primary GF as seen by the higher risk of primary GF in mismatched compared to both well-matched and partially matched unrelated grafts (Olsson et al. 2015).

2. ABO mismatching in the donor/recipient pair – ABO incompatibility between the donor and the recipient occurs in approximately 25% of HLA-matched transplants. Usually, it has no influence on the neutrophil engraftment, but certain donor/recipient mismatches have been associated with posttransplant pure red cell aplasia (Lowsky and Messner 2016). Olsson et al. (2013) observed that using ABO-incompatible grafts is no longer a risk factor for GF. They assume that removing the red cells from the graft decreases the number of SC by about 30% of the original dose and this might be the reason for GF and not the ABO incompatibility itself, although more recently, in the largest analysis of primary GF ($n = 23,272$), Olsson et al. (2015) concluded that major ABO incompatibility does in fact still remain a risk factor for primary GF.
3. Reduced-intensity conditioning (RIC) – RIC regimens have lower doses of chemoradiation therapy; the host immune system may persist, resulting with an increased rate of GF (Mattsson et al. 2008; Olsson et al. 2013; Locatelli et al. 2014). Those regimens may result in an intermediate phase, termed mixed chimerism, in which hematopoietic cells are derived from both donor and recipient cells, and thus do not fulfill the traditional definition of GF (Lowsky and Messner 2016).
4. Diagnosis – The primary disease may affect the probability of GF indirectly due to differences in the intensity of pretransplant chemotherapeutic protocols (Olsson et al. 2015).

Patients with severe aplastic anemia (SAA) have higher incidence of GF due to sensitiza-

tion to components of red blood cell caused by multiple transfusions; therefore, in SAA transfusions should be minimized prior to transplant.

Hemoglobinopathies (thalassemia, sickle-cell disease) – The incidence of GF or rejection remains high probably due to an intact immune system. GF is particularly high in patients who have heavy iron overload and organ damage due to excessive transfusion and inadequate chelation treatment (Gaziev et al. 2008).

Myeloid disorders (myelodysplastic syndrome (MDS) and myelofibrosis (MF)) – These patients, most probably, do not receive prior intensive chemotherapy and might resist donor cell engraftment, due to the presence of residual host cells (Lowsky and Messner 2016). In addition, patients with absence of complete remission (CR) prior to transplant have more GF compared to patients in CR ($P < 0.0001$) (Cluzeau et al. 2016).

5. Graft source – Graft type is the strongest risk factor in the multivariate model for primary GF, with three times higher risk in BM compared to PB grafts (Olsson et al. 2015). Passweg et al. (2011) described that the only characteristic that was associated with GF in that study was the use of BM compared with PB ($P = .002$). Unrelated CB transplants are associated with the highest engraftment failure rate (Kekre and Antin 2014).
6. Cell dose – The higher number of CD3 cells in PB is likely to facilitate engraftment and contributes to the lower incidence of primary GF. BM grafts with low cell dose (TNC doses $\leq 2.4 \times 10^8/\text{kg}$) result in a 40% increase in primary GF. PB products per se are associated with cell doses above the threshold that would affect primary GF, or other cell subtypes such as T cells may be equally or more important for engraftment. Nevertheless, while other factors seem more important for primary GF, CD34 cell dose is probably important for subsequent secondary graft failure (Olsson et al. 2015).
7. Graft manipulation – T-cell depletion (TCD) of the graft may cause a potential increased

risk for GF (Lowsky and Messner 2016). Various approaches to TCD are used by transplant centers, and they vary in the rates of GF (Kekre and Antin 2014), although Reisner et al. (2011) emphasize in a review of the developments in the last 15 years that haploidentical transplants demonstrate how obstacles to successful transplantation can be overcome making full haplotype-mismatched transplantation a clinical reality that provides similar outcomes to transplantation from matched unrelated donors (MUD). Encouragingly, in recent years, the graft failure rate for haploidentical transplantation has decreased to levels comparable to those of matched unrelated donors (MUD), matched related donors (MRD), and mismatched unrelated donors (MMURD) (Reisner et al. 2011; Kekre and Antin 2014).

8. Other risk factors that have been identified to cause an increased risk of graft failure are infections especially of viral origin, such as cytomegalovirus (CMV), human herpesvirus 6 (HHV-6), and parvovirus, and the use of drugs that may induce myelosuppression, such as ganciclovir (Locatelli et al. 2014).

Identifying and assessing the risk factors for GF, prior to transplant, allow clinicians to make more informed choices for their patients with respect to BM versus PB, donor selection, immunosuppressive regimens, and when to plan for a rescue transplant (Olsson et al. 2015).

13.9 Treatment Options for GF

Whatever the etiology of graft failure or rejection is, it should be identified as early as possible and recognized as a serious and life-threatening issue requiring immediate intervention (Wolff 2002). Routine monitoring of donor cell engraftment is recommended since the evaluation of chimerism status can be crucial for optimizing the chance of rescuing patients from graft failure (Locatelli et al. 2014). No single drug or strategy has incontrovertibly proven to be superior to others for

reversing graft failure; current approaches to limit the detrimental impact of this complication are primarily based on its prevention (Locatelli et al. 2014). No standard approach to the management of graft failure exists (Hege et al. 2016), and the rescue strategies are limited (Servais et al. 2013). The common approaches are listed below.

13.9.1 Changes to Immune Suppression

Early detection of decrease in donor chimerism enables to modify the immunosuppressive treatment (Dubovsky et al. 1999). Withdrawal of the immunosuppressive drugs is usually the first measure, which by itself can control leukemia in a limited number of patients (Yoshimi et al. 2005). In case of persistent mixed chimerism after allogeneic transplant, it remains unclear if withdrawal of immunosuppressive drugs will accelerate or prevent GF. The limitation of this method includes an increased risk of graft-versus-host disease.

13.9.2 Donor Lymphocyte Infusion

Donor lymphocyte infusion (DLI) has a potent immunological effect and has been increasingly used to treat relapse, especially molecular relapse, but may also be used to overcome rejection in cases of decreasing donor cell chimerism (Mattsson et al. 2008). Persistent mixed chimerism or declining level of donor cell chimerism is associated with increased risk for GF both in adult and pediatric transplant recipients. A large ($n = 163$) prospective multicenter trial of children with acute lymphoblastic leukemia (ALL) after allogeneic SCT demonstrated that children who developed increased mixed chimerism were at higher risk of developing relapse and can be rescued by preemptive DLI (Bader et al. 2004). Administration of preemptive DLI after day +100 to patients that were withdrawn from immunosuppressive medications enabled 50% of the

patients in that study to convert to complete donor type. The majority of the patients required multiple administrations of DLI's. Therefore, DLI may convert mixed donor-host chimerism to full donor chimerism as a surrogate measure to prevent relapse in patients with hematological malignancies (Hale and Petrovic 2014). Frugnoli et al. (2010) reported that escalating doses of DLI is a treatment option for emerging rejection in patients with mixed chimerism following SCT for β -thalassemia. The origin of lymphocytes for DLI could be either frozen aliquots collected from the donor at the time of the original harvest or collected peripherally by leukapheresis or phlebotomy from the donor before DLI (Haines et al. 2015). Side effects of DLI include increased risk of GvHD (Lowsky and Messner 2016) and, in few cases, can lead to marrow aplasia (Mattsson et al. 2008).

13.9.3 CD34+ Boost

Poor graft function is defined by cytopenia of at least two lineages beyond day +28 in patients with complete or near-complete chimerism (Lowsky and Messner 2016). As manifested by the development of a neutrophil count of $<1 \times 10^9/l$ (grade 4) and/or platelet count of $<50 \times 10^9/l$ (grade 3, $25\text{--}50 \times 10^9/l$; grade 4, $<25 \times 10^9/l$) (Frugnoli et al. 2010). Cytopenias may be due to viral infection, medication side effect, or GvHD (Lowsky and Messner 2016). In patients with continued poor graft function in the absence of graft rejection, a boost of donor stem cells without additional preparative chemotherapy may improve overall function of the graft. Because this boost may induce GvHD, T-cell depletion of the stem cells can prevent this and improve survival in some patients (Mattsson et al. 2008). CD34+ selected cell boosts without a conditioning regimen prior to infusion can be a valid option in order to improve poor graft function, and fully reverse graft failure, especially in patients with complete donor chimerism or predominance of donor hematopoiesis (Locatelli et al. 2014; Servais et al. 2013).

13.9.4 Autologous Backup

Infusion of autologous hematopoietic stem cells (HSC) that were collected and stored prior to transplant can restore hematopoiesis in case of GF. The collection of autologous backup prior to allogeneic transplant is according to center policy. In patients with hematological malignancies or with marrow failure syndromes, the collection of autologous backup is controversial (Lowsky and Messner 2016).

13.9.5 Growth Factors

Administration of growth factors, after autologous transplant, significantly shortens the time for neutrophil recovery. In case of poor graft function or GF, it is a reasonable approach until a more definitive intervention is decided. Following allogeneic transplants, the role of growth factors for patients with poor graft function or GF is unclear. It is a reasonable approach for the management of low blood counts, and depending on the cause, it may or may not be effective (Lowsky and Messner 2016). Certainly, hematopoietic growth factors should be considered in the management of graft dysfunction, especially with partial donor chimerism (Wolff 2002).

13.9.6 Regrafting

A second allogeneic transplant is the only potential long-term curative option for patients with GF and rejection (Remberger et al. 2011; Servais et al. 2013; Locatelli et al. 2014; Cesaro et al. 2015). There are no conclusive data for supporting the choice of using either the same donor of the first allograft or an alternative donor (Mattsson et al. 2008; Locatelli et al. 2014). Different studies recommend a variety of options depending on the availability of a donor, the patient's clinical condition, and the underlying disease. Gaziev et al. (2008) recommend using the initial donor for second transplant for patients with thalassemia recurrence following the first

graft. The use of the same donor was more frequent in the sibling group compared with the unrelated group, in a report of second transplant in SAA patients. This might be due to the availability of the donor for transplant (Cesaro et al. 2015). However, in patients with an immune-mediated graft rejection, the use of an alternative donor, whenever possible, is recommended (Locatelli et al. 2014). PB might be the best stem cell source for salvage transplantation (Servais et al. 2013) in order to improve engraftment and thus achieve faster hematopoietic recovery (Cesaro et al. 2015).

There are no uniform criteria about the best conditioning approach for a second SCT in patients who have developed GF although it should differ from that used at the first transplant (Mattsson et al. 2008; Cesaro et al. 2015). Many transplant teams favor using an immunosuppressive non-myeloablative, reduced-intensity conditioning (RIC) regimen in order to avoid unacceptable cumulative toxicities of two consecutive high-dose conditionings given in a short interval of time (Remberger et al. 2011; Servais et al. 2013; Ferrà et al. 2015; Cesaro et al. 2015; Cluzeau et al. 2016). The optimal reconditioning regimen after graft failure still needs to be defined, and standardized protocols are lacking (Teltschik et al. 2016).

In general, a second unrelated HSCT is considered a risky procedure with a lower probability of long-term survival on account of a high incidence of GF, noninfectious organ toxicity, and infectious complications. This negative outcome is also influenced by the type of underlying disease. However, second transplant using related and unrelated donors in SAA patients is feasible with a good chance of long-term overall survival in more than 60% of cases (Cesaro et al. 2015). Second transplant should be considered especially for patients with nonmalignant diseases (Remberger et al. 2011).

In conclusion, GF is a rare complication after allogeneic transplant but is associated with poor outcome. Early identification of the patients at risk and aggressive intervention could rescue or prevent some patients from developing GF.

13.10 Pediatric Considerations

The aim of allogeneic transplant in nonmalignant disease is to achieve sustained engraftment in order to improve the hematopoietic function, to correct the immunocompetence, and/or to increase or normalize the respective enzyme shortage (Bader et al. 2005). Children who may have more than 60- to 70-year life expectancy after undergoing allogeneic transplant may benefit from the approach of reduced-intensity conditioning (RIC) or reduced-toxicity conditioning regimens prior to transplant versus myeloablative conditioning. This is especially true in those with nonmalignant diseases and those with malignant diseases that may have a profound graft-versus-tumor effect (Satwani et al. 2013). In the last several years, the use of RIC has expanded from adults with high indices of comorbidity to candidates without comorbidities (Satwani et al. 2013) as well as to the pediatric population. In pediatric nonmalignant diseases, RIC is an attractive alternative with the potential for decreased regimen-related toxicities, lower incidence of long-term complications, as well as preserving fertility. Graft rejection rates are low, especially when stable mixed chimerism is curative if ensured in the lineage that corrects function (Madden et al. 2016). Graft rejection, in children with inborn errors of metabolism undergoing RIC transplants, still remains an obstacle to the success of the transplant since they are immunocompetent (Kato et al. 2016). The incidence of GF in children varies in the different studies. In a large report of 240 classical SCID patients who received allogeneic transplant between 2000 and 2009 by Pai et al. (2014), 18% of the patients received a boost, an additional transplant from the same donor without conditioning (23 children), or a second transplant from a different donor (with or without conditioning) or from the same donor with conditioning (34 children), and 11 children received both a boost and a second transplant at 5 years. A retrospective study by Mitchell et al. (2013) of 135 children with primary immunodeficiency reported that 18 patients (13%) required a second SCT due to

graft failure or rejection. Satwani et al. (2013) reported a large study of reduced-toxicity conditioning allo-SCT, using both related and unrelated allogeneic stem cell sources in pediatric recipients, with both malignant and nonmalignant diseases. Primary GF occurred in 16 patients (16%) all in unrelated CBT recipients and none in MUD/MSD graft recipients. Chemotherapy naivety was the only significant risk factor for primary GF. In a single-center study by Balashov et al. (2015), the incidence of primary and secondary GF in primary immunodeficient patients undergoing MUD and haploidentical transplants was 27% (10 out of 37 patients). This accrued in patients that were initially in high risk for graft failure, such as chronic granulomatous disease (CGD) and congenital neutropenia.

However, as with the adult patients, evidence on the optimal management of GF in children is limited; therefore, analysis of pediatric GF is important in order to establish a standard treatment strategy against this rare event (Kato et al. 2013). The case report (Fig. 13.2) demonstrates the process of graft rejection, its consequences, and treatment options.

13.11 Nursing Considerations

When a patient fails to engraft, he or she faces a life-threatening situation. Patients experiencing disappointment and fear from the failure of the transplant might express feelings of anger, betrayal, grief, depression, and hopelessness. Similarly, healthcare personnel involved in the patient's care may also feel a sense of failure and grief (Wilson and Sylvanus 2005). General nursing care of patients experiencing GF does not differ from the treatment during the neutropenic period of the transplant, as described in Chap. 7, although nurses should routinely monitor the patient engraftment by daily CBC during the engraftment phase, as it enables to assess for signs of GF as well as delayed engraftment. Chimerism analysis should be evaluated frequently as per local policy especially in patients that are at risk for GF (Fig. 13.3).

A 13 month old baby was transferred from another hospital to a specialist unit due to recurrent infections since he was one month old. He initially presented with a necrotic infected wound after a supra pubic aspiration and an extremely swollen belly. Family history: parents are cousins, have 6 children, one died of infection when he was a few months old.

The baby was diagnosed with Leukocyte adhesion deficiency-1 (LAD1), CD11 & CD18 deficiency and he underwent a BM transplant on 13.7.14 from his MRD sister. Conditioning regimen included Fludarabine, Treosulfan and ATG. Stem cell engraftment was on day +17. On day + 24 due to decreased donor chimerism, from 63% to 20%, Cyclosporine was stopped. Three days later on day + 27 he developed skin rash and was diagnosed with acute GvHD. He went on to develop severe acute GvHD (grade III-IV) involving skin, liver and GI tract. GvHD was treated with Solumedrol, CSA, ATG and one dose of mesenchymal stem cells (on day +56). GvHD improved and at discharge, two months post-transplant he had mixed chimerism of 43% donor cells according to XX FISH analysis. Subsequently donor chimerism continued to decrease and at one year post transplant was 3.5% donor cells by XX FISH analysis. CD 11 & CD 18 was measured only on lymphocytes and not on neutrophils (split chimerism). During that year he suffered again from recurrent infections. He underwent a second allogeneic BM transplant on 11.10.15 from another MRD sister. Conditioning therapy included Busulfan & Fludarabine. Engraftment was on day +14 and chimerism was 60% donor cells (XX). Except for CVC sepsis and removal of the central line the transplant went very well and he was discharged home on day +24 in a very good overall condition.

Currently, 11 months post second allogeneic transplant he is in a good general condition. He has stable mixed chimerism of 87% of donor cells (XX). During that period he was at home with no infections, no GvHD and no other complications post-transplant.

This case demonstrates two important points: discontinuation of cyclosporine does not always reverse the situation of increased mixed chimerism and carries the risk of developing severe GvHD. Second allogeneic transplant is feasible with good outcome.

Fig. 13.2 Case report

Routine monitoring of patient engraftment by daily complete blood count
Serial Chimerism testing
Emotional support for patient experiencing graft failure

Fig. 13.3 Be aware of:

Equally important to the physical care is the emotional support for the patient and family experiencing this devastating, disappointing, and life-threatening situation. Nurses can help to reduce patients' fears by providing accurate, timely information about procedures, symptoms, and feelings that the transplant recipient may experience or is experiencing. Nurses should provide support and education on the diagnosis of

GF, treatment options, and decisions regarding the care plan. All information must be individually tailored to the patient and family needs (Wilson and Sylvanus 2005).

Nurses caring for patients who undergo SCT should be aware of the possibility of graft failure following the transplant. They should know the risk factors associated with GF and the treatment options available. This will lead to a better understanding and recognition of this rare but life-threatening situation. The possibility of GF should be discussed with the patient and his family prior to transplant, and they should be counseled with regard to the risk factors for developing GF. The nursing literature regarding graft failure is scarce with no recent study on the implications and the support needed for the patient who develops graft failure.

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