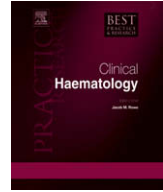




Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beh



13

Thrombotic complications after haematopoietic stem cell transplantation: early and late effects

Dimitrios A. Tsakiris, MD, Head of Haemostasis, Diagnostic Haematology *,
André Tichelli, MD, Head of Diagnostic Haematology

Department of Haematology, University Hospital Basel, CH-4031 Basel, Switzerland

Keywords:

haematopoietic stem cell transplantation
thromboembolism
atherosclerosis
arterial disease
thrombosis
veno-occlusive disease
microangiopathy

Haematopoietic stem cell transplantation is currently the only curative option for many haematological malignancies, but is characterized by a wide spectrum of complications, including haemostatic changes. Bleeding and thrombotic events occur in the early and late phases after transplantation. In the early phase, thrombotic events have a variable clinical picture and present either as venous thrombosis, mainly at the site of central venous lines, veno-occlusive disease (also known as sinusoid occlusion syndrome) or transplant-associated microangiopathy. The latter two occur in the context of an acute graft-vs-host reaction, which involves various organs including the endothelium. In the late phase, years or decades after transplantation, thrombotic events present either as common venous thromboses or as arterial occlusions because of the development of premature atherosclerosis combined with diabetes, hypertension and dyslipidaemia, all of which are accelerated under the influence of the post-transplant treatment. This chapter will discuss the incidence, possible causative associations and treatment options of early and late thrombotic events after haematopoietic stem cell transplantation.

© 2008 Elsevier Ltd. All rights reserved.

Haematopoietic stem cell transplantation (HSCT) is currently the only curative option for many malignant and non-malignant haematological diseases [1]. The conditioning regimen used before HSCT, the development of graft-vs-host disease (GVHD) in the allogeneic setting, and the delayed immune reconstitution are responsible for a wide variety of early and late complications.

* Corresponding author. Tel.: +41 612 654275; Fax: +41 612 654450.
E-mail address: dtsakiris@uhbs.ch (D.A. Tsakiris).

Haemostatic mechanisms before and after HSCT have been studied extensively, since they are involved in a number of adverse reactions [2,3]. In the early phase after HSCT, bleeding events are the most common and apparent haemostatic complications when myeloablative conditioning regimens are used [4]. During this early phase, thrombotic events are relatively rare, probably because cytopenias characterize a considerable time frame in this treatment. However, thrombosis can occur early and late after HSCT, involve various vascular regions and have various clinical manifestations (Table 1) [2,5–7].

This chapter discusses the incidence, pathophysiology and treatment options of thrombotic events, appearing early and late after HSCT, and presenting in a variable clinical spectrum.

Pathophysiology of haemostasis after HSCT

Haemostatic mechanisms undergo various changes after HSCT [8–11]. In the early phase after HSCT, myeloablative regimens usually cause prolonged cytopenias, which predispose to bleeding. However, simultaneously, a variety of other effects can favour the development of thrombotic complications. Residual tumour load at the time of HSCT is a recognized causative factor for thrombosis. Intensive conditioning regimens with total body irradiation (TBI) can cause endothelial damage and turn endothelial cells into a procoagulant surface [12–14]. Immunosuppression with cyclosporin or other calcineurin inhibitors can also stimulate endothelial cells, which in turn release von Willebrand factor and express surface adhesion molecules, thus promoting activation of haemostatic mechanisms [9]. Severe bacterial and fungal infections, a common complication after HSCT, induce acute-phase reactions, which translate into a prethrombotic state. More extensive complications, such as acute GVHD[15,16] or transplant-associated microangiopathy (TAM) involving multiple organs [17,18], are also associated with endothelial damage and/or changes in various coagulation and fibrinolysis proteins, thus facilitating thromboembolic events. All of these changes can contribute to thrombotic complications in the early post-transplant period.

With improvement in long-term survival after HSCT, new insights have been obtained with respect to arterial vascular events [7,19–21]. Chronic GVHD can activate endothelial cells in terms of release of procoagulant factors and surface adhesion molecules [22]. A tentative model of these mechanisms is shown in Fig. 1. Endothelial cells can be damaged or stimulated by cytokines, irradiation and toxic effects of conditioning chemotherapy, and cause lesions where platelets adhere by ligand–receptor interactions. Binding of certain ligands upregulates the expression of adhesion molecules on endothelial cells, which in turn attract and bind cytotoxic T lymphocytes. These can cause more damage, thus perpetuating the GVHD effects on the endothelium.

Data from retrospective studies suggest that long-term survivors after HSCT are at higher risk of developing atherosclerosis and suffer more arterial vascular events compared with the general population [7,19,20]. This risk is particularly exacerbated if established atherosclerotic risk factors co-exist, such as diabetes, hypertension or dyslipidaemia. In the following discussion, early and late thrombotic complications after HSCT will be described in detail (Table 1).

Table 1
Early and late thrombotic complications after haematopoietic stem cell transplantation.

<i>Early thrombotic complications</i>
Catheter thrombosis
Proximal or distal deep vein thrombosis
Pulmonary embolism
Arterial thrombosis
Hepatic veno-occlusive disease
Transplant-associated microangiopathy
<i>Late thrombotic complications</i>
Late venous thromboembolism
Late arterial thrombosis
Premature atherosclerosis

Download English Version:

<https://daneshyari.com/en/article/2100422>

Download Persian Version:

<https://daneshyari.com/article/2100422>

[Daneshyari.com](https://daneshyari.com)