Prevention of Graft-Versus-Host Disease

Introduction

Graft-versus-host disease (GVHD) often occurs in patients who have undergone allogeneic hematopoietic cell transplantation (HCT). This condition results from the immune response, primarily driven by differences between donor (graft) and recipient cells. The immune system of the donor recognizes the recipient cells as foreign, leading to the initiation of GVHD.

GVHD is mediated by T-lymphocytes, which recognize the recipient cells as foreign antigens. Antigenic sites are primarily HLA class I (HLA-A, -B, -C) and class II (HLA-DQ, -DR, -DP). Key sites for initiating GVHD are HLA-A, -B, -DR, which are critical for the recognition of antigenic sites by T-lymphocytes.

Apart from differences in cell types, other factors contributing to GVHD include T-lymphocytes from competent cells and recipient cells that cannot manage T-lymphocytes from the donor. Typically, GVHD occurs in patients with compromised hosts, as the incidence of GVHD after HCT ranges from 10-80%, depending on the factors involved.

Graft-versus-host disease (GVHD) can be prevented through various strategies, such as selecting compatible donors, using conditioning regimens, and reducing the number of T-lymphocytes from donors. Conditioning regimens, such as methotrexate and cyclosporine, can also be used to prevent GVHD.

Transfusion-associated graft versus host disease (TA-GVHD) is a less common but more severe form of GVHD, involving grafts that do not undergo HCT. The incidence of TA-GVHD is lower, but the mortality rate is higher, reaching 90-100% in some cases.

The risk factors for TA-GVHD are similar to those of GVHD, with additional concerns for patients receiving transfusions. Precautions include radiation of blood products to prevent GVHD.

Conclusion

Graft-versus-host disease is a significant challenge in HCT. Prevention strategies are crucial to reduce the incidence and severity of GVHD and TA-GVHD. Understanding the mechanisms and risk factors can help in developing effective preventive measures, ensuring better outcomes for patients undergoing HCT.

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Table 1  Risk Groups for Transfusion-Associated Graft-Versus-Host Disease

Risk Well Defined
- Congenital T-cell defects (known or suspected)
- Immunologic immaturity (fetus or premature infant)
- Intrauterine transfusion
- Neonates undergoing intrauterine exchange transfusion or extracorporeal membrane oxygenation
- Acquired T-cell defects
- Bone marrow or peripheral blood stem cell transplant recipients (allogeneic or autologous)
- Hodgkin lymphoma
- Haplotype sharing between donor and recipient
- Transfusions from blood relatives
- HLA-matched platelet

Risk Identified but Not Clearly Defined
- Hematologic malignancies (other than Hodgkin lymphoma)
- Solid tumors
- Immunologic immaturity or prematurity (in the context of small-volume transfusion)
- Certain immunosuppressive agents such as fludarabine

Risk Not Identified
- Acquired immunodeficiency syndrome (AIDS)
- Aplastic anemia (except in setting of bone marrow transplantation or immunosuppressive therapy)

Table 2  Indications for Irradiation of Blood Components for Prevention of TA-GVHD

<table>
<thead>
<tr>
<th>Indication</th>
<th>MGH</th>
<th>SBK/UHN</th>
<th>HSC</th>
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<tbody>
<tr>
<td>Stem cell transplant recipients                                           ✓</td>
<td>✓</td>
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<tr>
<td>Congenital immunodeficiencies or infants with features suggestive of an undiagnosed immunodeficiency</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Intrauterine transfusion                                                  ✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Premature, low birth weight                                               ✓</td>
<td>✓</td>
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<tr>
<td>Term infants (&lt; 6 months old)                                             ✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Acute lymphoplastic leukemia                                              ✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Other lymphoid leukemia                                                   ✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Acute myeloid leukemia                                                    ✓</td>
<td>✓</td>
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<tr>
<td>Chronic leukemias                                                         ✓</td>
<td></td>
<td>✓</td>
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<tr>
<td>Stem cell donors during harvest                                            ✓</td>
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<td>✓</td>
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<tr>
<td>Fludarabine, alemtuzumab, and ATG recipients                              ✓</td>
<td>✓</td>
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<tr>
<td>Children on intensive myeloablative chemotherapy regimens                ✓</td>
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<tr>
<td>Children with solid tumors of malignant hematologic disease               ✓</td>
<td></td>
<td>✓</td>
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<tr>
<td>Children with solid organ transplants                                     ✓</td>
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<td>✓</td>
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HSC, Hospital for Sick Children, Toronto, Canada; MGH, Massachusetts General Hospital, Boston, MA; SBK, Sunnybrook Health Sciences Centre, Toronto, Canada; UHN, University Health Network, Toronto, Canada.
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เอกสารอ้างอิง
