Graft-Versus-Host Disease

Case Study

Alien T cells React Against their New Host

BM transplant is useful therapy for some forms of leukemia, apalstic anemia, primary immunodeficiency diseases.

BM contains some mature T lymphocyes

If these T cells recognize new host tissue (MHC+MHA) as foreign , severe inflammatory disease can occur = GVHD

Rash, diarrhea, penumonitis, and liver damage

Acute= occurs less than 100 days after tansplant
Chronic= occurs after 100 days post-transplant

In the past, donor alloreactive T cells were investigated using MLR

Now, this is replaced by molecular HLA typing.

GVHD Rash

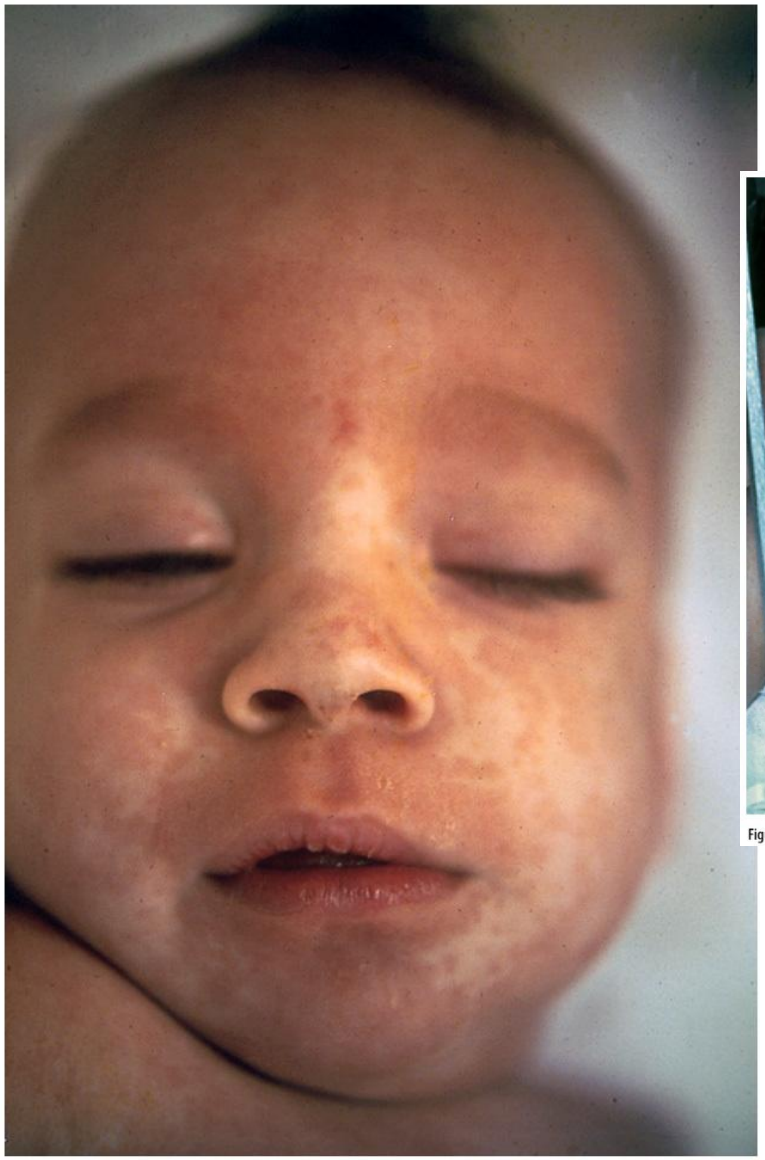


Figure 11.1 Case Studies in Immunology, 7th ed. (© Garland Science 2016)

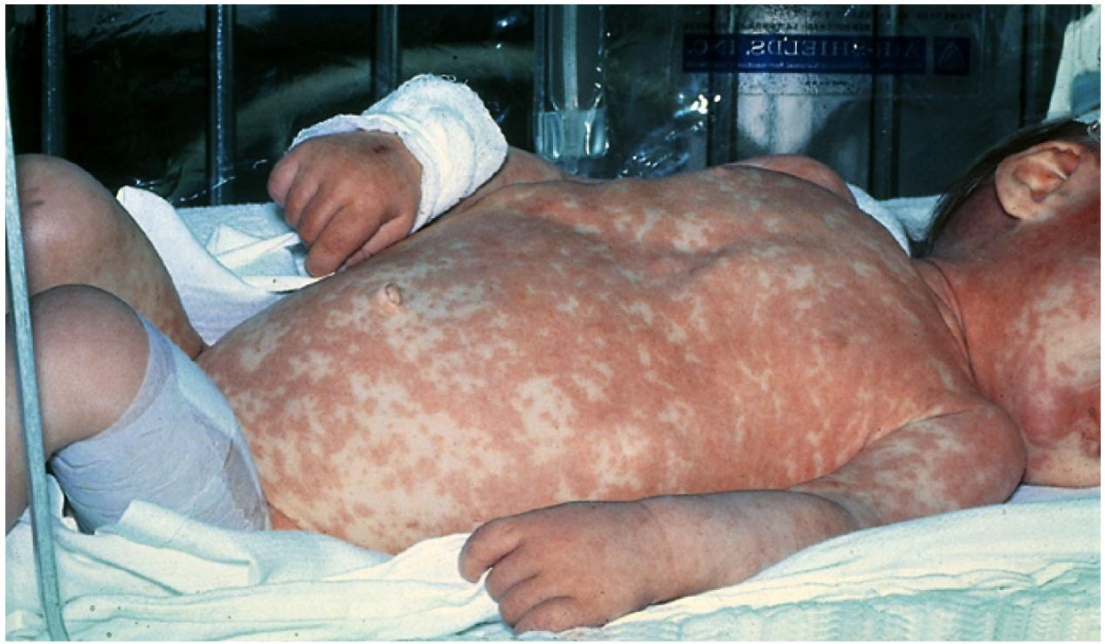


Figure 11.2 Case Studies in Immunology, 7th ed. (© Garland Science 2016)

The case of John W. Wells

Healthy until 7 years old, then pale and petechiae on the skin

Blood test, very anemic Hb=7 g/dl, platelets= 20,000/ul, low WBC count

Bone marrow biopsy= very few cells, almost complete absence of RBC, WBC, and Platelet precursors

Diagnosis of aplastic anemia

BM transplant from HLA-identical brother

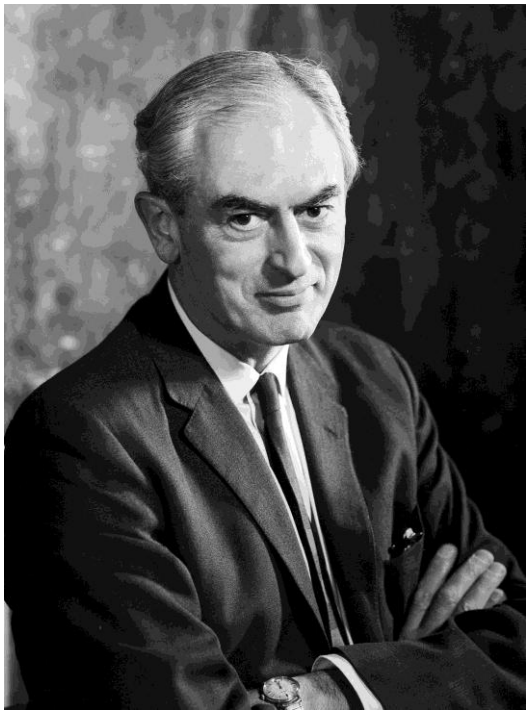
Course of horse anti-thymocyte globulin (ATG), fludarabine, and cyclophosphamide

BM performed, started on cyclosporin A to prevent GVHD

At 24th day post-transplant = acute GVHD, rash, diarrhea, no fever or hepatic involv.

Treated with coritcosteroids, and rabbit ATG. Improved, sent home after 2 weeks.

GVHD



First described by Medawar and colleagues 30 years ago.

Allogenic T cells administered to newborn mice: Growth retarded, destruction of lymphoid tissue, diarrhea, and liver necrosis.

First recognized in SCID infants who took blood transfusions.

To develop GVHD:

1- Graft must contain immunocompetent cells
2- Recipient must express major or minor histocompatibility molecules not found in donor
3- Recipient must be incapable of rejecting the graft

Symptoms: Rash face and spreading (Itchy), fever, GI tract, hepatic tissue, lungs, BM.

Treatment: Immunosuppressive drugs, T-cell depleting agents.

Half matched, or matched unrelated donors transplants carry risk of GVHD (T-cell depeletion) Unless “Graft-vs-Leukemia” reaction is desired.

GVHD in the Skin

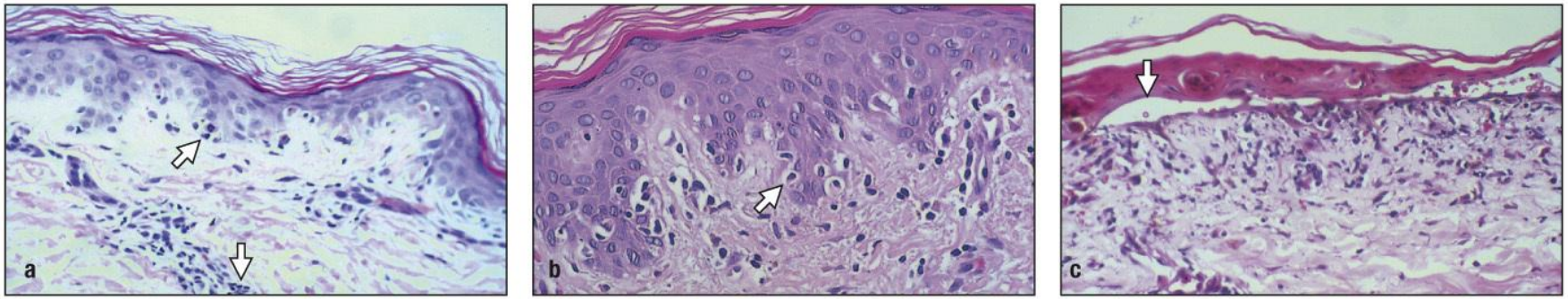


Figure 11.3 Case Studies in Immunology, 7th ed. (© Garland Science 2016)

GVHD in Colon and Liver

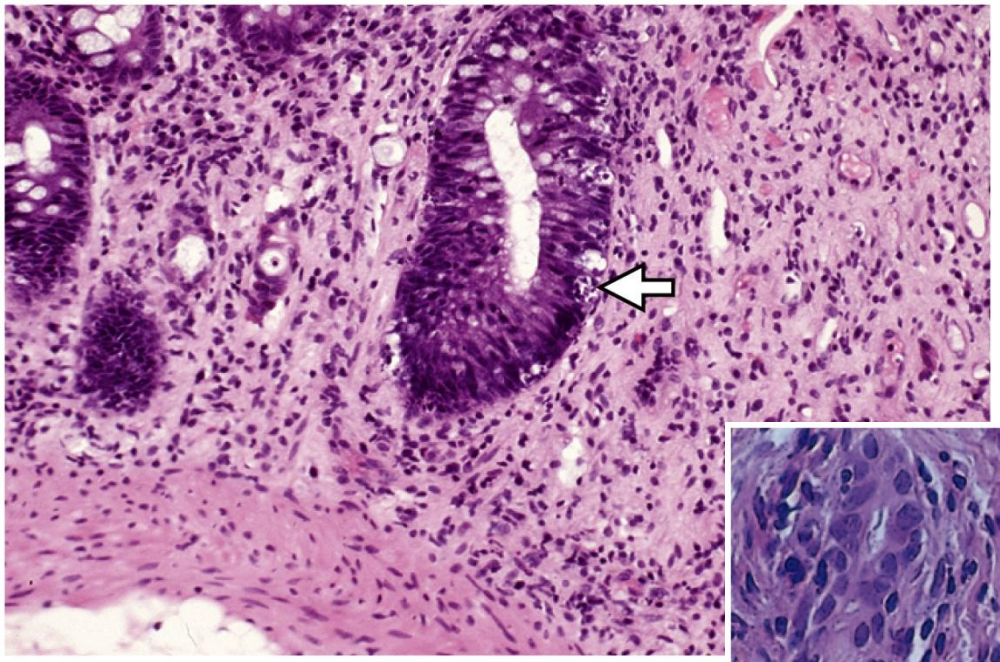


Figure 11.4 Case Studies in Immunology, 7th ed. (© Garland Science 2016)

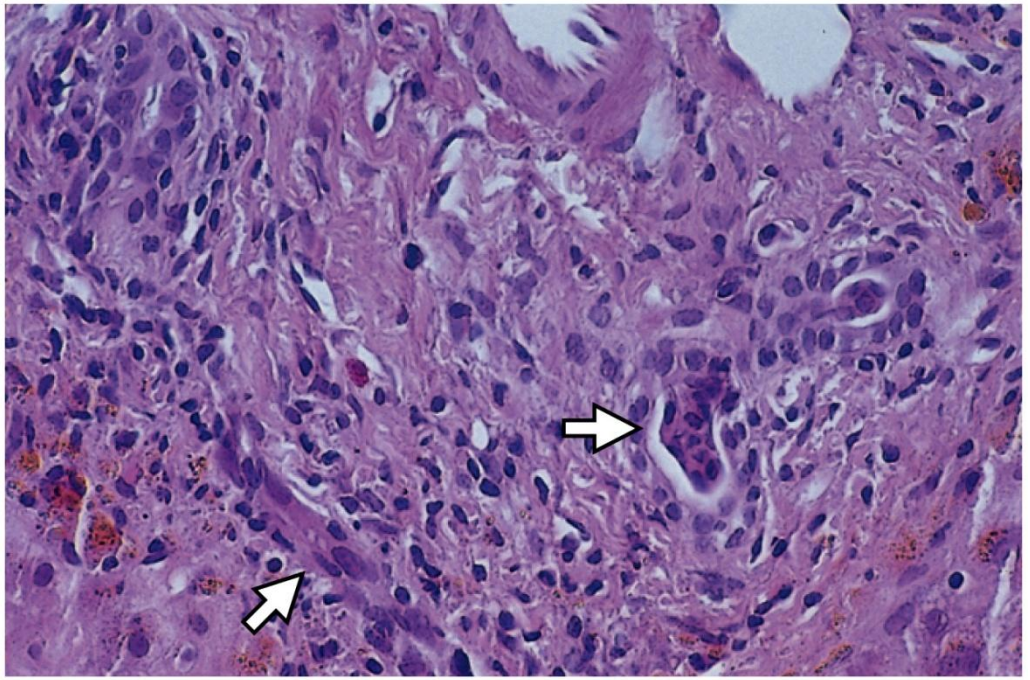


Figure 11.5 Case Studies in Immunology, 7th ed. (© Garland Science 2016)

Explain “Graft-vs-Leukemia” effect?

Engrafted T cells will attack allogenic antigens on leukemia cell. Example: HB-1 antigen expressed by acute lymphoblastic leukemia cells and EBV-transformed B-cells.

IFN-γ secreted by engrafted helper T-cells help sustain and increase GVHD, why?

This cytokine can induce expression of MHC molecules on cells.

ATG was given to deplete T cells and control GVHD, what other methods can be used to deplete T cells?

IV injection of monoclonal anti-CD3.

Antibodies against activated T cells (Anti- CD25, CD40L) to spare naive T cells (Maintain viruses at check ex: EBV)

Why are the skin and intestinal tract major sites for GVHD?

Skin and intestine express higher levels of MHC molecules than other tissues

GI tract is damaged by preparative cytotoxic treatment to BM. Damage induces cytokines and MHC molecule expression.