

Graft versus host disease associated with blood transfusion

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Graft versus Host Disease (GVHD) typically occurs after hematopoietic stem cell transplantation (HSCT) as the donor lymphocytes attack antigen presenting cells with a different HLA haplotype in host tissues, typically in the skin, liver and gastrointestinal tract. But can you get GVHD in non-transplant subjects? Normally, blood transfusions would not be expected to cause GVHD, as the recipient's immune system would destroy lymphocytes in the donor blood. However, GVHD has been demonstrated after blood transfusion in subjects who have not had a transplant. This typically occurs in two settings. Firstly, the subject is immunosuppressed, either because of an underlying T-cell disorder, as in children, or because of chemotherapy or radiotherapy for hematologic or solid cancer [1,2]. Hence the donor lymphocytes are free to run amok. The second setting is unique and occurs in **immunocompetent** subjects. This typically happens when a subject who is **heterozygous** for a HLA antigen receives a blood transfusion from a donor who is **homozygous** for that HLA antigen [3]. Thus, the host's lymphocytes do not recognise the blood donor's lymphocytes as foreign, but the donor lymphocytes recognise the "mismatched" HLA antigen in the host tissues as alien. This kind of mishap is likely to occur when there is limited genetic variability in the population, as in Japan, or when the blood donor is a family member, particularly if there is a high rate of consanguinity, thus causing shared HLA antigens, such as in rural Turkey [4] or on the subcontinent [5]. Unlike transplantation associated GVHD, transfusion associated GVHD is almost always fatal [6-8]. This is because apart from attacking the skin, liver and GI tract, lymphocytes in the donor blood also attack the host's bone marrow, causing aplasia. Remember, that in HSCT, the marrow has been ablated, and replaced by the donor marrow, which will therefore not be attacked by the graft lymphocytes.

Transfusion associated GVHD starts 2-30 days after transfusion [9], is usually mild and insidious in onset and is therefore often not recognised, and is usually attributed to the underlying disease. It starts with fever and rash, which can become erythrodermatous in severe cases, and proceeds to vomiting, severe diarrhoea, right upper quadrant pain, deranged LFTs, and pancytopenia [10].

Transfusion associated GVHD can be caused by transfusing whole blood, packed RBC, platelets, leucocytes and fresh unfrozen plasma. It does not occur when transfusing deglycerolated, frozen RBC or cryoprecipitate or FFP.

Diagnosis can be made by a skin biopsy and by demonstrating that the circulating lymphocytes are the donor's rather than the host's [11].

This devastating complication can be prevented by gamma-irradiating donor blood in the following 4 instances- in immunosuppressed subjects, in subjects who have had HSCT (although GVHD here would not affect the marrow), in instances where the blood donor is a relative and in HLA-matched platelet transfusions [12].

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