Laboratory Tests Performed in Blood Bank before and after Hematopoietic Stem Cell Transplantation

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Tests performed in the blood bank are performed in the pre- and post-hematopoietic stem cell transplantation (HSCT) setting as in other clinical contexts. However, the patterns of results and their causes differ. Interpreting test results and understanding the clinical situation are therefore different. Among the blood bank tests related to hematopoietic stem cells are the following: 1. ABO blood typing; 2. RhD typing; 3. antibody screening and identification; 4. direct and indirect antiglobulin tests; 5. isoagglutinin testing.

1. ABO blood typing

As with patients in other clinical contexts, ABO testing for HSCT recipients is important. First, any ABO typing discrepancies must be resolved. Patients anticipated to undergo HSCT often require many transfusions, so accurate blood typing is crucial to determine the optimal blood products. Determining blood type is also important after transplantation to assess relapse and to select optimal transfusions. ABO typing discrepancies can arise from Group 1: serum (reverse) typing abnormalities, Group 2: red cell (forward) typing abnormalities, Group 3: plasma abnormalities, and Group 4: other causes. Second, ABO incompatibilities frequently occur between donor and recipient in HSCT. Major incompatibility means the recipient has antibodies against donor red cell antigens—for example, an O recipient receiving stem cells from an A, B, or AB donor, or an A or B recipient receiving AB donor cells. Minor incompatibility means the donor's serum contains antibodies against the recipient—for example, A, B, or AB recipients receiving O donor stem cells, or AB recipient receiving A or B donor cells. Bidirectional incompatibility denotes mutual incompatibility such as an A recipient receiving B donor cells or vice versa.

2. RhD typing

First, D variants exist and should be characterized. Generally, D variants are considered RhD-positive if the donor and RhD-negative if the patient. Second, RhD mismatches include RhD-positive recipients receiving RhD-negative stem cells (minor incompatibility) or RhD-negative recipients receiving RhD-positive stem cells (major incompatibility). If the patient has anti-D and then receives RhD-positive stem cells, that is considered minor incompatibility; if the donor has anti-D, that is considered major incompatibility.

Consider an RhD mismatch where an RhD-negative recipient receives grafts from an RhD-positive donor. Pre-transplant transfusions may safely use RhD-negative blood. After transplant, RhD testing will show positivity ranging from 1+ to 4+. Theoretically, once the recipient reaches RhD 4+ one can safely transfuse RhD-positive blood, but in practice clinicians must decide when to switch—often considering RhD 2+ to 4+ as the decision window. Conversely, if an RhD-positive recipient receives grafts from an RhD-negative donor, pre-transplant transfusions use RhD-positive blood; after engraftment clinicians may switch to RhD-negative blood once testing shows approximately 3+ RhD negativity.

3. Antibody screening and identification

Antibody screening and identification are commonly seen pre-transplant, especially in heavily transfused patients such as those with myelodysplastic syndromes. If antibodies are present, blood lacking the corresponding antigens should be selected for transfusion. If antibodies persist after transplant, antigen-negative units should likewise be chosen.

4. Direct and indirect antiglobulin tests (DAT/IAT)

The direct antiglobulin test (DAT) detects IgG or C3d attached to red cells and uses reagents derived from animals (e.g., rabbit) or monoclonal sources. Washed red cells are mixed with antiglobulin reagents (polyclonal or monoclonal anti-IgG, anti-C3d) and observed for agglutination. It is reported that DAT becomes positive when roughly 150–500 IgG molecules are attached per red cell.

Factors influencing hemolysis related to antiglobulin testing include: higher antibody titer increases hemolysis; the affinity between antibody and antigen affects hemolysis; a broader temperature range of antibody reactivity increases hemolysis. The DAT detects IgG binding but not IgM or IgA. Among IgG subclasses, binding strength to Fcγ receptors and complement (C1q) is greatest for IgG3 > IgG1 >>> IgG2, IgG4; most hemolysis is caused by IgG1. Glycosylation of the Fc portion influences hemolytic activity: decreased glycosylation tends to increase hemolysis, and reduced galactosylation is associated with more hemolysis. Antigens located farther from the red cell membrane are more prone to destruction by macrophages—e.g., anti-K bound to membrane-distant antigens is more readily phagocytosed than anti-D. The ability of antibodies to fix complement also affects hemolytic potential; anti-Band3 fixes complement and causes hemolysis more effectively than anti-Rh. Understanding these properties of the antiglobulin test improves interpretation and clinical insight.

A positive DAT in pre-transplant patients often arises from underlying disease. Hematologic malignancies such as lymphoma or chronic lymphocytic leukemia can show DAT positivity, likely due to antibodies produced by malignant cells that bind red cells. After transplant, conditions such as pure red cell aplasia (PRCA) or autoimmune hemolytic anemia (AIHA) can occur, where the DAT is diagnostically useful. Distinguishing between antibody-mediated hemolysis and drug-induced immune hemolysis can be challenging.

5. Isoagglutinin titer testing

High-titer isoagglutinins can cause post-transplant pure red cell aplasia or delayed engraftment in minor-incompatible transplants. To prevent such complications, isoagglutinin titers are measured pre-transplant and, if above certain thresholds, treatment is initiated. Therapeutic plasma exchange is typically continued until titers are reduced to 1:8–1:32 or a fixed number of sessions is completed.

6. Conclusion

Blood bank testing before and after HSCT often produces atypical or complex results; care should be taken when performing and interpreting these tests.