A case of severe intravascular hemolysis in a young girl

Sir,

Correlating history and clinical findings of a patient with laboratory parameters is often helpful in directing the laboratory personnel to choose the correct test to be done on the sample, as illustrated in the present case.

Blood sample of a 10-year-old girl with acute severe anemia was sent for blood grouping and direct and indirect antiglobulin testing. Forward typing was ‘O’ Rh D positive and reverse typing showed 4+ agglutination with pooled ‘A’ and ‘B’ cells and 1+ agglutination with O cells in an automated column agglutination technique. Clumps with O cells observed on reverse grouping resolved after incubating the tubes at 37°C for one hour.

Visual inspection of the sample revealed large numbers of clumps in the blood. Both direct and indirect antiglobulin tests showed negative results, whereas the autocontrol by IAT was positive. Cold agglutination test was positive and thermal amplitude extended up to 22°C. Cold antibody titer was 32 at 4°C and 16 at 22°C. Low titer and thermal amplitude of the cold antibody did not correlate with clinical severity of hemolysis. Analysis of other investigations suggested severe hemolysis, with a hemoglobin value of 6 g/dl, reticulocyte count of 10%, polychromasia and clumps of red cells on peripheral smear and total bilirubin of 4.7 mg/dl (direct: 0.6 mg/dl).

On reviewing the history of the patient, she had an episode of fever and chills five days ago. Following that, she suffered back pain and passed brown colored urine. Since the history suggested an episode of acute hemolysis following fever, we proceeded with Donath–Landsteiner testing.

Three sets of test tubes (A1, A2, A3, B1, B2, B3 and C1, C2, C3) were labeled and 10 volumes of patient’s serum were added to tubes 1 and 2 of each set. Ten volumes of fresh normal serum were added to tubes 2 and 3 of each set. One volume of 50% suspension of washed P-positive red cells was added to all tubes. The first set (A1, A2, A3) was placed in a bath of melting ice for 30 minutes and then at 37°C for 1 hour. Three “B” tubes were placed in melting ice for 90 minutes. Three “C” tubes were placed at 37°C for 90 minutes. All test tubes were centrifuged after completion of incubation period and observed for hemolysis. Hemolysis was present in A1 and A2 but not with any other tubes, thus indicating a positive result. Detection of D-L antibody was also done by the indirect antiglobulin test after incubation of serum and group O cell mixture at 4°C and cold saline washing. This technique gave a weak positive report.

Patient recovered without any intervention and her hemoglobin level improved to 10 g/dl on discharge.

Donath–Landsteiner hemoglobinuria is the least common type of autoimmune hemolytic anemia, with an incidence of 1-2%. Red cell destruction occurs due to the biphasic hemolysin, which binds to the patient’s red blood cells at low temperatures and fixes complement and hemolysis sets in when body temperature rises.

In the present case, the clumping of blood indicated the presence of cold antibody, but its activity was limited to 22°C and the titer was very low to cause serious intravascular hemolysis. The negative direct antiglobulin test in this case is probably due to the elution of the antibody on washing red cells. However, a weak positive report was obtained after 4°C incubation and cold saline washing. It is unusual to obtain a combination of negative result in direct antiglobulin test and positive result in autocontrol as was noted in this case. This is explained by the presence of the complements on the surface of red blood cells at 37°C.

This case highlights the importance of correlating the clinical features with the laboratory findings and the need for good communication between the primary care physician and immunohematologist in the best interest of patient care.

Shamee Shastry, Sudha S. Bhat
Department of Transfusion Medicine, Kasturba Medical College, Manipal University, Manipal, Karnataka, India

Correspondence to: Dr. Shamee Shastry, Department of Transfusion Medicine, Kasturba Medical College, Manipal University, Manipal, Karnataka, India. E-mail: shameegirish@gmail.com

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