Severe hemolytic anemia due to auto anti-N

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Auto anti-N is infrequently encountered and, in most reported cases, does not cause clinical hemolysis. This case reports an auto anti-N associated with severe hemolytic anemia (Hb = 2.7 g/dL) in a 6-year-old Caucasian girl with a history of vomiting, fever, and abdominal pain. Upon admission, she was found to have a metabolic acidosis, secondary to her severe anemia, with abnormal liver function tests. As in three other case reports, the autoimmune hemolytic anemia resolved, with disappearance of the auto anti-N, after corticosteroid therapy. ***Immunohematology* 2005,21:63–65.**

Key Words: hemolysis, autoantibody, anemia, antigens, MNS blood group system, autoimmune hemolytic anemia

Autoimmune hemolytic anemia can be caused by a variety of underlying illnesses. We report a case of an auto anti-N that caused a severe hemolytic anemia.

Case Report

A 6-year-old Caucasian girl (28.9 kg) with a 2-day history of vomiting, fever, and abdominal pain presented to her local physician and was found to be jaundiced. That evening, her emesis worsened and her urine was noted to be red. She presented to a local hospital with an initial Hct of 8% and abnormal liver function tests. She was transferred to our hospital; her admission laboratory values were: Hb = 2.7 g/dL, Hct = 7.4%, WBC = 22.5 × 10^9/L, LDH = 7856 U/L (normal 470–900), AST = 587 U/L (normal 14–38), ALT = 434 U/L (normal 15–48), alkaline phosphatase = 232 U/L (normal 150–380), gamma glutamyl transferase (GGT) = 63 (normal 11–48), and total bilirubin = 12.3 mg/dL (Fig. 1). Peripheral smear showed lymphocytosis, with atypical lymphocytes, promyelocytes, myelocytes, and plasmacytoid lymphocytes; polychromasia; and varying shapes and sizes of RBCs with rouleaux. Anti-nuclear antibody (ANA) was positive (speckled pattern, 1:80). Tests for double-stranded DNA, Smith antigen (sm), ribonucleoprotein (RNP), Sjogren's syndrome A (SSA), and Sjogren's syndrome B (SSB) were all negative. The test for infectious mononucleosis was negative. EBV serologies were positive for IgG, but negative for IgM, suggestive of a previous, nonrecent infection. In addition, blood cultures were negative. At time of transfer, the patient was in severe metabolic acidosis, secondary to her severe anemia, with a pH of 7.17, pCO_2 of 23 mm Hg, pO_2 of 47 mm Hg, and bicarbonate (HCO_3) of 9.3 mmol/L.

Two units of group O, D– RBCs were released and transfused upon admission without pretransfusion testing. Antibody screening performed, after release of the units, showed a 1+ reaction with two cells of a three-cell screening panel, using the ID-MTS gel test (Ortho-Clinical Diagnostics, Raritan, NJ). Antibody panel results showed reactivity with N+ cells in saline room temperature and AHG tests using PEG. All other clinically significant antibodies were excluded. The autocontrol was positive in the same phases of testing as the panel cells. The DAT was 4+ with polyspecific AHG, 2+ with anti-IgG, and 3+ with anti-C3d. ABO/Rh typing was initially discrepant between forward and reverse typing, and the Rh control was positive.

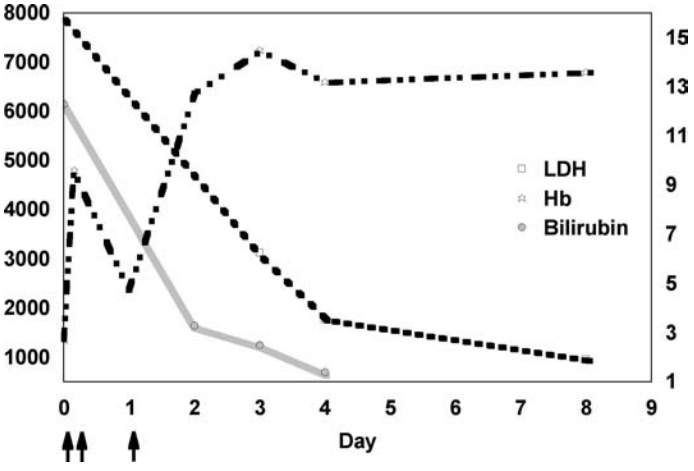

Fig. 1. Progression of patient's LDH, bilirubin, and Hb levels by day of hospitalization. Steroid therapy was initiated at the time of presentation to the hospital. The patient was transfused with two emergency-released uncrossmatched units of RBCs on Day 0 and one unit of crossmatched RBCs on Day 1. (Arrows indicate RBC transfusion.)

Table 1. Features of the cases of hemolytic anemia caused by auto anti-N

Study	Case no.	Age	Sex	Race	Initial Hb (g/dL)	LDH (U/L)	Bilirubin (mg/dL)	Underlying diagnosis	Steroids	Transfusion	Discharge Hb
Bowman et al.[1]	1	18	M	UNK*	6.9	2200	3.1	Infectious mononucleosis	Yes	Yes (2 units)	10.2 (24 days)
Dube et al.[2]	2	7	M	UNK*	6.0	UNK*	1.7	UNK*	Yes	Yes (1 unit)	10 (10 days)
Cohen et al.[3]	3	21	F	Caucasian	5.5	540	1.7	SLE†	Yes	No	12.8 (hospital stay unreported)
This report	4	6	F	Caucasian	2.7	7856	12.3	Questionable viral origin	Yes	Yes (3 units)	13.2 (4 days)

* Unknown
† Systemic lupus erythematosus

A 1-hour chloroquine diphosphate (Gamma-Quin, Gamma Biologicals, Inc., Houston, TX) treatment of the RBCs resolved the ABO typing and Rh control problem, and the patient's RBCs typed as group A, D+. The antibody was interpreted as a warm autoantibody with anti-N specificity. EDTA glycine-acid (EGA) treatment of the RBCs (Gamma EGA kit, Gamma Biologicals, Inc.) reduced the IgG reactivity from 2+ to w+, and the patient's EGA-treated RBCs typed 2+ for the N antigen. An AHG crossmatch of the two group O, D– emergency-released RBC units showed that one of the units was incompatible with the patient's serum. Further testing determined that the incompatible unit was N+; the other unit was N– and compatible. The patient received one additional unit of N–, AHG-crossmatch–compatible RBCs. Corticosteroid therapy was administered and the patient's Hb increased to 12.9 g/dL (Fig. 1).

Eight days after admission, a DAT of the patient's RBCs did not react with polyspecific AHG. The patient was discharged on corticosteroids with laboratory values of Hb = 13.2 g/dL, Hct = 36.7%, WBC = 9.2 × 10^9/L, LDH = 1773 U/L, and total bilirubin = 1.4 mg/dL. Follow-up transfusion testing two months later showed a negative antibody screen, negative DAT, and no ABO/Rh typing discrepancy.

Conclusion

After corticosteroid therapy, the autoimmune hemolytic anemia resolved and the auto anti-N disappeared. The etiology of the autoimmune hemolytic anemia was assumed to be related to the acute illness which was suspected to be of viral origin. There have been at least three other case reports of auto anti-N hemolytic anemia published (Table 1).[1–3] Two of the three reports were of pediatric patients (< 18 years old) and, as in our patient, all had antibody resolution after steroid therapy.[1,2]

Although infrequent, there have been at least 11 additional cases of naturally occurring auto anti-N in four healthy individuals and seven patients, all without evidence of clinical hemolysis or an associated etiology.[4–8] In addition, hemodialysis-associated anti-N–like antibodies have been described when formaldehyde was used to sterilize dialysis equipment. These antibodies were able to be adsorbed onto and eluted from NN RBCs as well as from formaldehyde-treated RBCs regardless of MN phenotype.[9–12]

Auto anti-N is infrequently encountered. In most reported cases, the antibody did not cause clinical hemolysis. In those few cases associated with hemolysis, as in the present case, the hemolysis resolved with steroid therapy.

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