HEMOLYSIS AFTER HIGH-DOSE INTRAVENOUS Ig

To the Editor:

Intravenous Ig (IVIg) is well established as replacement therapy in primary immunodeficiencies at doses of 0.2 to 0.6 g/kg/mo. It is considered safe with minor side effects usually related to rapid infusion. As IVIg becomes more widely used at higher immunomodulatory doses of 1 to 2 g/kg, other rare but more serious adverse reactions are becoming increasingly important.

We report a case in which acute hemolysis followed high-dose IVIg. A 50-year-old Caucasian man with Lambert Eaton myasthenic syndrome received 1 g/kg of IVIg on 2 consecutive days as part of a double-blind, placebo-controlled trial. The following day, he felt unwell and was passing brown urine. His hemoglobin level decreased from 15 g/dL to 8.7 g/dL. Free hemoglobin was detected in his serum and urine. His serum haptoglobin level decreased, his bilirubin level increased, and his creatinine level remained normal. His red blood cells (previously negative) became weakly positive on polyclonal IgG Coomb's testing. The patient's blood group was A1, and the eluate from his postinfusion red blood cells showed anti-A1 activity. The Ig batch used contained isohemagglutinins at a titer of 1/32 to A1 cells, 1/8 to A2 cells, and 1/16 to B cells. A cross match between the patient's pretreatment red blood cells and the Ig batch used gave negative results by saline hemagglutination but a strongly positive cross match by indirect Coomb's assay. A red blood cell panel covering several antigens (Rhesus D, MN, Ss, and P1; Lewis a and b; Kk; Jka and b; and Fya and b) was used to exclude an unusual antibody in the Ig preparation. The patient required a single transfusion. He also developed nephrotic syndrome, and renal biopsy showed minimal change glomerulonephritis. A review of his records found asymptomatic proteinuria before treatment with IVIg. He has made a good recovery with some improvement in his neuromuscular problems.

Deterioration of renal function has been reported after high-dose IVIg in patients with active glomerulonephritis. It would be prudent to avoid high-dose IVIg in this patient group in the future.[1]

Positive Coomb's tests are well recognized after infusion with many blood products, including Ig.[2] Hemolysis has not been reported after standard replacement doses of IVIg, but has rarely followed high-dose IVIg.[3,4] Anti-A and anti-D have been implicated, and a variety of commercial products have been involved.

Two main approaches may prevent such hemolytic reactions. First, the Ig product should be screened for blood group antibodies. The World Health Organization has laid down guidelines for the composition of IVIg,[5] but there are no internationally agreed limits for the levels of isohemagglutinins. A monograph for the European Pharmacopoeia is in preparation and is expected to include such guidelines. Current manufacturing practice varies considerably; some limit isohemagglutinins to a maximum titer of 1:32 by indirect Coomb's testing, whereas others do not routinely measure isohemagglutinins. Secondly, cross-matching before infusion would identify batches that might cause hemolysis in the recipient. This is now our routine practice.

It is important that physicians using high-dose IVIg are aware of the risks of hemolysis and reduced renal function and take appropriate preventative action.

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