Brief Communication
Communication abrégée

DELAYED ONSET OF LIFE-THREATENING IMMUNE HEMOLYSIS AFTER PERIOPERATIVE ANTIMICROBIAL PROPHYLAXIS WITH CEFOTETAN

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Cefotetan is a cephalosporin recommended for perioperative antimicrobial prophylaxis. A number of reports indicate that severe immune-mediated hemolysis can occur during use of this drug. We report on a patient who presented with life-threatening hemolysis 7 days after receiving the last of 3 doses of antimicrobial prophylaxis with cefotetan given perioperatively for incisional hernia repair and incidental cholecystectomy. The delay between use of cefotetan, and subsequent cefotetan-induced immune hemolysis led to delayed recognition of the correct diagnosis.

CASE REPORT

A 63-year-old woman was brought to the Emergency Department after being found by her family to be confused, tachypneic, vomiting and dizzy. She had been discharged from the same hospital 3 days earlier, after uncomplicated repair of an incisional hernia and incidental cholecystectomy, performed 9 days earlier. No blood transfusions had been given.

Blood tests showed a hemoglobin level of 38 g/L, a leukocyte count of 30.9 × 10⁹/L with a normal platelet count and evidence of immune hemolysis (polychromasia, spherocytes, reticulocytosis, elevated lactate dehydrogenase), but the initial direct antiglobulin (Coombs) test was negative (probable false-negative result from massive immune hemolysis, with few residual immunoglobulin G-coated red cells).

The patient was immediately transfused with 4 units of red cell concentrates, which raised the hemoglobin level to 91 g/L. Both computed tomography and ultrasonography ruled out intra-abdominal hemorrhage as a cause for the profound anemia. The patient recovered without complications, and was discharged with suspected hemolysis of uncertain etiology for follow-up by a hematologist.

The consulting hematologist suspected a delayed-onset of immune hemolysis, perhaps from a perioperative medication. It was noted that 3 doses of cefotetan had been given perioperatively for prophylaxis (total, 3 g over 48 hours); 1 year earlier, she had received 9 doses of cefotetan without incident after surgery for a colocutaneous fistula. Although there had been an interval of 7 days between the last dose of cefotetan and the patient’s presentation to the emergency department, cefotetan was investigated as a possible causative agent.

One of the other drugs given (anesthetic agents: sufentanil, vecuronium bromide, propofol, neostigmine, glycopyrrolate; postoperative drugs: meperidine, morphine, dimenhydrinate, prochlorperazine, lorazepam, ranitidine) are known to cause immune hemolysis.

The repeat direct antiglobulin (Coombs’) test was positive (both IgG and complement); potent IgG (1/32 000) and IgM (1/10 240) cefotetan-dependent antibodies were demonstrated in patient serum by agglutination and antiglobulin end points; both immune complex and drug adsorption (hapten) techniques, performed as described, gave positive results. Control serum and control antibiotics (penicillin, cefazolin) gave negative test results.

DISCUSSION

Since 1989, at least 8 cases of cefotetan-induced immune hemolysis have been reported. In all cases but 1, the anemia began while the patient was receiving cefotetan; in 1 patient, anemia developed 4 days after completing a 5-day course of cefotetan.

Our patient is remarkable in that she received only 3 doses of cefotetan perioperatively and presented to the hospital 7 days after receiving the final dose with a hemoglobin level of only 38 g/L. This delay made it difficult to establish the correct diagnosis. The presence of very potent cefotetan-dependent antibodies in this patient’s serum represent strong laboratory evidence for immune hemolysis. It is possible that subclinical immune sensitization from the course of cefotetan 1 year earlier contributed to this woman’s subsequent severe clinical course.

Cefotetan has been recommended for perioperative antimicrobial prophylaxis for patients undergoing appendectomy, bowel surgery, biliary tract surgery, hysterectomy, and for postoperative infections of the genitourinary system. This case emphasizes that life-threatening hemolytic reactions of delayed onset some-
times can complicate the use of cefotetan. If cefotetan continues to be used for antimicrobial prophylaxis, surgeons must be aware that delayed onset of severe hemolysis can complicate even a brief exposure to this drug.

References