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.[1–3] A number of reports indicate that severe immune-mediated hemolysis can occur during use of this drug.[4–10] 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 30.9×10^9/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. None 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,[4–6] 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.[4–10] 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.[1–3] This case emphasizes that life-threatening hemolytic reactions of delayed onset some-

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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.

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SESAP Critique / Critique SESAP

CATEGORY 5, ITEMS 20 AND 21

This patient's hypokalemia is most likely caused by his use of a thiazide diuretic twice a day. He did not have a potassium supplement, and excessive urinary loss of potassium is the most likely explanation for hypokalemia with the other electrolytes remaining in the normal range.

Preoperative bowel preparation with Golytely did not cause the hypokalemia. Golytely is an isotonic bowel preparation with close to serum values for sodium, potassium, chloride, and bicarbonate; large volumes can be administered without significant changes in water or electrolyte balance. Except for a villous adenoma with a focus of colon carcinoma, adenocarcinoma of the colon does not produce an excess loss of potassium. Although a clear liquid diet eliminates dietary fiber, the diet can still include sodium and potassium salts, which will maintain electrolyte balance if there is not excessive loss.

Accurately estimating the amount of total body loss of potassium is difficult and variable because 98% is intracellular and only 2% is extracellular. Because the serum potassium level is extracellular, small changes in serum potassium represent much larger deficits in the intracellular fluid. The Na-K ATPase pump, pH of the blood, and the patient's hydration — total body water excess or deficit — can also change the serum potassium level.

From a serum drop in potassium from 4.0 to 3.0 mEq/L, the serum studies showed the effect of an uncomplicated potassium depletion on serum potassium to be a fall of 0.25 in mEq/L of serum potassium, representing a 25 to 50 mEq drop of deficit of total body potassium. Starting with normal serum potassium of 4, a drop of 1 mEq/L in serum potassium represents a potassium deficit of 100 to 200 mEq/L. A further drop from 3.0 to 2.5 represents a loss of 100 to 200 mEq/L for each drop of 0.25 mEq/L, or a 200 to 400 mEq deficit of potassium. Therefore, the total potassium deficit for a serum potassium = 2.5 = 100 to 200 plus 200 to 400 = 300 to 600 mEq of potassium deficit.

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