Defective Platelet Function After Cephalosporin Administration

To the Editor:

Large doses of penicillin will alter platelet function, according to the excellent study of Brown et al.¹ These authors emphasize that if large doses of penicillin are given to patients with impaired renal function, attention to dosage is necessary to prevent exceedingly high blood levels, which in turn may compromise platelet function and lead to bleeding.

We recently observed a patient with renal incompetence who bled following Cefazolin—a semisynthetic cephalosporin—therapy. She was a 29-yr-old mentally retarded lady with chronic pyelonephritis admitted with sepsis due to Klebsiella. Initial therapy was with Keflin, 1 g every 6 hr for 10 days. Owing to persistent fever, Keflin was discontinued and Cefazolin, 2 g every 4 hr, and gentamicin, 10 mg every 8 hr, were given for the next 5 days. The serum creatinine during the period of antibiotic therapy ranged from 4.7 to 5.1 mg/100 g, eventually returning to normal levels.

On the third day of this regimen severe bleeding from the nose, mouth, and venipuncture sites was noted. The prothrombin time (PT) and partial thromboplastin times (PTT) were 96/12 and 100/34 sec, respectively. Aqua-mephyton 10 mg and banked whole blood were administered. The PT and PTT on the fourth day were 13/12 and 33/31 sec, respectively. The platelet count ranged between 210,000 and 495,000/cu mm during the period of Cefazolin therapy. The serum Cefazolin levels during the fifth and seventh days of this regimen were 246 and 206 μg/ml.

Minimal bleeding continued, and on the fifth day of this regimen the template bleeding time was over 20 min (normal 4-6 min). Platelet aggregation in vitro (kindly performed by Dr. G. Koneyer, USC/LAC Medical Center, Los Angeles, Calif.) with ADP (2 μM), epinephrine, collagen, and thrombin was impaired, suggesting both primary and secondary wave defects. The Cefazolin was discontinued at this time and the bleeding ceased.

Lerner and Lubin² reported on a uremic patient with a prolonged PT and PTT while receiving Cefazolin. However, platelet function studies were not done in that case. Our experience suggests that Cefazolin at high blood concentrations is capable of producing both a humoral and platelet-mediated coagulation dysfunction.

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REFERENCES


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To the Editor:

The patient described by Dr. Khaleeli and Dr. Giorgio certainly seems to represent an example of bleeding induced by Cefazolin through its effects on platelet function and coagulation. At least one explanation for bleeding in this uremic patient is that the drug presumably augmented an existing defect in platelet function. The dose of Cephazolin was 2 g every 4 hr, or somewhere between 200 and 300 mg/kg/day. This dose in a patient with uremia could be expected to result in quite high serum levels of drug.

Since cephalosporins are closely related in chemical structure to penicillin, one might expect that they would affect platelets in a manner similar to that of the penicillins. A recent
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M Khaleeli and AJ Giorgio