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Case Report

Acute Thrombocytopenia After IV Administration of a Radiographic Contrast Medium

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Although adverse effects of radiographic contrast medium, ranging from minor rashes to anaphylactic reactions, are not rare during various radiologic procedures, thrombocytopenia has been extremely rare, and only a few cases of acute severe thrombocytopenia have been described [1–8]. In five reported patients, thrombocytopenia developed after oral administration of radiographic contrast material [1–4, 6], and in four patients it followed IV injection [5, 7, 8]. In this report, another case of acute severe thrombocytopenia due to an IV contrast medium is described.

Case Report

A 66-year-old woman was admitted to the hospital for evaluation and treatment of recurrent angina. The medication at the time of the admission was diltiazem hydrochloride, chlorzoxazone with acetaminophen, and lorazepam. The patient denied any history of allergy and had no history of exposure to a contrast medium. The hemogram revealed a hemoglobin of 13.3 g/dl, hematocrit 38.3%, white cell count 9000/μl, and platelet count 230,000/μl. After initial cardiac evaluation, the patient underwent a right and left cardiac catheterization, left ventriculography, and selective coronary angiography. Moderate stenosis of the anterior descending branch of the left coronary artery was shown. During the procedure, 90 ml of Renografin-76 (diatrizoate: sodium 10% and meglumine 66%; Squibb Diagnostics, Inc., New Brunswick, NJ), with 1000 units of heparin flush, were used. Four hours after cardiac catheterization, the platelet count decreased markedly to 10,000/μl (Fig. 1). Both prothrombin time and activated partial thromboplastin time were normal. Fibrinogen level was 280 mg/dl, Factor VIII level was 100%, and fibrin split product was absent. On the basis of these findings, disseminated intravascular coagulation was excluded. No cause of thrombocytopenia was evident; the patient was not taking any drug known to cause acute thrombocytopenia, and heparin-induced thrombocytopenia was ruled out on clinical grounds and the lack of the heparin-dependent, platelet-aggregating factor [9]. Six units of platelet concentrates were transfused, and the patient had no unusual bleeding. The platelet count gradually returned to normal in several days (Fig. 1). Because of the thrombocytopenic episode, no immediate coronary artery surgery was advised, and the patient was discharged on medical treatment of the angina.

Three weeks later the patient was readmitted for percutaneous coronary angioplasty because of unstable angina despite treatment with nitroglycerin, dipyridamole, and verapamil hydrochloride. The platelet count was 320,000/μl on admission. During the angioplasty, the patient again received 90 ml of Renografin-76. The patient tolerated the procedure well, and angioplasty was successfully completed. Heparin was not used. However, 3 hr later, marked thrombocytopenia of 9000/μl developed. The diagnosis of acute thrombocytopenia induced by Renografin-76 was well established. The patient was not given a platelet transfusion, but the platelet count was closely monitored. Over the next several days, the platelet count increased spontaneously to more than 300,000/μl (Fig. 1). Bone-marrow aspiration showed normal erythroid and granulocytic precursors with abundant megakaryocytes during the thrombocytopenic stage, which was consistent with thrombocytopenia due to increased peripheral destruction.

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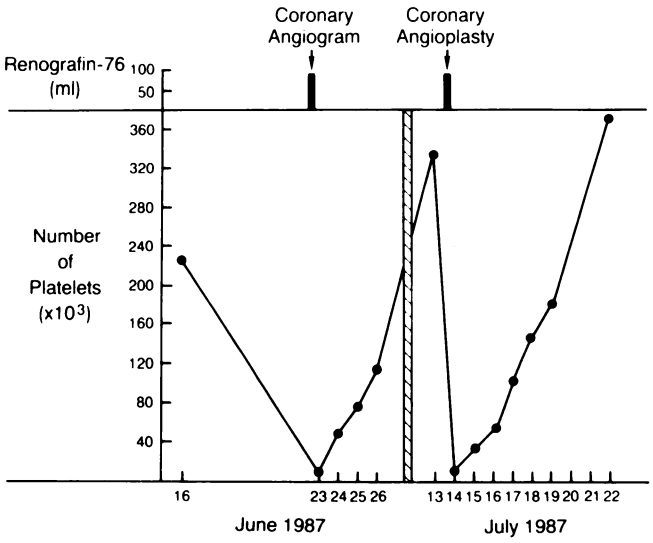

Fig. 1.—Graph showing changes in platelet count after IV administration of Renografin-76 during coronary angiogram and coronary angioplasty. Note sudden onset of severe thrombocytopenia and gradual return to normal platelet counts in about 4 days.

Laboratory Investigation

Immunologic Study

When the patient recovered from acute thrombocytopenia after the percutaneous coronary angioplasty, her serum and platelets were collected for immunologic studies. Platelet-associated immunoglobulin was not detected, and the platelet antigen was positive for PL^{A1}. The complement-dependent cytotoxicity test using the patient's platelets and Renografin-76 was negative. These results suggest thrombocytopenia was not immunologically mediated and tend to exclude drug-induced immune thrombocytopenia and thrombocytopenia due to alloantibody anti-PL^{A1}. Also, these findings suggest Renografin-76 caused thrombocytopenia through a mechanism other than immune pathogenesis.

Platelet Aggregation Test

To rule out the possibility of in-vivo consumption of platelets by aggregation, the Renografin-induced platelet aggregation test was performed by using the patient's plasma and Renografin-76 in a similar manner to show the heparin-dependent, platelet-aggregating factor [9]. No Renografin-76–dependent platelet-aggregating factor was shown. This finding suggests Renografin-induced thrombocytopenia was not caused by in-vivo aggregation of platelets.

In-Vitro Effect of Renografin-76 on Platelets

To examine the possibility of a direct chemical effect of Renografin-76 on the patient's platelets, the patient's platelet-rich plasma was incubated in various concentrations of Renografin-76, and the platelet count was done at 30-min intervals from 0 to 2 hr. No significant changes in platelet count were observed between samples with and without the radiographic contrast medium. This result tends to exclude a direct chemical destruction of the patient's platelets by Renografin-76.

Comments

It is now well established that various radiographic contrast media can cause acute severe thrombocytopenia. A review of the literature reveals that thrombocytopenia has occurred after administration of four agents: iopanoic acid, ipodate, and iocetamic acid administered orally for cholecystogram [1–4, 6], and diatrizoate administered IV for cardiac catheterization or percutaneous nephrostography (Table 1) [5, 7, 8]. Our patient is added to the cases with diatrizoate. In all five reported cases with diatrizoate, thrombocytopenia followed IV administration of the contrast material, and all cases involved the use of mixed meglumine and sodium salts. Four of the five cases involved cardiac angiography. Radiologic contrast media also are known to cause in-vivo and in-vitro abnormalities of platelet function [10]. Because of possible induction of functional abnormalities of platelets by contrast media, acute severe thrombocytopenia may cause serious bleeding in certain patients.

The mechanism for acute thrombocytopenia due to contrast media is essentially unknown. In our patient, the laboratory investigation suggests that Renografin-76–induced thrombocytopenia is not caused by the immune mechanism,

TABLE 1: Reported Cases of Acute Thrombocytopenia Due to Contrast Medium

Case	Contrast Medium[a]	Radiologic Procedure	Lowest Platelet Count (per μl)	Reference Citation
1	Iopanoic acid (PO)	Cholecystogram	N.D.[b]	1
2	Ipodate (PO)	Cholecystogram	N.D.	2
3	Iopanoic acid (PO)	Cholecystogram	1,000	3
4	Iopanoic acid (PO)	Cholecystogram	21,000	4
5	Diatrizoate (IV)	Cardiac catheterization	4,000	5
6	Iocetamic acid (PO)	Cholecystogram	N.D.	6
7	Diatrizoate (IV)	Cardiac catheterization	20,000	7
8	Diatrizoate (IV)	Percutaneous nephrostogram	6,000	7
9	Diatrizoate (IV)	Cardiac catheterization	2,000	8
10	Diatrizoate (IV)	Cardiac catheterization	9,000	Present case

[a] PO = oral administration, IV = intravenous administration.
[b] N.D. = platelet not detected on peripheral blood smear.

in-vivo aggregation resulting in platelet consumption, or direct chemical destruction. Also, clinically, the lack of history of previous exposure to contrast medium tends to argue against antibody-mediated immune destruction. On the other hand, proliferation of megakaryocytes in the marrow, sudden-onset thrombocytopenia and rapid rise in platelet count after Renografin administration are consistent with thrombocytopenia due to rapid destruction of platelets. A more complicated immune mediation, however, cannot be excluded.

As seen in Table 1, thrombocytopenia has occurred after both oral and IV administration of contrast media. Fortunately, all the reported cases have recovered without serious complications, which was possible because of timely recognition of the problem and the shortness of the thrombocytopenic episodes. Often, contrast media are considered not to be drugs, and clinicians generally overlook these agents in the list of drugs when evaluating acute thrombocytopenia. In such instances, thrombocytopenia may be diagnosed as idiopathic, and another radiographic examination with the contrast medium may cause bleeding.

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