CASE REPORT

Contrast-induced thrombocytopenia following percutaneous coronary intervention

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Contrast-induced thrombocytopenia is a rare complication distinguished by acute and severe platelet consumption, with spontaneous recovery within days. We describe a case of acute thrombocytopenia 6 hours after coronary angioplasty in a patient with a negative antiplatelet factor 4 test. The count reached $1 \times 10^3/\mu L$, but improved spontaneously to $210 \times 10^3/\mu L$ after 8 days. In conclusion, physicians should be aware of this complication, particularly when dual antiplatelet therapy is being considered.

Keywords: Cardiovascular disease, Contrast media, Thrombocytopenia

Introduction

Many physicians are not aware of the association between contrast exposure and thrombocytopenia because it is a rare event, and therefore very few reports have been published. There is still much to learn about the disease's clinical characteristics and management, particularly in the context of percutaneous coronary interventions (PCI). Such cases require difficult decision making especially regarding the management of dual antiplatelet therapy, whereas most previously published case studies described the complication after contrast-based diagnostic tests. Currently, contrast-induced thrombocytopenia has no clinical diagnostic criteria or specific blood test, and therefore it is a presumed diagnosis based on the exclusion of other possibilities, particularly heparin-induced thrombocytopenia (HIT).

Case report

A 71-year-old woman with dyslipidemia, active smoking, and progressive angina, despite regular

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aspirin and beta-blocker use, was admitted for an elective PCI. Additional comorbidities and allergies were excluded. Diagnostic angiography with the administration of unfractionated heparin was performed 10 days earlier without complications, and revealed proximal and middle segment lesions of the left anterior descending artery. Aspirin and clopidogrel were given on admission, and an initial complete blood count was normal (platelet count $198 \times 10^3/\mu L$). The patient was asymptomatic and with an unremarkable physical exam.

Only midazolam, fentanyl, 10,000 U of unfractionated heparin, and 200 mL of a low-osmolar iodinated contrast medium were administered during the procedure. Optical coherence tomography was also used, and two drug eluting stents were placed in the left anterior descending artery without difficulties. After the arterial sheath was removed from the right femoral artery, a hemostatic vascular closure device was successfully placed, and the patient was transferred to the intensive care unit.

Five hours later she suddenly experienced nausea, vomiting, and chills, without fever or hypotension. Profuse bleeding was observed at the puncture site and local pressure was applied for 60 minutes. Partial thromboplastin time was unrecordable, international normalized ratio and fibrinogen were normal (STAGO automated coagulation analyzer), hemoglobin was 10.5 mg/dL, and leukocytes $5.9 \times 10^9/L$; however, the platelet count dropped to $1 \times 10^3/\mu L$. Protamine was administered and a new sample collected in a sodium citrate tube confirmed the thrombocytopenia. On microscopic evaluation platelets were scarcely identified and there was no evidence of platelet clumping. An emergency computed tomography scan excluded retroperitoneal bleeding. Given that the patient remained stable and without recurrent hemorrhage, platelet transfusions were withheld because of the possibility of HIT.

On the next day, the platelet count was unchanged but the partial thromboplastin time had normalized. Antiplatelets remained withdrawn and an antiplatelet factor 4 (antiPF4) assay was ordered to rule out HIT (HemosIL HIT-$Ab_{(PF4-H)}$). As the result was negative (0.1 U/mL; reference <1.0 U/mL), the contrast medium was believed to be responsible for the thrombocytopenia. On the 4th day, aspirin and clopidogrel were reinitiated once the platelet count reached $24 \times 10^3/\mu L$. After 8 days, the value was $210 \times 10^3/\mu L$ and the patient had an uneventful recovery (Fig. 1).

Discussion

Our case illustrates the importance of acknowledging different diagnostic possibilities when thrombocytopenia develops after PCI, even when heparin is potentially involved (Table 1) [1]. Although HIT type 2 was considered, the very low platelet count, concomitant contrast exposure, and absence of thrombosis yielded a 4 T's score of only 3. Such a low likelihood was further supported by the negative anti-PF4 assay. Among the other medications, none are typically associated with thrombocytopenia and the platelets continued to rise even after reinitiating aspirin and clopidogrel. Furthermore, pseudothrombocytopenia was excluded both by microscopic evaluation and collection of the second sample in a citrate tube.

Contrast-induced adverse reactions include several manifestations such as skin rashes, nausea, anaphylaxis, pulmonary edema and nephropathy. Low-osmolar iodinated agents are associated with fewer events, occurring in 0.15% of cases [2]. Thrombocytopenia is rare, although reports have been described since the early 1980s, with differ-

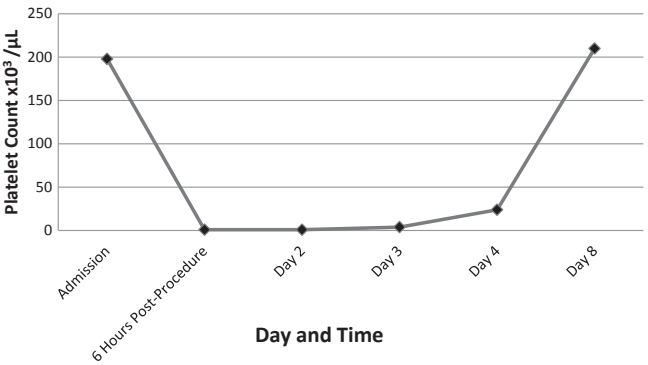

Figure 1. Platelet counts before and after contrast exposure.

Table 1. Causes of thrombocytopenia and time of onset after percutaneous coronary interventions (PCI) [1].

Causes of thrombocytopenia according to time of onset after PCI		
H	D	Wk
Contrast media	Protamine	Ticlopidine
Protamine	Heparin (typical)	Heparin (rare)
Heparin (rare)	Glycoprotein IIb/IIIa inhibitors (rare)	Pseudothrombocytopenia
Glycoprotein IIb/IIIa inhibitors (typical)	Clopidogrel	
Pseudothrombocytopenia	Pseudothrombocytopenia	
Intra-aortic balloon pump	Intra-aortic balloon pump	

ent types of intravenous contrast media [3]. Patients typically manifest systemic symptoms within 1 hour after contrast administration, including fever, chills, dyspnea, wheezing, abdominal pain, and blood pressure variability. Thrombocytopenia is usually diagnosed within hours, characteristically with very low platelet counts [3–5]. The lowest reported value had been $2 \times 10^3/\mu L$, after a contrast enhanced abdominal computed tomography with a nonionic low-osmolar agent [2].

An autoimmune antibody mediated mechanism has been proposed, although *in vitro* tests using iodixanol have yielded variable results [2] Additionally, an anaphylactoid response has also been suggested, chiefly because of the preceding systemic symptoms and recurrent nature [4] However, reports of mild clinical manifestations accompanying severe thrombocytopenia have been described. Management may include the administration of high dose steroids and while this has not been shown to halt the thrombocytopenia, it may be an effective preventive measure if recurrent contrast exposure is necessary. Platelet transfusion should only be considered during clinically relevant bleeding and when HIT is deemed unlikely or has been excluded.

Considering the large number of contrast-mediated diagnostic and therapeutic procedures worldwide, it is imperative that physicians become aware of this rare but potentially severe complication. Given the high degree of platelet consumption in these cases, physicians must be prepared to balance the benefits and risks of antiplatelet therapy, especially after coronary interventions. Until novel diagnostic tests become available, it seems prudent to carefully assess the necessity of contrast exposure in patients with a history of such a complication.

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