

# Acute Life-Threatening Contrast Induced Thrombocytopenia Following Diagnostic Coronary Angiography: A Case Report and Literature Review

Debanshu D Roy<sup>1</sup>, Callie S Marshall<sup>2</sup>, Son V Pham<sup>3</sup>, and Robert J Chilton<sup>4\*</sup>

<sup>1</sup>Cardiovascular Fellow, University of Texas Health, San Antonio, USA

<sup>2</sup>Medical Student, University of Texas Health, San Antonio, USA

<sup>3</sup>Assistant Professor and Chief of Cardiology, Audie L Murphy VA Hospital, San Antonio, USA

<sup>4</sup>Professor and Director, Catherization Lab, Audie L Murphy VA Hospital, San Antonio, USA

\*Corresponding authors: Robert J Chilton, Professor and Director, Catherization Lab, Audie L Murphy VA Hospital, San Antonio, USA, E-mail: RoyD@uthscsa.edu; chilton@uthscsa.edu

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## Abstract

Acute severe thrombocytopenia following contrast administration is incredibly rare, but it can lead to significant morbidity. This case details the experience of a 63-year-old male whose diagnostic coronary angiography quickly led to severe thrombocytopenia with cardiovascular compromise in the absence of any immediate symptoms of anaphylaxis. His platelet count normalized within a week, increasing from  $2 \times 10^3/\mu\text{L}$  to  $328 \times 10^3/\mu\text{L}$ . A thorough review of the literature along with the present case is being reported.

## Introduction

Severe thrombocytopenia following contrast administration is a rare phenomenon. As per our literature search derived from PubMed, there have been a net fourteen reported cases of acute, severe thrombocytopenia following contrast administration. Due to rarity of this phenomenon, a drastic drop in platelet counts is not anticipated, which could be disastrous in the context of recent femoral access. Platelet count usually responds well to conservative therapy and spontaneously returns to normal within a week.

The patient described here presented for an elective left heart catheterization complicated by severe thrombocytopenia two hours post-procedure leading to a large inguinal hematoma at the access site and life-threatening hemodynamic compromise requiring vasopressors.

## Case Report

A male patient aged 63 years with a history of atrial flutter, smoking and hypertension was referred for a left heart catheterization for further evaluation following abnormal myocardial perfusion stress test. He had no prior cardiac procedures, known drug allergies or contrast exposures. On the day of the procedure, he presented with normal vital signs and a platelet count of  $269 \times 10^3$ . 6-Fr access was obtained in the right common femoral artery. During the coronary angiography, the patient received intracoronary (IC) adenosine and nitroglycerin, unfractionated heparin (intra-arterial), intravenous fentanyl, midazolam, phenylephrine and 100mL of Visipaque-320, a non-ionic iso-osmolar contrast medium. Neither Aspirin nor a

P2Y12 inhibitor was given before or during the procedure. Coronary angiography showed three-vessel disease with a Fractional Flow Reserve (FFR) positive Right Coronary Artery (RCA) lesion; Percutaneous Coronary Intervention (PCI) was deferred in favor of a potential Coronary Artery Bypass Graft (CABG). Intraoperative hypotension was attributed to nitroglycerin and adenosine rather than anaphylaxis since it was not associated with other symptoms including dyspnea, throat tightness, pruritis or flush. Vascade vascular closure system (Cardiva Medical, Inc.) was used along with ten minutes of manual pressure. Good hemostasis at the access site was achieved.

However, within two hours of the procedure, femoral access site was found to develop a large hematoma complicated by hypotension and supraventricular tachycardia. Resuscitation was done with intravenous normal saline and twenty-five minutes of direct manual pressure applied to the access site. A FemoStop® plus compression system was then placed. Intravenous vasopressors and amiodarone were initiated to stabilize the condition.

Patient was emergently taken to the catheterization lab for a right iliac and femoral angiogram *via* contralateral access using an additional 40mL of visipaque which ruled out retroperitoneal hemorrhage. Mild access site active extravasation was noted. Decision was made to perform prolonged manual compression which eventually achieved hemostasis. Immediately afterwards, he was found to have platelets of  $2 \times 10^3$ . Peripheral smear confirmed thrombocytopenia and identified rare schistocytes. Doppler studies of all four extremities were performed to rule out Deep Venous Thrombosis (DVT). Normal INR/

PTT, LDH and fibrinogen ruled out DIC. A second peripheral smear found no schistocytes and identified only a single platelet in addition to increased eosinophils. HIT (Heparin Induced Thrombocytopenia) antibodies were negative. Indirect antibodies to platelets detected by flow cytometry were positive. Provisional diagnosis of contrast induced thrombocytopenia was made.

The patient ultimately received four units of platelets and two units of packed RBCs. He had melena for next 48 hours which, on colonoscopy, were found to be due to diffuse mucosal bleeding. This complication was likely due to the severe thrombocytopenia as no focal spot of gastrointestinal hemorrhage was found on esophagogastroduodenoscopy or colonoscopy.

Although a few case reports [1-3] have documented corticosteroid administration in similar situations, there is insufficient literature to support this intervention. Hence, we decided not to use IV corticosteroids. Platelet counts increased to  $127 \times 10^3$  by discharge three days later and were  $328 \times 10^3$  in one week. Due to prompt improvement in platelet count, marked improvement in patient's clinical condition and logistic constraints, allergy specialist was not involved in the case.

Patient subsequently underwent successful three-vessel CABG and was reportedly event free since the last clinical encounter. Temporal trend of platelet count is represented in figure 1.

## Discussion

There are fourteen reported cases of acute, severe thrombocytopenia following contrast administration as per our literature search derived from PubMed (Table 1). Both ionic and non-ionic, low and high osmolar contrast agents have been reported to be associated with this phenomenon. Repeat exposure within weeks of the primary exposure were invariably associated with recurrent thrombocytopenia [1,2,4].

Clinical profile, temporal trend of platelet reduction and recovery noted in these handful of contrast-induced thrombocytopenia

cases closely resemble the thrombocytopenia induced by Ligand-Mimetic Fibrinogen receptor antagonists (GpIIb-IIIa inhibitors) [5]. Thrombocytopenia associated with GpIIb-IIIa inhibitors is a well-known phenomenon where a severe, acute drop in platelet counts occurs within hours of exposure followed by recovery within a week. This can be associated with fever, chills and other systemic symptoms. These antibodies can be naturally occurring, accounting for the observation that platelet destruction can occur within a few hours of the first exposure to one of these medications [6,7].

Maintaining a high clinical suspicion for contrast induced thrombocytopenia is paramount. Thrombocytopenia can be the only manifestation; however, systemic symptoms like fever, chills and hemodynamic instability have been reported. Avoidance of the contrast exposure especially in close temporal proximity with the earlier exposure is of utmost importance. Once established, sensitivity to contrast causing immune thrombocytopenia is usually permanent; hence, patients should avoid future exposure [7]. Glucocorticoids use is controversial, but often administered. It is difficult to attribute the improvement in platelet count to steroid administration as this could be simply due to withdrawal of the sensitizing agent itself. IV immunoglobulin's and plasma exchange are used for other forms of drug induced thrombocytopenia; however, in the context of contrast induced thrombocytopenia, we found only one reported case of IV immunoglobulin's [4] while none reported use of plasma exchange. Platelet counts invariably improved within next one to two weeks, regardless of the treatment options.

## Conclusion

Contrast induced thrombocytopenia is rare but clinically important entity especially in a busy cardiovascular practice. Awareness of this phenomenon is paramount in avoiding future contrast exposures and management of the patient. Platelet count invariably improve within days, however, supportive care during this interval is critical.

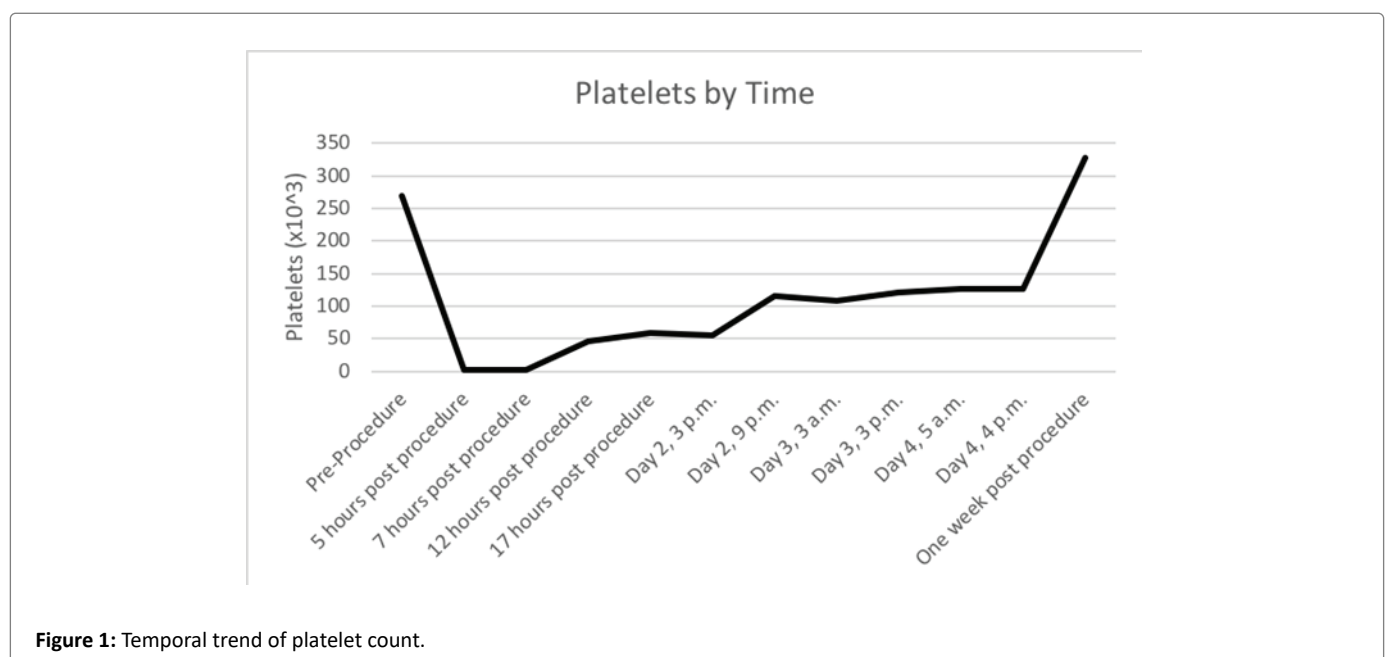


Figure 1: Temporal trend of platelet count.

**Table 1:** Literature review of case reports of intravenous contrast induced thrombocytopenia.

Author, Year	Case Description	Lowest Platelet Count ( $\times 10^3/\mu\text{L}$ )	Contrast Name and Quantity	Investigations/ Treatment	Time to Recovery (days)/platelet count ( $\times 10^3/\mu\text{L}$ )
Park M, et al. [3]	63-year-old male with chronic alcohol intake underwent CT Liver with contrast for assessment of abnormal liver function test. Patient presented to the emergency room 6 hours after discharge with hematoma around the IV site and stable vital signs. No anaphylaxis signs.	2	Non-ionic, low osmolarity contrast agent Ioversol (Optiray 350), 120mL	10 units of platelets and 1 mg/kg Methylprednisolone for 5 days. Discharged on day 5 without complication ns.	May-64
Ferreira RM, et al. [8]	71-year-old woman underwent elective PCI to LAD. 5 hours after exposure, she developed chills, nausea, vomiting along with bleeding from the femoral access site.	1	Low-osmolar iodinated contrast	Protamine, DAPT held, no transfusions used as bleeding had stopped and patient was stable; negative PF4 antibody	8/210
Cubero-Gomez, et al. [1]	47-year-old man with history of renal transplantation, on dialysis, underwent diagnostic LHC. Within 24 hours, platelets dropped from 242 to 74 ( $\times 10^3/\mu\text{L}$ ), reaching 25 ( $\times 10^3/\mu\text{L}$ ) in 48 hours. He then underwent placement of 7 stents. After 6 hours, platelet counts dropped to 0 ( $\times 10^3/\mu\text{L}$ ). Reportedly, he had had a similar episode of thrombocytopenia after an LHC which was attributed to Clopidogrel.	0	High osmolar ionic iodinated contrast (ioxaglate sodium/ioxaglate meglumine) and Bivalirudin	IV Methylprednisolone; next PCI was done with Gadolinium and IVUS guidance	6/181
Keach JW, et al. [2]	74-year-old man with ADHF and NSTEMI underwent diagnostic LHC. 4.5 hours later, he developed a hematoma at the femoral access site. Platelets dropped to undetectable levels. He refused to undergo CABG and instead underwent PCI 6 days later. Similar drop in platelets was noted; however, this episode was accompanied by dyspnea and tachycardia.	0	Iodixanol (non-ionic, low osmolar)	IV methylprednisolone, famotidine and diphenhydramine, HIT panel negative	6/100
McCaulley JA, et al. [9]	22-year-old pregnant woman who underwent CT with contrast (pulmonary embolism protocol). Suffered from immediate onset of throat tightness, dyspnea and facial flushing. Platelet counts dropped to 4 ( $\times 10^3/\mu\text{L}$ ) in several hours.	4	Not reported	Not reported	Not reported
Bata P, et al. [10]	72-year-old man underwent CT-Urogram. Within hours, he developed paradoxical hypertension, respiratory distress and petechiae. Platelet counts had dropped from 300 to 2 ( $\times 10^3/\mu\text{L}$ ) in 20 hours.	2	Optiray 350 (low osmolar, non-ionic), 120 cc	Platelet transfusion and IV methylprednisolone. <i>In vitro</i> testing of patients' blood with the contrast agent did not exhibit similar drop in platelet counts.	6/157
Garcia Bueno MJ, et al. [7]	65-year-old woman underwent whole body CT scan with contrast. 12 hours later, she presented to emergency department with headache, fever, vomiting, diffuse petechia, ecchymoses and gingival bleeding. Previous episodes of contrast exposure were associated with chills and fever; however, no bleeding was noted.	6	lomeprol (non-ionic, low osmolality), 100 cc	Normal complements, negative anti-platelet antibodies, negative anti-PF4 antibody, normal IgE levels. Received 5 units of platelets.	6/162

Saitoh T, et al. [11]	70-year-old man who presented with hemiparesis underwent CT head with contrast. 3 hours later, he developed purpura and his platelets dropped to $5 \times 10^3/\mu\text{L}$ .	5	lopamidol (non-ionic), 100 cc	IV corticosteroids and platelet transfusions; negative anti-PF4 antibody; platelet aggregation seen on <i>in vitro</i> contrast exposure to the patient's whole blood.	2 days
Wiemer M, et al. [4]	66-year-old woman with unstable angina underwent coronary angiography. 8 hours later platelet counts dropped from 310 to $1 \times 10^3/\mu\text{L}$ . This was complicated by access site hematoma and renal failure requiring hemodialysis. Three weeks later, she underwent another angioplasty and had a similar drop in platelets.	1	lopromide (low-osmolar, non-ionic), 90 cc	Cortisone and immunoglobulins	8 Days
Kudoh Y, et al. [12]	52-year-old man underwent drip infusion pyelography. 2 hours later, he developed chills and fever. Platelet counts had decreased from 233 to $8 \times 10^3/\mu\text{L}$	8	Not reported	Treated with hydrocortisone. <i>In vitro</i> platelet aggregation test and anti-platelet antibody test were negative	"several days"
Chang JC, et al. [13]	66-year-old woman underwent diagnostic LHC for evaluation of chest pain. 4 hours after the procedure, platelets dropped to $10 \times 10^3/\mu\text{L}$ with no systemic signs or symptoms. Three weeks later, patient required another procedure which led to another episode of transient thrombocytopenia.	10	Renografin 76 (Ionic, high osmolar), 90 cc	Treated with platelet transfusion. Bone marrow biopsy showed abundance of megakaryocytes suggestive of peripheral destruction. HIT panel, platelet associated immunoglobulin and complement-mediated cytotoxicity testing were negative. <i>In vitro</i> platelet aggregation and direct chemical destruction was not seen.	4/120
Shojania AM, et al. [14]	<b>Case 1:</b> 57-year-old female with chronic renal failure underwent left ventricular arteriography. The next day, she was drowsy with generalized ecchymoses and petechiae with a hemorrhage in the left fundus.	21	5mL 75% diatrizoate sodium (Hypaque-M) and 60mL diatrizoate meglumine and diatrizoate sodium (Renografin-76)	None	Not reported
Shojania AM, et al. [14]	<b>Case 2:</b> 60-year-old male with renal failure underwent bilateral percutaneous nephrostography leading to leakage of contrast medium into perinephric region. 14 hours later, bleeding from nephrostomy tubes was noted.	8	20mL of 60% diatrizoate meglumine (Reno-M-60)	6 units of platelets	5/252
Lacy J, et al. [15]	79-year-old male with diabetes and aortic stenosis underwent cardiac catheterization. Immediately after procedure, he experienced chills, fever and hypotension. Within 8 hours, his platelets were $30 \times 10^3$ and dropped to $2 \times 10^3$ by the next day.	2	190mL Renografin-76 (diatrizoate meglumine)	Benadryl and dopamine. No evidence of microangiopathic hemolysis on peripheral smear. Megakaryocytes on bone marrow aspirate.	24/280

LHC: left heart catheterization; PCI: percutaneous coronary intervention; IVUS: intravascular ultrasound; ADHF: acute decompensated heart failure; CT: Computed Tomography; HIT: Heparin-induced thrombocytopenia

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