Case Report

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Acute severe thrombocytopenia following iodinated radiographic contrast medium infusion: a case report

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Introduction: Acute contrast-induced thrombocytopenia is an unusual complication, and it is a rare event with the use of modern low-osmolarity iodinated contrast medium. There are only a few reports that exist in English literature.

Case presentation: The authors report the case of a 79-year-old male patient with severe, life-threatening thrombocytopenia after administration of intravenous nonionic low-osmolarity contrast medium. His platelet count dropped from 179×10^9/l to 2×10^9/l after 1 h of radiocontrast infusion. Which has returned gradually to normal level within days with corticosteroid administration and platelet transfusion.

Conclusion: Iodinated contrast-induced thrombocytopenia is a rare complication with an unknown causative mechanism. There is no definitive treatment for this condition, with corticosteroids being used in most cases. The platelet count normalizes within a few days regardless of any interventions, but supportive treatment is important to avoid any unwanted complications. Further studies are still needed for a better understanding of the exact mechanism of this condition.

Keywords: iodinated contrast medium, case report, thrombocytopenia

Introduction

Acute contrast-induced thrombocytopenia is a very rare event with the use of modern low-osmolarity iodinated contrast media. Only a few cases have been published so far[1–6]. No causative mechanism has yet been identified. However, direct toxicity or an idiosyncratic reaction after a previous exposure may be part of its etiopathogenesis[7]. 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[8]. Corticosteroids are often given, but there is no evidence that they are helpful if the thrombocytopenia is drug induced[9].

Here, we report the case of a 79-year-old male patient with severe acute thrombocytopenia 1 h following intravenous (i.v.) nonionic contrast medium presented with extensive purpuric rash on the skin and mucosal surfaces, followed by hematuria, and gastrointestinal hemorrhage without any signs or symptoms of immediate allergic reactions. The platelet count returned gradually to normal within days with corticosteroid administration and platelet transfusion.

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HIGHLIGHTS

- Acute severe thrombocytopenia is one of the rarest complications associated with iodinated contrast, with few cases reported in the literature.
- The causative mechanism that causes this phenomenon has not yet been identified. Although immune-mediated platelet destruction should be considered.
- There is no established treatment, and the use of steroids is controversial.

This case report has been reported in line with the SCARE criteria[10].

Case presentation

A 79-year-old male patient who underwent laparoscopic sigmoidectomy for adenocarcinoma of the sigmoid colon (p T3 N0) 4 months ago has presented to our oncology outpatient clinic for routine computed tomography (CT) scan follow-up. The patient had a history of lymphoma which had been treated by chemotherapy 15 years ago prostate cancer, which had been treated with radiation 10 years ago, diabetes mellitus type 2, hypertension, and atrial fibrillation. His daily medication consisted of Digoxin 0.25 mg, Verapamil 120 mg, Rivaroxaban 20 mg, Metformin 1000 mg BID, Gabapentin 300 mg, and Atorvastatin 10 mg.

A nonionic low-osmolarity contrast agent [120 ml Omnipaque 350 (Iohexol)] enhanced whole-body CT scan was performed. During the infusion of contrast media, no specific signs or symptoms were observed. At the end of the examination, while the patient was still on the CT table, he developed transient shortness of breath and chills.

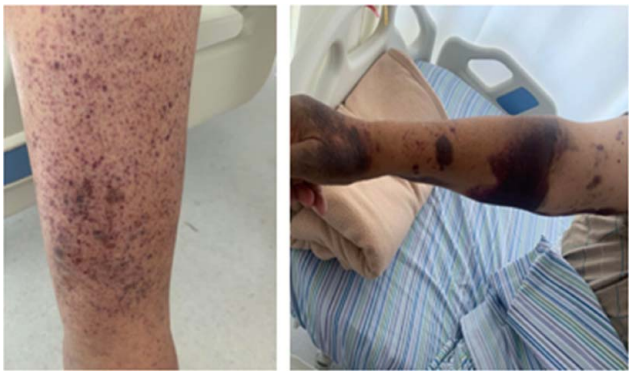

Figure 1. The petechial rash and the ecchymosis that appeared on the patient's upper and lower limbs 30 min after the computed tomography scan.

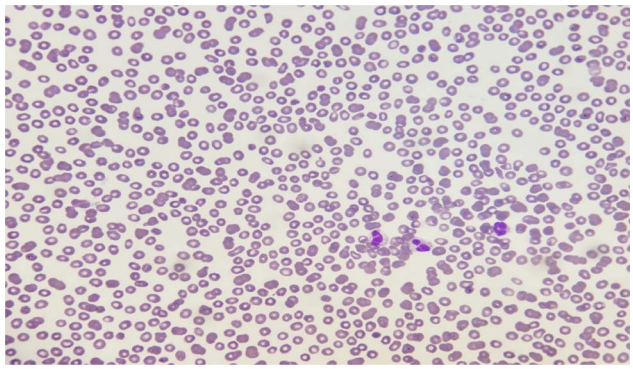

Figure 2. Peripheral blood film showed thrombocytopenia, and no schistocytes were seen.

Thirty minutes later, he presented to our emergency room with worsening shortness of breath, along with diffuse petechial hemorrhages in both lower extremities, and multiple large ecchymosis in different part of his body (Fig. 1). No fever, urticarial, or pruritus were observed. Vital signs: blood pressure: 103/57 mm Hg, pulse: 89 per minute, temperature: 36.4°C, and SpO_2: 94% on room air. He received immediately hydrocortisone 200 mg and promethazine 25 mg. Initial laboratory testing showed severe thrombocytopenia with a platelet count of 2×10^9/l, which was 179×10^9/l at the aforementioned clinic 4 h prior. A new sample collected in a sodium citrate tube confirmed the thrombocytopenia. Other laboratory parameters, including prothrombin time and activated partial thromboplastin time, fibrinogen, and C-reactive protein were unremarkable, and thrombocytopenia was the only laboratory abnormality (Table 1). The peripheral blood film showed thrombocytopenia, and no schistocytes were seen (Fig. 2).

He denied any recent changes in his medication, and he did not receive any drugs on the day he did the CT scan. No other causes of thrombocytopenia were evident. Only the administration of the contrast could therefore have caused this acute thrombocytopenia. The patient only known allergy is penicillin allergy, and he received i.v. contrast multiple times during the CT scans he underwent in multiple hospitals in the USA as a part of the evaluation and follow-up of his previous diseases. Unfortunately, there is no documentation of the type of contrast used before, but there were no complications or drops in the platelet count back then.

On the same day of admission, he developed gross hematuria, melena, and more extensive ecchymosis. The patient's hemoglobin dropped from 12.6 to 8.5 g/dl. He received 2 units of packed red blood cells, and he needed a 5-unit platelet transfusion twice daily for 2 days until the platelet count started to rise and the bleeding stopped. On the second day of admission bone marrow aspiration and biopsy were done which revealed megakaryocytes, and excluded any hematological diseases or actual malignancies (Fig. 3).

After a literature review, we found a few case reports that documented corticosteroid administration as management in similar situations. So methylprednisolone 80 mg twice daily was started after 2 days of contrast exposure and administered for 3 days. The patient was discharged from the hospital after 4 days with a platelet count 74×10^9/l. The platelet count returned gradually to baseline by day 10, and no significant drop was observed during follow-up (Fig. 4).

Table 1

Laboratory result before and after development of acute thrombocytopenia

	4 h before	1 h after	6 h after	1 day after 6 a.m.	2 days after 6 a.m.	2 days after 6 p.m.	3 days after	4 days after
WBC (10^3/μl)	4.5	4.96	5.86	4.27	4.63	4.70	4.18	6.39
PLT ($\times 10^3$/μl)	179	2	5	1	8	30	33	74
Hb (g/dl)	12.6	11.5	11.1	8.5	9.1	8.9	9.4	9.2
Hct (%)	36.5	35.9	30.1	28.9	29	29.4	29.6	29.6
Neutrophil (10^3/μl)	1.89	2.7	4.4	–	2.28	4	2.9	4.87
Eosinophils (10^3/μl)	0.2	0.05	0.09	–	0.04	0.01	0.01	0.05
Creatinine (mg/dl)	0.98	0.81	0.97	0.74	–	–	–	0.87
Total bilirubin (mg/dl)	0.498	–	0.36	0.784	–	–	–	0.948
AST (IU/l)	17	–	–	–	23	–	–	15
ALT (IU/l)	17.8	–	–	–	29.1	–	–	26.7
aPTT (s)	38.9	–	–	34.4	38.4	–	–	–
INR	1.21	–	–	1.42	1.24	–	–	–
CRP (mg/l)	–	15.53	–	–	–	–	–	–
LDH	124	–	–	136	–	134	–	147
Fibrinogen	–	–	–	250	–	–	–	–

ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CRP, C-reactive protein; Hb, hemoglobin; Hct, hematocrit; INR, international normalized ratio; LDH, lactate dehydrogenase; PLT, platelet; WBC, white blood cell.

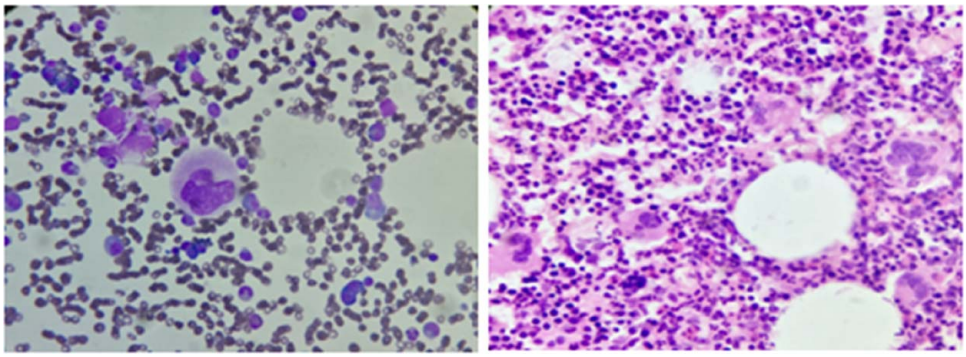

Figure 3. Bone marrow aspiration and biopsy were done and revealed megakaryocytes with megakaryocytic hyperplasia.

Discussion

Acute severe thrombocytopenia is one of the rarest complications associated with iodinated contrast, with few cases reported in the literature. Iodinated contras media are generally associated with a very low rate of adverse effects, which are undoubtedly lower with nonionic low osmolar agents. Most previously reported cases were associated with ionic contrast media used for coronary angiography[1].

In our case, acute severe thrombocytopenia was caused by nonionic low-osmolar contrast medium, without any immediate signs of an allergic reaction. The lowest platelet count was 1×10^9/l 18 h after contrast medium administration. Such low platelet counts are rarely been reported previously with a non-ionic low osmolar agent, and there are only three cases in English literature[8,11,12] (Table 2).

The causative mechanism that causes this phenomenon has not yet been identified. A sudden onset of thrombocytopenia, followed by a proliferation of megakaryocytes in the bone marrow, indicates either peripheral platelet consumption or destruction[2]. The drop in platelet count due to disseminated intravascular coagulation after iodinated contrast media infusion has been reported in a few cases[9,13,14]. In our case, disseminated intravascular coagulation was excluded by laboratory tests.

In this case, thrombocytopenia was confirmed both by microscopic evaluation and the collection of the second sample in a citrate tube. Contrast exposure was the only trigger for the acute drop in the platelet level. The platelet count was 178×10^9/l 4 h before contrast exposure. Furthermore, no drugs or other chemical agents were used, and no sign of an ongoing viral infection or other infection was detected. And the acute inflammatory reactant within range. No other causes of thrombocytopenia were evident.

Immune-mediated platelet destruction should be considered in this patient due to cytotoxicity after previous exposure to contrast[5]. Although antibody-mediated mechanisms of contrast medium-induced reactions have never been conclusively documented, it has been shown that contrast medium can act as a hapten and induce antibody formation in animals[15].

Conflicting results were seen regarding the effect of iodinated contrast media on platelets *in vitro*. One study showed that when whole blood is preincubated with high concentrations of contrast media and then exposed to platelet-rich plasma, it induces fibrinogen consumption with platelet aggregation, which results in thrombocytopenia. Another study showed that no direct toxicity on the platelets was seen when i.v. contrast was added to blood sample[3].

There is no established treatment, and the use of steroids is controversial. In our case, we administered corticosteroids after 48 h of contrast exposure, as suggested in the literature. It was fortunate that platelet count increased immediately after the use of steroids, from 8×10^9/l to 33×10^9/l, but it is difficult to attribute the improvement in platelet count to steroid administration. I.v. immunoglobulin and plasma exchange have been used in the management of drug-induced thrombocytopenia, but the benefit of these treatments in the context of contrast-induced thrombocytopenia is uncertain[1].

The time needed for recovery from thrombocytopenia was several days regardless of the treatment option, but, rarely, thrombocytopenia persisted for several weeks[16]. Life-threatening bleeding is unusual, and all the reported cases have recovered without catastrophic complications.

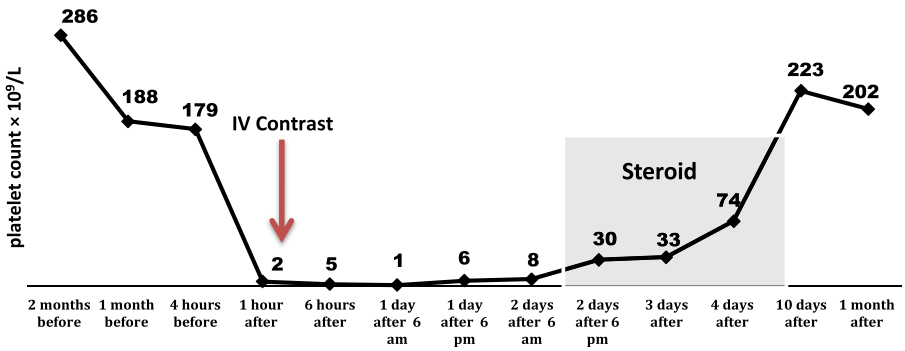

Figure 4. The patient's platelet count before and after being exposed to intravenous iodinated contrast media.

Table 2

Reported cases of nonionic low osmolar contrast media-induced acute thrombocytopenia with nadir platelet counts one or less ($\times 10^3/\mu l$)

References	Case description	Contrast media	Nadir platelet counts ($\times 10^3/\mu l$)
Ferreira *et al.*[8]	71-year-old female underwent elective coronary angiography. Five hours later, she developed chills, vomiting along with bleeding from the femoral access site	Low-osmolar iodinated contrast	1
Keach *et al.*[11]	74-year-old man developed a hematoma at the femoral access site after therapeutic coronary angiography	Nonionic, low osmolar (Iodixanol)	0
Wiemer *et al.*[12]	66-year-old female underwent coronary angiography, 8 h later, her platelet count drop from 310 to 1 ($\times 10^3/\mu l$). She also underwent another angioplasty after 3 weeks and she had a similar drop in platelets counts	Low-osmolar, nonionic (Iopromide)	1

Conclusion

Iodinated contrast-induced thrombocytopenia is a rare complication with an unknown causative mechanism, although immune-mediated platelet destruction should be considered. There is no definitive treatment for this condition, with corticosteroids being used in most cases. The platelet count normalizes within a few days regardless of any interventions, but supportive treatment is important to avoid any unwanted complications. Further studies are still needed for a better understanding of the exact mechanism of this condition.

Ethical approval

The study is exempt from ethical approval at our institution. This is a case report. The patient was informed that the data concerning his case would be submitted for publication.

Consent

Written informed consent was obtained from the patient for the publication of this case report, images, and all information contained in it. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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No funding was obtained for this study.

Author contribution

B.M.M.S. and M.H. were involved in literature review, data collection, and design. All authors were involved in interpretation and all read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no competing interests.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Baraa M.M. Sharawi.

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References

[1] Park M, Kim M, Park J, *et al*, Life-threatening thrombocytopenia following intravenous contrast media infusion. Yonsei Med J 2018; 59:158.
[2] Barillari G, Pasca S. Acute thrombocytopenia after infusion of an iodinated contrast medium: a case report. J Clin Case Rep 2012;2:15
[3] Bata P, Tarnoki A, Tarnoki D, *et al*. Acute severe thrombocytopenia following non-ionic low-osmolarity intravenous contrast medium injection. Korean J Radiol 2012;13:505.
[4] DD R, CS M, SV P, *et al*. Acute life-threatening contrast induced thrombocytopenia following diagnostic coronary angiography: a case report and literature review. J Clin Case Stud 2021;6. doi:10.16966/2471-4925.218
[5] Cubero-Gómez J, Guerrero Márquez F, Diaz-de la-Llera L, *et al*. Severe thrombocytopenia induced by iodinated contrast after coronary angiography: the use of gadolinium contrast and intravascular ultrasound as an alternative to guide percutaneous coronary intervention. Rev Port Cardiol 2017;36:61.e1–4.
[6] Chang J, Lee D, Gross H. Acute thrombocytopenia after i.v. administration of a radiographic contrast medium. AJR Am J Roentgenol 1989;152:947–49.
[7] Guerrero-Márquez F. Thrombocytopenia induced by iodinated contrasts. Utility of gadolinium and intravascular ultrasound. J Rare Dis Res Treat 2018;3:17–21.
[8] Ferreira R, Mansur Filho J, Villela P, *et al*. Contrast-induced thrombocytopenia following percutaneous coronary intervention. J Saudi Heart Assoc 2017;29:227–9.
[9] Aster R, Bougie D. Drug-induced immune thrombocytopenia. N Engl J Med 2007;357:580–7.
[10] Agha RA, Franchi T, Sohrabi C, *et al*. SCARE Group. The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84(December):226–30.
[11] Keach J, Huang J, Garcia J, *et al*. Acute severe thrombocytopenia secondary to intraarterial low-osmolar iodinated contrast administered during coronary angiography. J Vasc Interv Radiol 2014;25: 2003–5.
[12] Wiemer M, Kreuzpaintner G, Lauer B, *et al*. Recurrent immune thrombocytopenia: a rare complication after contrast medium injection. Dtsch Med Wochenschr 1995;120:1236–40.
[13] Lacy J, Bober-Sorcinelli KE, Farber LR, *et al*. Acute thrombocytopenia induced by parenteral radiographic contrast medium. Am J Roentgenol 1986;146:1298–9.
[14] Shojania AM. Immune-mediated thrombocytopenia due to an iodinated contrast medium (diatrizoate). Can Med Assoc J 1985;133:123.
[15] Brasch R, Caldwell J. The allergic theory of radiocontrast agent toxicity. Invest Radiol 1976;11:366.
[16] Aster R, Curtis B, Mcfarland J, *et al*. Drug-induced immune thrombocytopenia: pathogenesis, diagnosis, and management. J Thromb Haemost 2009;7:911–8.