



# Life-Threatening Thrombocytopenia Following Intravenous Contrast Media Infusion

Mihwa Park<sup>1</sup>, Minjeong Kim<sup>1</sup>, Jisun Park<sup>2</sup>, and Jinhyun Cho<sup>2</sup>

<sup>1</sup>Department of Internal Medicine and <sup>2</sup>Division of Hematology-Oncology, Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, Incheon, Korea.

Radiocontrast media-induced acute severe thrombocytopenia is a very rare complication and potentially life-threatening. Here, we report the case of a 63-year-old male patient with severe acute thrombocytopenia following first exposure to intravenous non-ionic contrast media without immediate allergic reactions. His platelet count dropped from 107000/ $\mu$ L to 2000/ $\mu$ L after six hours of radiocontrast infusion. After administration of corticosteroid and transfusion of platelet concentrates, the platelet count returned gradually to normal within 5 days. To the best of our knowledge, non-ionic contrast media-induced isolated acute severe thrombocytopenia following no signs or symptoms of immediate allergic reaction has never been described.

**Key Words:** Thrombocytopenia, contrast media, non-ionic, hypersensitivity

## INTRODUCTION

Contrast media can occasionally produce allergic reactions, ranging from minor to life-threatening anaphylactoid responses. Intravenous contrast media can also induce acute thrombocytopenia, although it is a very rare complication that has been mostly reported in patients who received ionic contrast media, which was usually used for coronary arteriography.<sup>1-3</sup> Non-ionic contrast-induced acute thrombocytopenia is far more rare and has been usually accompanied by signs or symptoms of immediate allergic reaction, including respiratory distress, chest discomfort, facial flushing, or skin rash.<sup>4,5</sup>

Here, we report the case of a 63-year-old male patient with a self-limiting severe acute thrombocytopenia following first exposure to intravenous non-ionic contrast medium without any signs or symptoms of immediate allergic reactions.

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**Corresponding author:** Dr. Jinhyun Cho, Division of Hematology-Oncology, Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, 27 Inhang-ro, Jung-gu, Incheon 22332, Korea.

Tel: 82-32-890-2581, Fax: 82-32-890-2585, E-mail: henkengun@gmail.com

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## CASE REPORT

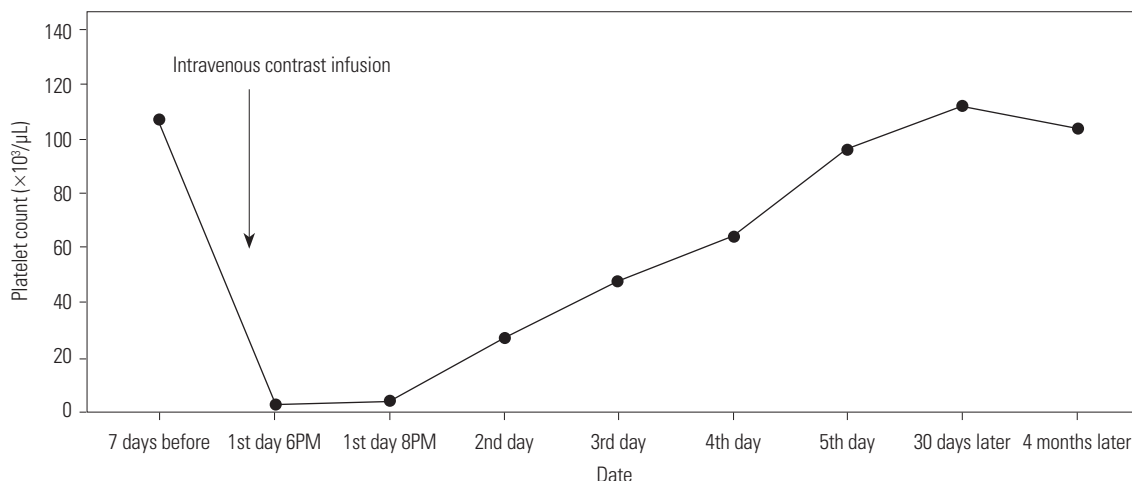
A 63-year-old male had visited an outside clinic with easy fatigue. Laboratory evaluation revealed elevation of liver transaminases with alanine aminotransaminase of 47 IU/L, aspartate aminotransferase of 106 IU/L, and gamma-glutamyl transpeptidase of 935 IU/L. The patient had a history of chronic alcohol intake over 30 years and hypertension for 8 years. His daily medication consisted of felodipine 5 mg, losartan 50 mg, atorvastatin 20 mg, and aspirin 100 mg, and he denied any recent changes in medication.

A non-ionic low osmolality contrast agent [120 mL, Ioversol (Optiray 350®)] enhanced computed tomography (CT) scan was performed to clarify the cause of abnormal liver function test. During infusion of contrast media, no specific signs or symptoms were observed. CT scan detected chronic liver disease with mild splenomegaly, which was consistent with alcoholic liver disease. The patient returned home with no signs or symptoms of immediate allergic reactions. Six hours after examination, he was admitted to our emergency room (ER) reporting sudden onset bleeding from his intravenous site, along with a huge bruise and hematoma. At presentation to the ER, he had a blood pressure of 105/58 mm Hg, a heart rate of 71/min, and a respiration rate of 18/min. No fever, urticaria, itches, rash, respiratory distress, or chest discomfort was recorded. Laboratory test showed severe thrombocytopenia with a platelet count of 2000/ $\mu$ L, which was 107000/ $\mu$ L at the afore-

**Table 1.** Results of Laboratory Evaluation before and after Development of Acute Thrombocytopenia

	7 days before	1st day	2nd day	3rd day	5th day	Normal range
WBC (/ $\mu$ L)	8100	8750	8510	7340	8610	4000–10000
Hb (g/dL)	12.7	13.2	11.7	11.0	12.5	13.0–17.0
Hct (%)	35.2	37.2	32.3	32	35.9	36–51
PLT ( $\times 10^3$ / $\mu$ L)	109	2	27	48	64	140–400
MCV (fL)	-	94	93	96	95	83–100
MCH (Pg)	-	33.5	33.6	33.1	33.1	27–34
MCHC (g/dL)	-	35.6	36.3	34.5	34.8	31–35
Neutrophil (%)	-	92.6	81.7	66.1	82.1	40–75
BUN (mg/dL)	10.9	19.5	23.1	30	25.1	6–20
Creatinine (mg/dL)	0.86	1.19	1.35	1.14	1.04	0.5–1.3
Total bilirubin (mg/dL)	-	0.7	0.9	0.9	0.6	0.0–1.2
AST (IU/L)	106	114	80	44	37	5–40
ALT (IU/L)	47	22	21	17	16	5–41
ALP (IU/L)	-	221	157	135	105	35–130
PT (INR)	-	1.22	1.19	-	1.13	0.85–1.30
aPTT (sec)	-	38.1	40.4	-	33.5	29.0–44.0

WBC, white blood cell; Hb, hemoglobin; Hct, hematocrit; PLT, platelet; MCV, mean cell volume; MCH, mean cell hemoglobin content; MCHC, mean cell hemoglobin concentration; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; PT, prothrombin time; aPTT, activated partial thromboplastin time.

**Fig. 1.** Changes in platelet level before and after development of acute thrombocytopenia.

mentioned clinic 7 days prior. Mild anemia and elevated liver transaminases were also reported, which were considered to be associated with chronic alcohol intake (Table 1). Other laboratory parameters, including prothrombin time and activated partial thromboplastin time, were within normal limits. Peripheral blood smear showed normal size and shape of white blood and red blood cells, except a markedly decreased number of platelets. Serological studies showed no evidence of viral hepatitis or autoimmune disease, and there were no signs or symptoms of infectious disease.

Since drug-induced thrombocytopenia was highly suspected, the patient received platelet concentrates (10 units) and methylprednisolone (1 mg/kg for 5 days) intravenously. The platelet count returned gradually to baseline by day 5, and no further exacerbation of thrombocytopenia was observed dur-

ing follow-up (Fig. 1). Liver transaminases were also recovered upon drinking cessation, and there were no significant changes in other laboratory tests. He was discharged on the fifth day.

## DISCUSSION

Since their introduction in the 1920s, radiographic iodinated contrast media have been among the most commonly used drugs in modern medicine. The advent of low-osmolar iodinated contrast media has decreased the overall incidence of contrast-induced adverse events; the majority of adverse effects are mild and self-limited.<sup>6</sup> Nonetheless, severe or life-threatening complications, including cardiovascular collapse, bronchospasm, laryngeal edema, loss of consciousness, and

**Table 2.** Reported Cases of Non-Ionic Contrast Media-Induced Acute Thrombocytopenia

Author/contrast media	Age/sex	Symptoms and signs of allergic reaction	Onset of allergic reactions	Nadir platelet counts
Bata, et al. <sup>4</sup> /Ioversol (Optiray 350 <sup>®</sup> )	72/male	Respiratory distress, creeps, elevated blood pressure	40 minutes after contrast infusion	2×10 <sup>3</sup> /μL
McCaulley, et al. <sup>5</sup> /Iopamidol	22/female	Facial flushing, throat tightness, dyspnea	During contrast infusion	4×10 <sup>3</sup> /μL
Saitoh, et al. <sup>7</sup> /Iopamidol	70/male	No documentation (abstract only)		5×10 <sup>3</sup> /μL

seizure, can still occur occasionally. Acute severe thrombocytopenia induced by contrast media is extremely rare, with few cases reported in the literature. Most previous cases were associated with ionic contrast media used for coronary angiography.

In our case, isolated acute severe thrombocytopenia was caused by non-ionic low osmolar contrast media without any signs or symptoms of immediate allergic reaction, which has never been described before. Three cases of non-ionic contrast-induced acute severe thrombocytopenia have been reported so far: Two cases demonstrated acute thrombocytopenia following symptoms of immediate allergic reaction after contrast infusion (Table 2).<sup>4,5</sup> The other case did not describe whether any signs or symptoms of allergic reaction were observed after contrast infusion or not.<sup>7</sup>

Adverse reactions to contrast media are typically divided into two categories, chemotoxic reactions and hypersensitivity reactions.<sup>8,9</sup> Chemotoxic reactions are associated with the chemical properties of radiocontrast agent and dependent upon dose and infusion rate. These reactions, including emesis, flushing, warmth, increased vagal tone, and organ toxicities, are relatively common, usually transient, and self-limited. Hypersensitivity reactions are idiosyncratic and dose-independent, which include angioedema, bronchospasm, shock, and loss of consciousness. Several non-IgE mediated mechanisms have been proposed for hypersensitivity reactions.<sup>10,11</sup> Drug-induced platelet destruction is usually caused by drug-induced antibodies; however, this can be difficult to prove.<sup>12</sup> Most instances of drug-induced thrombocytopenia are considered as idiosyncratic, and no predisposing genetic or environmental factors have been identified.<sup>13</sup> Although the mechanism of contrast-induced thrombocytopenia remains unclear, an immunological mechanism is also postulated. Furthermore, previous studies demonstrated that radiocontrast media could activate coagulation, kinin, and/or complement cascade,<sup>10,11,14</sup> which might result in platelet aggregation with resultant thrombocytopenia. However, *in vitro* studies evaluating the effects of contrast media on platelets have showed conflicting results.<sup>15,16</sup> Further investigations are needed to clarify the pathophysiology of contrast-induced thrombocytopenia.

There is no established treatment for contrast-induced thrombocytopenia because of its rarity and uncertain pathophysiology. In many cases, patients have received treatment with high dose intravenous corticosteroids, which are widely used in management of anaphylaxis. However, the role of corticosteroids

in contrast-induced thrombocytopenia has never been studied to date. In our opinion, corticosteroids may be beneficial in preventing or reducing the severity of possible delayed adverse effects of radiocontrast media. Intravenous immune globulin and plasma exchange have been used in management of drug-induced thrombocytopenia, although the benefit of these treatments is still uncertain.

The present case demonstrated a rare but severe hematologic adverse effect of non-ionic low osmolar contrast media. Contrast-induced acute severe thrombocytopenia can occur even in patients without no symptoms or signs of immediate allergic reactions. Given the wide-spread use of intravenous contrast media, this case reminds clinicians to be aware of a rare, but life-threatening, hematologic complication caused by contrast media.

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## ORCID

Mihwa Park <https://orcid.org/0000-0003-2013-0972>  
 Jinhyun Cho <https://orcid.org/0000-0002-0641-5210>

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