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CASE REPORT

Contrast medium-induced severe thrombocytopenia in patient on maintenance hemodialysis: a case report and literature review

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Abstract
A 43-year-old male patient on maintenance hemodialysis had an enhanced computed tomography scan examination with iohexol for the first time 10 min before regular hemodialysis therapy. At the start of hemodialysis, no symptoms were observed, and the platelet count was 148,000/μl. Approximately 1 h after starting hemodialysis, dyspnea and chest discomfort appeared. Since oxygen saturation of the peripheral artery decreased to 87%, oxygen administration was immediately started while continuing hemodialysis therapy. Furthermore, gingival hemorrhage was observed, and the platelet count decreased to 5000/μl. We were carefully monitoring his conditions while continuing hemodialysis and oxygen administration, but no further deterioration was observed. Thereafter, these symptoms and severe thrombocytopenia gradually improved without additional treatment. At the end of hemodialysis, these symptoms completely disappeared. As well, the platelet count recovered to 35,000/μl at the end of hemodialysis and increased to 92,000/μl the next morning. From the clinical course, we diagnosed with contrast medium-induced thrombocytopenia. Acute thrombocytopenia is a rare complication induced by the contrast medium. Until now, 16 cases on contrast medium-induced thrombocytopenia have been reported. Our case spontaneously recovered from severe thrombocytopenia relatively earlier than previous reports. Our patient started hemodialysis therapy 10 min after an enhanced computed tomography examination. Early removal of contrast medium by hemodialysis might be associated with early improvement. We should acknowledge that contrast media have potential to induce severe thrombocytopenia, even in patients on maintenance hemodialysis.

Keywords Contrast medium · Iohexol · Thrombocytopenia · Hemodialysis · Adverse effect

Introduction

Contrast media, also known as contrast agents, are commonly used to enhance the contrast of structures or fluids within tissues in medical imaging examinations. Contrast media also enables detection of abnormalities more clearly. However, use of contrast media is not completely devoid of risk, although currently available contrast media are generally considered to be relatively safe. Adverse complications induced by the administration of contrast media vary from minor physiological and mild allergic reactions to severe life-threatening events. Most of these are mild non-life-threatening events that usually require only observation, reassurance, and/or supportive measures. However, severe and potentially life-threatening adverse events can rarely and unpredictably be experienced. Contrast-induced nephropathy, characterized by development of acute renal injury after exposure to contrast media, is a serious condition, which is likely to develop in patients with renal dysfunction. Patients on maintenance hemodialysis can receive intravascular contrast medium without risk of further renal damage because their kidneys are no longer functioning. The American College of Radiology manual on contrast media states that there is no need for urgent dialysis after intravascular iodinated contrast medium administration, unless an unusually large volume of contrast medium is administered, or there is substantial underlying cardiac dysfunction [1]. Therefore, we tend to underestimate the risk of using contrast media in patients on maintenance dialysis. However, even in patients

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on maintenance dialysis, a variety of adverse reactions induced by contrast media occur, as well as in those without renal dysfunction. Therefore, the risk of using contrast media needs to be recognized and we need to know how to treat these patients properly.

Acute thrombocytopenia is a contrast medium-induced serious complication, but its incidence is rare. We report here a case of a 43-year-old male patient on maintenance hemodialysis who developed severe acute thrombocytopenia after his first exposure to intravenous non-ionic contrast medium.

Case report

A 43-year-old Japanese man with end-stage renal failure was hospitalized because of general fatigue, loss of appetite, and considerable body weight loss. He had regularly undergone maintenance hemodialysis at another hospital because of chronic renal failure from chronic glomerulonephritis for approximately 1 year. He had no history of blood disease or autoimmune disease. Since starting hemodialysis therapy, he continuously had general fatigue and loss of appetite, and then lost 14 kg in body weight in 1 year. Because of the reduction in his body weight, he attempted to appropriately adjust his dry weight, but this was insufficient. At admission to our hospital, electrocardiography and echocardiography examinations did not indicate the possibility of ischemic heart diseases. After admission, an enhanced computed tomography (CT) examination of the chest and abdomen was performed with a total of 150 ml of a non-ionic low osmolality contrast agent, iohexol. This examination was performed to rule out the complication of any malignant diseases or infectious diseases. The CT examination did not show any evidence of these diseases. The patient had never used a contrast medium before this time. During the enhanced CT scan examination, no specific symptoms were observed. Approximately 10 min later, he started regular hemodialysis therapy and his blood was drawn for a routine examination (Table 1). On examination at the beginning of hemodialysis, his blood pressure and pulse rate were 135/85 mmHg and 62 beats per minute, respectively. His temperature, respiratory rate, and oxygen saturation were normal. The platelet count, which was 244,000/μl in a routine examination at another hospital 2 months previously, was 148,000/μl (Fig. 1). He started hemodialysis with a polysulfone dialyzer, APS-21SA (Asahi Kasei Medical, Tokyo, Japan), and low molecular weight heparin of a 1000 U bolus, followed by 1000 U/h infusion, according to his previous hemodialysis condition. One hour after starting hemodialysis therapy, he complained of dyspnea and chest discomfort. At that time, his blood pressure was 105/64 mm Hg, pulse was 60 beats per minute, and oxygen saturation

Table 1 Laboratory data at the start of hemodialysis

Peripheral blood		Blood chemistry	
Hematocrit	33.3%	Total protein	6.6 g/dl
Hemoglobin	11.3 g/dl	Albumin	4.0 g/dl
White blood cells	6500/μl	Aspartate aminotransferase	7.0 IU/l
Neutrophils	64.8%	Alanine aminotransferase	6.0 IU/l
Lymphocytes	21.5%	Lactate dehydrogenase	146 IU/l
Eosinophil	4%	Alkaline phosphatase	123 IU/l
Platelets	148,000/μl	Sodium	136 mmol/l
		Chloride	101 mmol/l
		Potassium	4.8 mmol/l
		Urea nitrogen	38.7 mg/dl
		Creatinine	12.56 mg/dl
		Uric acid	4.3 mg/dl
		Calcium	8.6 mg/dl
		Phosphorus	4.6 mg/dl

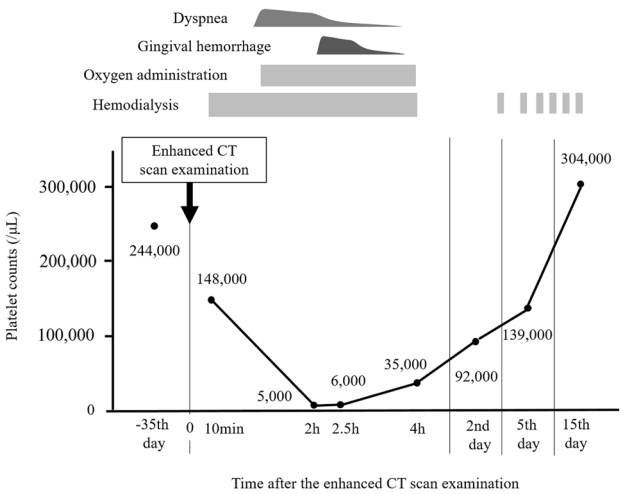

Fig. 1 A clinical course after an enhanced CT scan examination. *CT* computed tomography

of the peripheral artery had decreased to 87%. No fever, urticaria, itches, or rash was observed. Electrocardiography did not show any specific abnormalities. Oxygen administration was immediately started. Two hours later, gingival hemorrhage appeared and severe thrombocytopenia with a platelet count of 5000/μl was simultaneously observed. We carefully monitored his condition while he continued hemodialysis therapy and oxygen administration, but no further deterioration of his condition was observed. Thereafter, his symptoms gradually improved without any specific treatment, except for hemodialysis and oxygen administration. At the end of hemodialysis, his symptoms had completely disappeared, and the platelet count spontaneously recovered to

35,000/μl (Fig. 1). From the next day onward, these contrast media-induced symptoms were not observed. The platelet count recovered to 92,000/μl on the following day and then increased to 139,000/μl 4 days later. As the changes in other blood cell counts except the platelet count, the white blood cell counts were temporarily increased at the end of hemodialysis and, then, were spontaneously recovered as well (Table 2). The level of platelet-associated immunoglobulin G (PAIgG) in this patient was 28.6 ng/10^7 platelets (normal range: < 30.2 ng/10^7 platelets). Anti-cardiolipin antibody and anti-nuclear antibody were negative, and the immature platelet proportion was not increased to 2.9%. This patient had no other diseases that could cause thrombocytopenia. In addition, the onset of severe thrombocytopenia in this patient appeared to be associated with the administration of contrast medium, considering from his clinical course. Thus, we finally diagnosed with contrast medium-induced severe thrombocytopenia. He was discharged on the 4th day after reducing his body weight to his appropriate dry weight. He has not recurred thrombocytopenia thereafter.

Discussion

Contrast-induced adverse reactions include a variety of manifestations, such as skin rashes, nausea, anaphylaxis, pulmonary edema, and nephropathy. Acute severe thrombocytopenia is an extremely rare and severe adverse complication induced by contrast media. To the best of our knowledge, 16 cases of this serious adverse reaction have been reported with different types of contrast media since the early 1980s (Table 3) [2–17]. In most patients, any symptoms, including bleeding, fever, chills, dyspnea, wheezing, abdominal pain, and blood pressure variability, were observed within 24 h after contrast administration and the platelet count was decreased to below 10,000/μl. The lowest reported value of the platelet count was 0/μl [16]. With regard to treatment, high-dose intravenous corticosteroids, which are widely used in management of anaphylaxis, were used in nine patients [2, 4, 6, 7, 10, 12, 13, 16, 17]. Eight patients received platelet transfusions [3, 5–8, 10, 12, 17]. However, five patients spontaneously recovered their platelet count in 1–9 days without any treatment [3, 9, 11, 14, 15]. For the underlying disease of patients, three patients were on maintenance hemodialysis [3, 11, 16] and five had renal dysfunction [3, 4, 6, 7, 10]. Taken together with our case and previous reports, patients with renal dysfunction appear to be at higher risk for contrast medium-induced thrombocytopenia.

The mechanism of contrast medium-induced thrombocytopenia remains unclear. An immunological mechanism is proposed as a plausible mechanism [3]. According to this hypothesis, high-dose intravenous corticosteroids have been used as a treatment in some reports. Some reports have shown that radiocontrast media induce excessive coagulation and activate the complement cascade [18–22], which result in abnormal platelet aggregation with resultant thrombocytopenia. In our case, iohexol (non-ionic low osmolar contrast media) as a contrast medium for enhanced CT examinations was used. Adverse symptoms appeared in our patient approximately 2 h after administration of contrast medium. The nadir platelet count was 5000/μl. However, his symptoms and platelet count spontaneously recovered without any specific treatment, except for hemodialysis and oxygen administration. The time required for recovery was 4 h, which is relatively shorter than that in other previous cases. In our case, he coincidentally started regular hemodialysis therapy approximately 10 min after an enhanced CT examination. Most contrast media must be readily eliminated from the body by hemodialysis therapy. Therefore, removal of contrast media by hemodialysis therapy might be associated with early recovery from severe thrombocytopenia. Further accumulation of evidence is required to prove this possibility.

There is a large number of contrast-mediated diagnostic and therapeutic procedures worldwide. Therefore, complications induced by contrast media need to be recognized and any changes in the general condition need to

Table 2 Changes in blood cell counts before and after contrast medium infusion

	− 35 day	10 min	2 h	2.5 h	4 h	2nd day	5th day	15th day
PLTs(× 10^3/μl)	244	148	5	6	35	92	135	304
Ht (%)	37.1	33.3	33.6	32.9	36.6	34.6	33.9	37.9
Hb (g/dl)	12.2	11.3	11.3	11.1	12.7	11.4	11.2	12.5
RBC (× 10^4 /μl)	389	357	357	352	398	366	360	401
WBC(/μl)	6,000	6,500	4,200	5,200	10,000	7,300	5,300	6,800
Seg/neut (%)	70.6	64.8	72.9	81.0	75.3	57.3	59.7	71.7
Eosin (%)	3.7	4.0	0.7	1.0	1.4	4.8	4.9	3.7
Baso (%)	0.5	0.5	0.2	0.2	0.2	0.5	0.8	0.7
Lymph (%)	18.8	21.5	24.5	15.9	13.5	27.2	27.0	17.3
Mono (%)	6.4	9.2	1.7	1.9	9.6	10.2	7.6	6.6

Table 3 Summary of our case and previous cases reported

References	Age/sex	Contrast media	Nadir platelet counts	Time after contrast medium infusion	Coexisting kidney disorder[a]	Treatment	Recovery time
Our case	43 M	Iohexol	5000	2 h	HD	HD	4 h
2	29 M	Diatrizoate	4000	Next day	NA	Steroid	NA
3	57F	Diatrizoate	21,000	Next day	HD	(–)	9 days
3	60 M	Diatrizoate	6000	12 h	AKI	PT	4 days
4	79 M	Diatrizoate	2000	Next day	AKI	PD, steroid	8 days
5	66F	Diatrizoate	9000	3 h	NA	PT	Next day
6	52 M	Diatrizoate	8000	4 h	AKI	PT, steroid	NA
7	66F	Iopamidol	1000	2 h	AKI	HD, PT, steroid	NA
8	50 M	Iopamidol	19,000	5 h	NA	PT	NA
9	NA/F	Iopamidol	8000	48 h	NA	(–)	NA
10	70 M	Iopamidol	5000	3 h	CKD	PT, steroid	Next day
11	74 M	Iopamidol	30,000	1 h	HD	(–)	Next day
12	72 M	Ioversol	2000	Next day	(–)	PT, steroid	Next day
13	22F	Iopamidol	4000	Several hours	(–)	Steroid	Next day
14	75 M	Iodixanol	9000	4.5 h	(–)	(–)	3 days
15	71F	NA	1000	6 h	(–)	(–)	4 days
16	47 M	Ioversol	0	6 h	HD	steroid	NA
17	63 M	Ioversol	2000	6 h	(–)	PT, steroid	Next day

PD peritoneal dialysis, *PT* platelet transfusion, *NA* data not available

[a]Patients with chronic kidney disease (CKD), acute kidney injury (AKI), or on maintenance hemodialysis (HD) when contrast medium is administered

be carefully observed over several hours after the use of contrast agent, even in maintenance hemodialysis.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Human animal rights This article does not contain any studies with human participants performed by any of the authors.

Informed consent We have received a permission and written informed consent on the publication of this case report from this patient.

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