

〈Case Report〉

## A Case of Cholesterol Crystal Embolization with Hemorrhagic Intestinal Ulcer

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**ABSTRACT** Cholesterol crystal embolization (CCE) is a rare systemic embolism caused by formation of cholesterol crystals from atherosclerotic plaques. CCE usually occurs during vascular manipulation such as vascular surgery or endovascular catheter manipulation, or due to anticoagulation or thrombolytic therapy. We report a rare case of localized intestinal ulcer with active hemorrhage caused by spontaneous CCE. An 83-year-old man with a history of hypertension and diabetes was treated with a percutaneous coronary intervention (PCI) for myocardial infarction. Melena occurred eight days after PCI. An abdominal computed tomography revealed small intestinal ulcer, extravasation of the gastrointestinal tract and bleeding in the abdominal cavity. The patient was diagnosed as bleeding from the small intestinal ulcer, so an emergency laparotomy was performed. Partial resection of the small intestine was performed. A histopathological examination indicated that small intestine obstruction was caused by CCE. A histopathological examination indicated that small intestinal obstruction was caused by CCE. Therefore, in cases of intestinal obstruction after vascular manipulation, CCE should also be considered. doi:10.11482/KMJ-E43(1)29 (Accepted on March 9, 2017)

Key words : Cholesterol embolization, Intestinal necrosis, Percutaneous transluminal Coronary angioplasty

### INTRODUCTION

Cholesterol crystal embolization (CCE) is an

occlusion in a peripheral artery that occurs when atherosclerosis formed on the aortic wall ruptures

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and becomes an embolus containing cholesterol crystals<sup>1)</sup>. There are various factors that cause an atherosclerosis rupture, including interventional, anticoagulant and fibrinolytic therapies. Peripheral artery occlusions often cause problems in organs such as the kidneys, spleen, pancreas, liver and adrenal glands<sup>1)</sup>. Cases with embolization in the arteries of the toes are called Blue Toe Syndrome due to the skin color of the toes<sup>2)</sup>. CCE is often seen among elderly men, with risk factors including smoking, hyperuricemia, kidney failure and arteriosclerosis. In general, the prognosis of this disease is very poor and the diagnosis rates are not high<sup>1, 3)</sup>. The case in this report was a very rare embolization that appeared only in the ileum, without any problems in the toes or other organs.

## CASE REPORT

### *Patient*

83 year-old male

Main complaint: fever

Previous medical history: The patient had a right upper lobectomy due to lung cancer at the age of 65. He underwent a nephroureterectomy of the left kidney due to cancer of the right urinary tract. He also had bladder cancer, hypertension and type II diabetes.

### *Present history*

On August 12, 2016, the patient came to our hospital due to a fever and after an abdominal CT, he was suspected of having choledocholithiasis and choledochitis and was admitted. An endoscopic retrograde cholangio-pancreatography (ERCP) was scheduled, however he had an acute myocardial infarction (AMI). On August 12, a coronary angiogram (CAG) was immediately performed and a percutaneous coronary intervention (PCI) was performed in coronary artery #1 based on American Heart Association (AHA) classification.

On August 15, the patient vomited. After abdominal CTs, he was diagnosed with ileus

and referred to the surgical department. The CTs showed a partial thickening and edema of the small intestinal wall, which led to the diagnosis of localized enteritis. The images didn't show a clear finding of ischemia. After an ileus tube placement, conservative treatment continued. Later, even though ultrasonography showed a suspicious finding of small intestinal ischemia, his condition and blood test findings improved. However, melena started on August 20, and the amount increased by the 22. Additional abdominal CTs revealed a small intestinal ulcer, extravasation of the gastrointestinal tract and bleeding in the abdominal cavity (Fig. 1). The patient was diagnosed as bleeding from the small intestinal ulcer, so an emergency laparotomy was performed.

Medical condition at the time of hospitalization: His blood pressure was 118/66 mm Hg, pulse 90 beats per minute, body temperature of 38.0°C. No heart murmur was found. There were no diminished lung sounds, no color changes of the toes or fingers nor temperature changes. The dorsal arteries of both feet were palpable.

Test findings at the time of hospitalization: Urine tests were all positive for glucose, protein and occult blood. White blood cells increased in the peripheral blood which had a mild increase in the percentage of eosinophil, and normocytic normochromic anemia was also confirmed. A biochemical exam showed a distinct increase of LDH (LDH-2), which seemed to be from the heart. Increases of blood urea nitrogen (BUN), creatinine and C-reactive protein (CRP) were also confirmed. An electrocardiogram showed a normal sinus rhythm, left axis deviation and ST segment depressions in leads I, aVL, V4-6. A chest x-ray confirmed ground-glass opacity (GGO) possibly caused by pneumonia in the upper right lung field. The cardio thoracic ratio (CTR) was 60%, indicating heart enlargement.

Surgical finding: A substantial amount of light-colored hemorrhagic ascites was found.

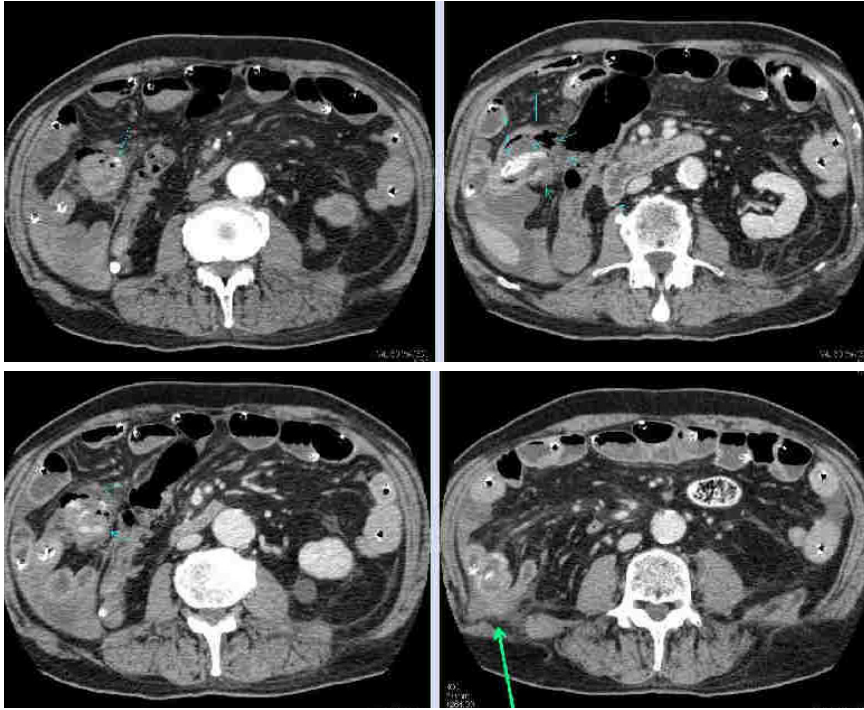


Fig. 1 The abdominal CT showed an intestinal ulcer, extravasation of the gastrointestinal tract (Blue arrows) and bleeding in the abdominal cavity (Green arrow).

A hematoma 5 cm in diameter was found in the mesentery of the ileum 330 cm away from the Treitz ligament. Eight centimeters of the ileum, with the hematoma in the middle, was resected and end to end anastomosis was performed.

**Post-operative course:** At the time of hospitalization, the patient had an intra-aortic balloon pump (IABP) inserted, then it was removed after his hemodynamic stabilized. However, along with renal function decrease, a distinct lung parenchymal shadow and hypoxemia were confirmed. Therefore, respiratory management began, including the administration of anti-biotics and continuous dialysis. The parenchymal shadow and hypoxemia temporarily improved, then a prominent lung shadow was again detected. MRSA (methicillin-resistant staphylococcus aureus) was detected in the patient's sputum, which led to an administration of vancomycin hydrochloride. Later, hemodynamic compromise and hypoxemia suddenly

occurred. A prominent depression of the ST segment in V4-6 of the electrocardiogram, and a mild elevation of creatin phosphokinase, CPK: 572U, appeared. A cardiac ultrasound revealed hypokinesia from the posterior portion of the septal wall to the basal posterior wall, which led to a diagnosis of a new myocardial infarction. A percutaneous coronary intervention (PCI) was performed to cure the stenosis of the left anterior descending artery (#6). After surgery, the total condition of the patient gradually recovered and he was transferred to the care of a nearby doctor on October 3.

Physical and pathological findings of the removed specimen showed the ischemic hemorrhagic ulcer (Fig. 2A) with mesenteric hematoma (Fig. 2B) due to the cholesterol embolization. Pathological findings revealed the ischemic hemorrhagic ulcer with mesenteric hematoma with CCE in small intestine (Fig. 3A) and CCE in the ileac wall vessel as well as an organic thrombus beneath the serosa (Fig. 3B).

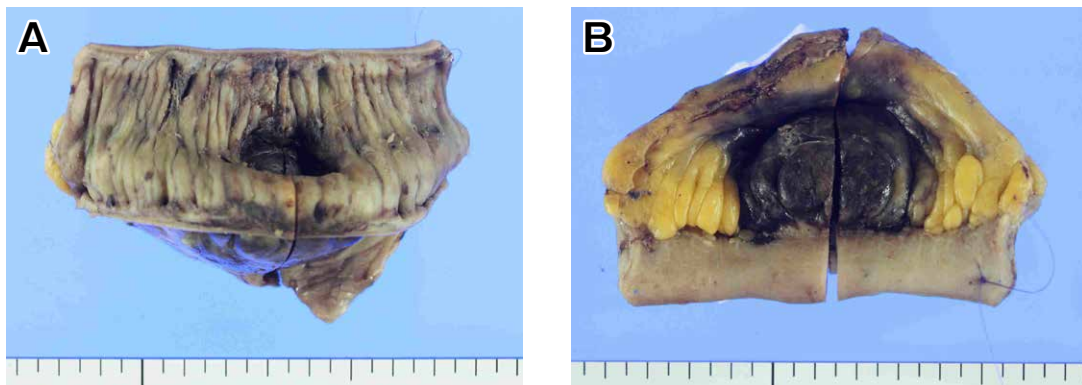


Fig. 2 Resected specimens; Ileal deep ulcer with hemorrhage (A), Hematoma in the ileal mesentery (B).

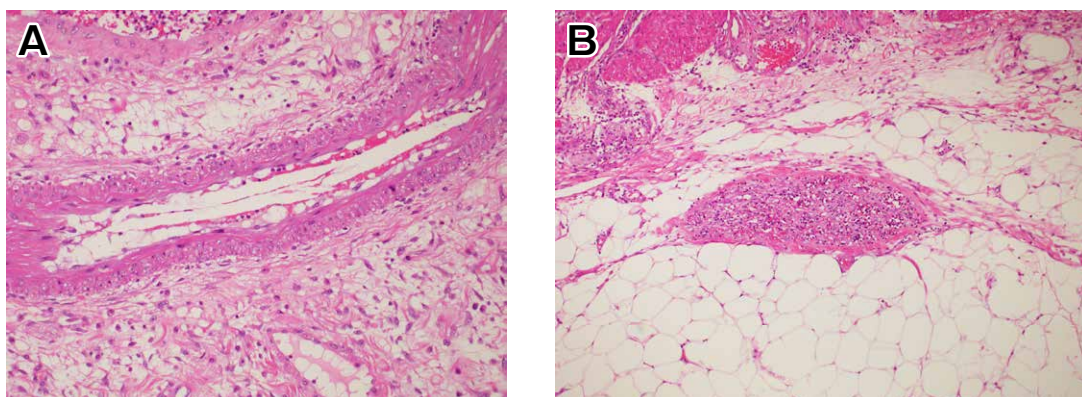


Fig. 3 Pathological findings; Small intestine showed the ischemic hemorrhagic ulcer with mesenteric hematoma due to cholesterol crystal embolization (A). Cholesterol crystal embolization in the ileac wall vessel was found as well as an organized thrombus beneath the serosa (B).

## DISCUSSION

CCE is caused by an atherosclerosis rupture in the aortic wall, with the resulting embolus of cholesterol crystals and/or microthrombi occluding a small peripheral artery<sup>1-3)</sup>. Ischemia occurs in the organs on the peripheral side due to the embolization by cholesterol crystal and the inflammation triggered by a foreign substance around the occluded region<sup>1-3)</sup>. Many cases with cholesterol embolism are often secondary, and the cholesterol embolism has been reported to occur after intravascular operations, such as cardiovascular surgery catheter operations, anticoagulant and fibrinolytic therapies<sup>1-3)</sup>. CCE is considered to be caused by a mechanical vascular occlusion from an embolus and an angitis-like

immune response of the local region<sup>1-3)</sup>. Recently, intravascular treatments to treat aortic aneurysms have been increasing, including stent-grafting and percutaneous coronary angioplasty for coronary diseases. Therefore, cases similar to the one in this case report can be expected to increase in the future<sup>1)</sup>.

The risk factors for CCE are hyperlipemia, cardiovascular disease such as hypertension, diabetes, smoking, hyperuricemia and kidney failure, which are all more likely among older men. CCE occurrence of aorta and CCE occurrence during intervention radiology of aorta are reported to be 0.08 to 0.31%<sup>1, 4)</sup>. On the other hand, there are reported cases of CCE revealed by autopsy, and

approximately half of those cases had had some kind of intravascular operation<sup>5, 6</sup>).

CCE could occur in any part of the body, such as kidneys, spleens and foot<sup>2, 5</sup>). In general, symptoms that lead to a diagnosis of CCE are kidney failure and/or skin problems. A histopathological diagnosis with a biopsy could be useful in cases with skin problems. However, this case didn't have any skin symptoms. Of the toe related symptoms, a bilateral symptom is most common and can occur suddenly. Cases with an embolus in the dorsal artery are called Blue Toe Syndrome due to the color of the toes<sup>2, 7, 8</sup>). An embolus in the pancreatic arteries often causes acute necrotic pancreatitis and an embolus in the ophthalmic arteries often leads to blindness. When an embolus occurs in an artery that controls the intestinal tract, it causes a stomachache with melena and/or abdominal cavity hemorrhage. However, it sometimes produces symptoms such as diarrhea or ileus, thus making a differential diagnosis difficult.

To treat CCE occurred in the intestine, an enterectomy is applicable for cases that have an intestinal ischemia, necrosis or bleeding<sup>8-10</sup>). Patients with a CCE often have a condition such as hypertension, arterial sclerosis or diabetes, which require special attention due to possible complications. There is no report of an effective treatment that can dissolve or remove the thrombotic cholesterol crystal. Most treatments are conservative and intended to maintain organ function and to reduce pain while collateral circulation develops<sup>7-10</sup>). Plasmapheresis and hemodiafiltration can sometimes be used, however they haven't been proven to be effective enough. Antiplatelet drugs are sometimes administered to prevent a new thrombus and prostaglandin is administered to improve circulation. There is a report stating that anticoagulant treatment with heparin or warfarin could accelerate the development of an embolus<sup>11</sup>). Despite of all these treatments, the prognosis of this

disease is very poor with a fatality rate as high as 80%<sup>1, 7-10</sup>).

## CONCLUSION

This is a case report of CCE that occurred secondarily during intravascular treatment. Cases are expected to increase due to an increase in intravascular treatments. Therefore, it is important to be knowledgeable about the clinical conditions, diagnosis decision process and therapy options to treat this disease. Careful observation is indispensable if a patient was just treated with catheter therapy or is in the middle of an anticoagulant treatment.

## REFERENCES

- 1) Toya N, Baba T, Kanaoka Y, Ohki T: Embolic complications after endovascular repair of abdominal aortic aneurysms. *Surg Today* 44: 1893-1899, 2014
- 2) Devy L, Brunet-Possenti F: IMAGES IN CLINICAL MEDICINE. Cholesterol Embolization after Transcatheter Aortic-Valve Replacement *N Engl J Med* 15: 375(11): e25, 2016
- 3) Fujiyama A, Mori Y, Yamamoto S, *et al.*: Multiple spontaneous small bowel perforations due to systemic cholesterol atheromatous embolism. *Intern Med* 38: 580-584, 1999
- 4) Caron F, Anand SS: Antithrombotic therapy in aortic diseases: A narrative review. *Vasc Med* 22: 57-65, 2017
- 5) Ueda M, Fujimoto T, Ogawa N, Shoji S: An autopsy case of cholesterol embolism following percutaneous transluminal coronary angioplasty and aortography. *Acta Pathol Jpn* 39: 203-236, 1989
- 6) Turnbull RG, Hayashi AH, McLean DR: Multiple spontaneous intestinal perforations from atheroembolism after thrombolytic therapy: a case report. *Can J Surg* 37: 325-328, 1994
- 7) Roque Castellano C, Marchena Gómez J, Hernández Navarro JA, Hernández Romero JM: Perforation of the small intestine due to cholesterol embolism. *Gastroenterol Hepatol* 28: 362-363, 2005
- 8) Blair NP, Hayes GW: Perforation of the small bowel: a case report. *Can J Surg* 38: 281-282, 1995
- 9) Jimenez-Heffernan JA, Martinez-Garcia CM, Sanchez

- MA, Jimenez C, Perna C, Burgos E: Small bowel perforation due to cholesterol atheromatous embolism. *Dig Dis Sci* 40: 481-484, 1995
- 10) Amendolara M, Carpentieri L, Balbi T, D'Elia A, Perri S, Baldon S, Farruggio A, Biasiato R: Two cases of small bowel ischemia due to unusual cause. *Minerva Chir* 59: 517-522, 2004
- 11) Mooney T, Joseph P: Purple toes syndrome following stroke thrombolysis and warfarin therapy. *Intern Med J* 44: 107-108, 2014