Acute type B aortic dissection with multiple cholesterol embolism: an autopsy case report

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Background	Most cases of cholesterol embolism are known to be triggered by cardiac catheterization, cardiovascular surgery, anticoagulation, or fibrinolytic therapy; however, spontaneous cases after aortic dissection are rare. In this report, we describe a case of cholesterol embolism after type B aortic dissection, which rapidly developed into multiple organ failure and death.
Case summary	A 65-year-old man with untreated hypertension was admitted to our hospital with sudden back pain and diagnosed with type B aortic dissection. The patient experienced a rapid progression of inflammation and developed respiratory and renal failure, despite computed tomography showing no obvious progression of dissection. We attributed them to a cytokine storm and acute respiratory distress syndrome, but steroid pulse therapy did not alleviate the symptoms. Finally, the patient died on Day 6 after admission, and an autopsy was performed, which revealed cholesterol crystal occlusions in the kidney, spleen, and the left lower leg. The lumen in the aorta is filled with atheroma and thrombus, and we suspect that aortic dissection triggered failure of the aortic plaques and released cholesterol crystals to distal arteries that led to cholesterol embolism.
Discussion	We experienced a patient with a type B aortic dissection that led to cholesterol embolism and rapid progression of respiratory and renal failure, resulting in death. The aortic dissection combined with cholesterol embolism was considered to trigger the subsequent severe inflammation, leading to rapid respiratory and renal failure. Our case points to the possibility that cholesterol embolism can extensively escalate inflammation after aortic dissection.
Keywords	Cholesterol embolism • Acute type B aortic dissection • Autopsy • Case report
ESC curriculum	9.1 Aortic disease • 2.1 Imaging modalities • 8.2 Arterial hypertension

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Learning points

- Spontaneous cases of cholesterol embolism after aortic dissection are rare.
- Cholesterol embolization triggered by aortic dissection can arouse subsequent severe inflammation, leading to acute renal and respiratory failure, resulting in death.
- We should be aware of the possibility of cholesterol embolization after aortic dissection even if skin biopsy is negative and attempt anti-inflammatory therapy as much as possible.

Introduction

Cholesterol embolism occurs when cholesterol crystals from a proximal arterial wall plaque embolize into peripheral small- and medium-sized blood vessels, resulting in organ damage due to physical embolization and inflammatory mechanisms. The reported incidence of clinically evident cholesterol embolism is 0.09–2.9%.[1–3] However, it is believed that many cases remain undiagnosed in practice, given the higher rate of diagnosis through autopsy. Risk factors include male gender, age, hypertension, diabetes, dyslipidaemia, smoking, cardiovascular surgery, inflammation, and anticoagulant therapy.[1] While most cases are triggered by invasive procedures such as cardiac catheterization or cardiovascular surgery, spontaneous cases after aortic dissection are rare.[1,4] Subjective symptoms vary depending on which organ is affected, but systemic constitutional symptoms such as fever, fatigue, anorexia, weight loss, and myalgia are frequently observed during the course of cholesterol embolism. Common inflammatory markers, such as elevated white blood cell count, increased erythrocyte sedimentation rate, elevated C-reactive protein, decreased serum complement levels, and elevated eosinophils can be seen in clinical tests. Nevertheless, these are not specific symptoms or findings for cholesterol embolism syndrome, and the definitive diagnostic method is pathological tissue diagnosis through biopsy.[5] Treatment options include corticosteroids, lipid-lowering therapy (such as statins and LDL apheresis), and dialysis, but treatment remains empirical due to limited evidence and the prognosis is generally considered poor.[6] However, the prognosis of cholesterol embolism following aortic dissection is unclear as there have been only two reported cases, both of which were non-fatal.[7,8]

In this report, we describe a suggestive case of cholesterol embolism after type B aortic dissection, which rapidly developed into multiple organ failure and death.

Summary figure

Case presentation

A 65-year-old man with untreated hypertension and a history of smoking was admitted to our hospital with a chief complaint of sudden back pain. He had undergone regular check-ups but had no history of taking any oral treatments, including antihypertensive or anticoagulant medications. Furthermore, he had never been diagnosed with aortic aneurysm or cardiovascular disease, nor had he ever undergone any invasive procedures such as catheterization. At the time of admission, his blood pressure was markedly elevated at 237/149 mmHg, and there was a livedo in the left lower limb, but no apparent heart murmurs or rales were noted. Blood tests showed a mildly elevated C-reactive protein of 0.45 mg/dL (normal range: ≦0.30 mg/dL) and an elevated D-dimer of 12.5 µg/mL (normal range: <1.0 µg/mL) (*Table 1*). Contrast-enhanced computed tomography (CT) showed a type B dissection with a patent false lumen from the distal aortic arch to the abdominal aorta. The arteries to the major organs including the kidneys were all derived from the true lumen, and no obvious occlusion was detected. However, we confirmed bilateral heterogeneous contrast-impaired areas in the kidneys on contrast-enhanced CT (*Figure 1*). After the patient was admitted to the intensive care unit, antihypertensive therapy and heart rate control with intravenous nicardipine 4.3 µg/kg/min and transdermal bisoprolol 4 mg were initiated immediately along with mild sedation. On the second day, as the back pain worsened again, blood pressure rose with decreased oxygenation. We again performed contrast-enhanced CT which showed no obvious progression of aortic dissection but only pleural effusion and atelectasis. Hypotension and decreased oxygenation occurred, leading to invasive mechanical ventilator management. The cause of the rapid respiratory failure and worsening inflammatory reaction could not be identified. The patient was treated with methylprednisolone pulses 500 mg/day for 3 days, based on the hypothesis that the patient had a cytokine storm associated with inflammation of the aortic dissection itself. We also suspected the coexistence of cholesterol embolization

A 65-year-old man was admitted due to type B aortic dissection, but the development of cholesterol embolism caused rapid worsening of inflammation, leading to progressive respiratory and renal failure, ultimately resulting in death.
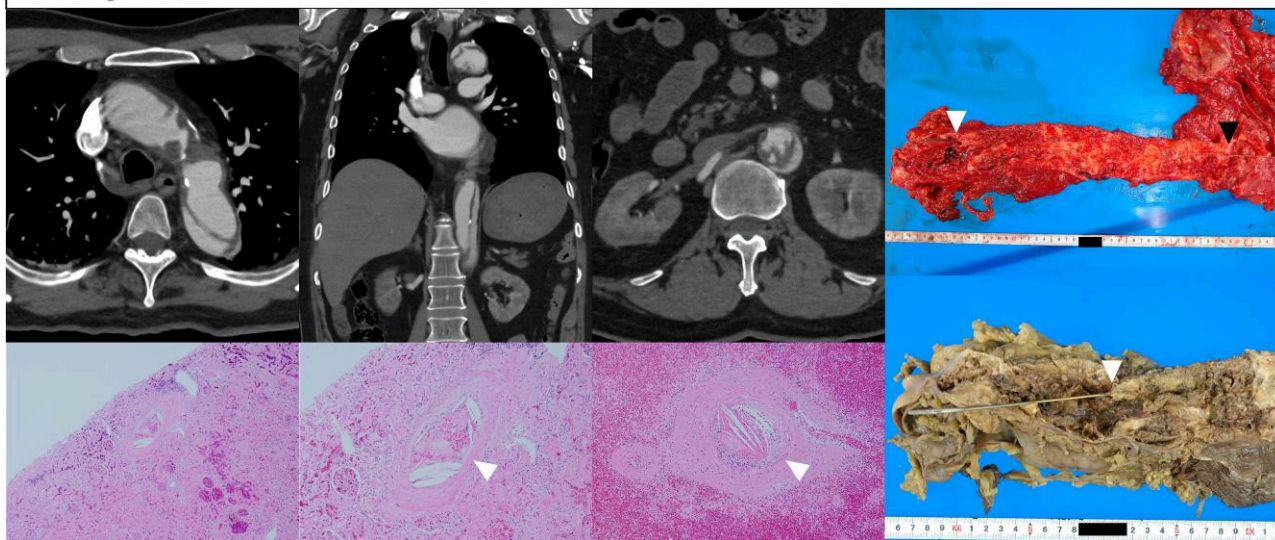
Table 1 Patient laboratory test results

Test item (unit) (normal range)	Date (+time)						
	Day 1	Day 2 (6:00)	Day 2 (12:00)	Day 3	Day 4	Day 5	Day 6
AST (U/L) (13–30)	35	91	87	177	3440	7260	6340
LDH (U/L) (124–222)	345	459	476	617	3880	7120	8836
Creatine kinase (U/L) (59–248)	97	2886	2366	4969	11,414	39,580	50,600
White blood cell (/μL) (3300–8600)	7900	16,100	1400	1000	2900	8300	11,800
C-reactive protein (mg/dL) (≦0.30)	0.45	4.65	9.16	34.49	50.07	55.83	49.56
D-dimer(μg/mL) (<1.0)	12.5	14.4	31.3	13.5	10.5	14.4	20.4
BUN (mg/dL) (8.0–20.0)	12.1						
Creatinin (mg/dL) (0.65–1.07)	1.37						
Total cholesterol (mg/dL) (130–219)	247						
Triglyceride (mg/dL) (30–149)	254						
LDL-C (mg/dL) (70–139)	169						
HDL-C (mg/dL) (40–80)	43						
Glucose (mg/dL) (70–109)	127						
HbA1c (%) (4.9–6.0)	5.9						
NT-proBNP (pg/mL) (≦125)	560						
Immunoglobulin G (mg/dL) (870–1700)		704					
Immunoglobulin A (mg/dL) (110–410)		121					
Immunoglobulin M (mg/dL) (33–190)		56					
Complement 3 (mg/dL) (86–160)		70					
Complement 4 (mg/dL) (17–45)		14.4					
CH50 (U/mL) (30–45)		21					
Anti-nuclear antibody (−)		Negative					
PR3-ANCA (−)		Negative					
MPO-ANCA (−)		Negative					
Urine–protein (mg/day) (3–60)		168					
Urine–creatinin (mg/day)		298					
α1-Microglobulin (mg/L) (0.8–14.1)		130					
NGAL (ng/mL) (<30.5)		5710					

AST, aspartate aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; HbA1c, haemoglobin A1c; NT-proBNP, N-terminal pro-brain natriuretic peptide; CH50, total haemolytic complement; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasmic antibody; MPO-ANCA, myeloperoxidase anti-neutrophil cytoplasmic antibody; NGAL, neutrophil gelatinase-associated lipocalin.
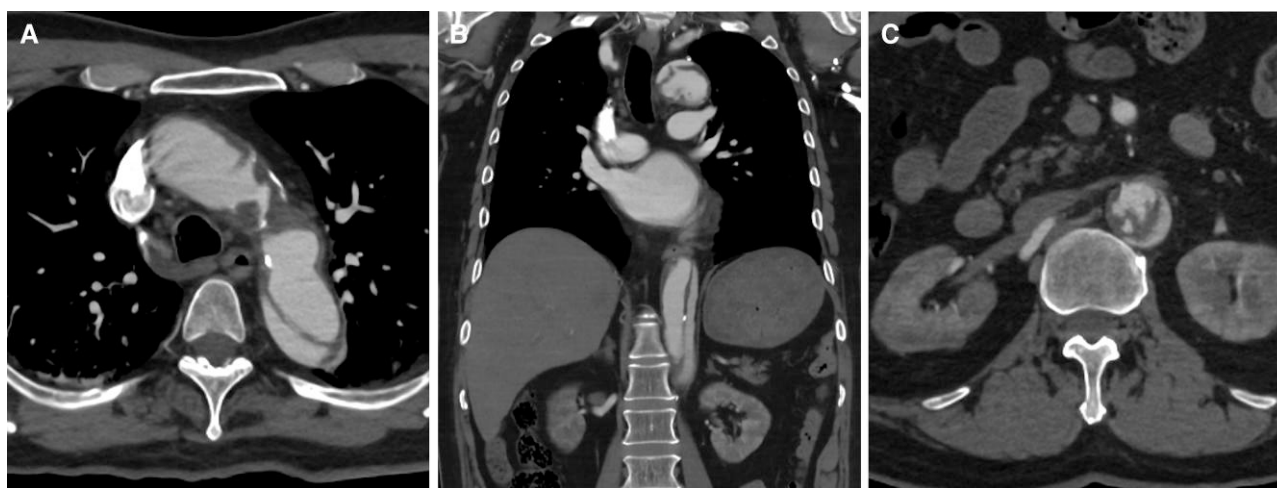

Figure 1 Arterial phase contrast-enhanced computed tomography of type B aortic dissection with a patent false lumen from the distal aortic arch to the abdominal aorta. (*A*) Axial view of the thorax showing vulnerable and irregular plaque along the aortic wall. (*B*) Coronal view. (*C*) Axial view of the abdomen showing heterogenous contrast-impaired areas in the bilateral kidneys.
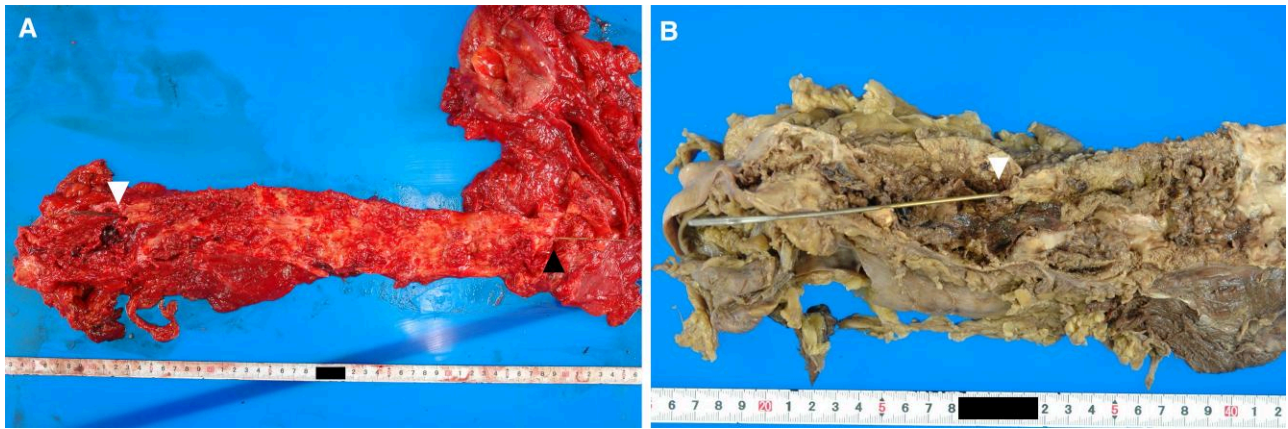
Figure 2 Pathological autopsy of the thoracic descending aorta. (*A*) Aortic dissection with the entry of the false lumen in the descending thoracic artery (upward arrow) and re-entry into the true lumen in the abdominal aorta (downward arrow). (*B*) The lumen around the re-entry (downward arrow) is filled with brown to dark reddish substances mixed with atheroma and thrombus.
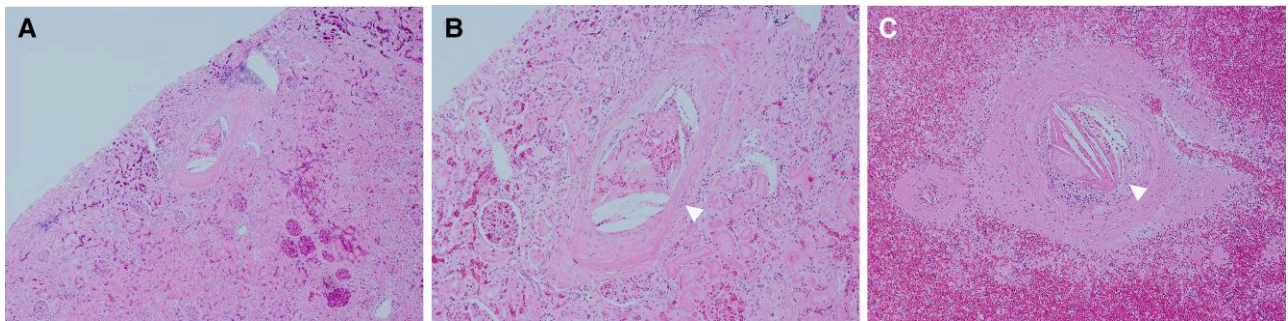

Figure 3 Histopathology of the kidney and spleen. (*A*) Glomeruli are retained in non-infarcted areas; however, tubular and glomerular structures are disrupted in some infarcted areas in the kidneys. (*B*) Cholesterol embolization in the vessels distal to arcuate arteries in the right renal cortex.(*C*) Cholesterol embolization in the spleen. Occluded vessels containing cholesterol crystals are marked with arrows in (B) and (C).

based on the livedo and the decline in complement and expected that steroid therapy would have favourable effects on both sides. We were able to perform a skin biopsy on the fifth day but could not find any obvious sign of cholesterol embolization in the skin tissue. Continuous haemodiafiltration (CHDF) was also initiated due to persistent anuria and progression of acidosis on the second day. However, the patient's condition continued to deteriorate, with worsening of multiorgan failure and unfortunately died on the sixth day. Pathological autopsy was performed, which revealed that the lumen of the aorta from the entry of the descending thoracic aorta to the re-entry of the abdominal aorta was narrowed due to thrombus and disrupted atherosclerotic plaque (*Figure 2*). In addition, the presence of cholesterol crystal occlusions in the kidney, spleen, and soft tissue arteries of the left lower leg led to the definitive diagnosis of cholesterol embolization (*Figure 3*). Moreover, the bilateral lower lobes of the lungs showed neutrophilic infiltration, pulmonary haemorrhage, and destruction of some alveolar structures, all indicative of an inflammatory response, but no obvious pathogens were detected.

Discussion

In this case, a type B aortic dissection led to rapid respiratory and renal failure and death. There are two points unique to this case. First, the cholesterol embolization was considered to have occurred as a result of aortic dissection. Previous reports have suggested that cholesterol embolization is often triggered by invasive procedures such as catheterization or surgery.[4,6] In this case, the patient had livedo in the left lower leg at the time of arrival, and the initial contrast-enhanced CT showed heterogeneous contrast poor areas in the bilateral kidneys. Therefore, it is possible that cholesterol crystals were released from the atheroma in the aorta by its dissection, which led to cholesterol embolization. To the best of our knowledge, only two cases of cholesterol embolization triggered by aortic dissection have been reported.[7,8] The current case is also valuable because it is the only one with a clear onset point.

The second unique feature is the rapid progression to death. One of the two reported cases was diagnosed with lower limb cholesterol embolism 1 month after the diagnosis of aortic dissection, and the patient

had to undergo lower limb amputation surgery.[7] The other case was initially diagnosed with cholesterol embolism, and subsequently, involvement of aortic dissection was suspected.[8] While chronic renal failure persisted after subsequent treatment, lower limb pain and skin lesions healed within several months. In both the cases, the process from diagnosis to treatment progressed with a month-long course.[7,8] However, the patient in this case died within 6 days from onset. Considering the clinical course and laboratory findings (Table 1) in our case, it is obvious that the general condition deteriorated rapidly on the second day. Since the repetitive CTs did not show any sign of the development of aortic dissection, we cannot attribute the rapid worsening of the inflammatory response to the aortic dissection itself, and it is highly likely that cholesterol embolization occurred repeatedly and accelerated the inflammation as a second attack. While the vivid laboratory findings insinuated extensive tissue necrosis, the autopsy specimens did not demonstrate occlusion of major vessels but only showed embolization of small vessels consistent with cholesterol embolization. Kronzon et al.[4] emphasize that the pathogenesis of arterio-arterial thromboembolism and cholesterol embolization is different, but it is suggested that in cases of cholesterol embolization secondary to aortic dissection, the volume and extent of embolization may become greater, which directly relates to the severity of inflammation.

In addition, the autopsy showed the signs of alveolar damage, but no pathogens or cholesterol embolization were detected in the lungs. It is known that respiratory failure triggered by aortic dissection is a common occurrence; the underlying mechanism is thought to involve activated neutrophils releasing mediators that damage the alveolar epithelium and increase vascular permeability.[9] On the other hand, as for pulmonary lesions of cholesterol embolization, Vacher-Coponat et al.[10] have reported the effectiveness of steroids for pulmonary haemorrhage and acute renal failure, suggesting alveolar injury via an immunologic mechanism. Furthermore, cholesterol embolization is thought to cause end-organ damage through subsequent inflammation rather than acute organ ischaemia, and the mechanisms include activation of the NLRP3/IL-1 pathway, leucocyte infiltration, complement activation, and activation of the renin–angiotensin–aldosterone system.[11] Similarly in this case, the alveolar damage seemed to be induced by severe systemic inflammation, but as both aortic dissection and cholesterol embolization can cause respiratory failure via an inflammatory response, it is difficult to completely distinguish between the two conditions. It is considered that in this case, cholesterol embolization triggered by aortic dissection caused acute ischaemia reflected in lactic acidosis and acute renal failure and aroused severe subsequent inflammation that was not responsive to steroid pulse therapy, leading to multiple organ failure and death.

Conclusion

In this case, we experienced a patient with a type B aortic dissection that led to cholesterol embolization and rapid progression of respiratory and renal failure, resulting in death. Cholesterol embolization may be a key trigger for induction of severe inflammation after aortic dissection, and it is important to suspect the possibility in future cases. However, the frequency of its occurrence, mechanism, and treatment have not been established; thus, further cases need to be accumulated.

Lead author biography
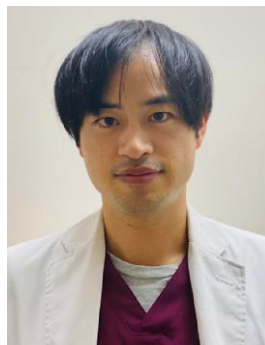
I have finished senior resident course at NTT Medical Center Tokyo. From April 2022, I have started working as a PhD student at the University of Tokyo Hospital.

Data availability

The data underlying this article are available within the article.

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