

A penetrating atherosclerotic ulcer rapidly growing into a saccular aortic aneurysm during treatment of leukaemia: a case report

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Background

The clinical course of penetrating atherosclerotic ulcers is variable and can be complicated with intramural haematomas, dissection, pseudoaneurysms, or aortic rupture. Because it can lead to life-threatening conditions, it needs to be managed carefully.

Case summary

A 68-year-old woman, who was treated for acute myeloid leukaemia (subtype: M0-FAB) approximately 1 year before presentation, visited the hospital with complaints of a headache and lumbar pain. After hospitalization, investigations revealed miliary tuberculosis. On the same day, she developed a Stanford type A acute aortic dissection (AAD) with cardiac tamponade; during the course of the previous leukaemia treatment, a small ulcerative lesion at the distal aortic arch grew into a small saccular aortic aneurysm (SAA) that expanded rapidly and finally developed into a Stanford type A AAD. However, the relationship between the SAA and aortic dissection could not be confirmed.

Discussion

The chronological changes in the atherosclerotic lesion at the distal aortic arch could be clearly observed because computed tomography scans were repeatedly obtained until just before the onset of AAD. The rapid progression of atherosclerotic lesions in the unique context of leukaemia treatment and miliary tuberculosis was considered to be a pathological characteristic, and the mechanism underlying this process was investigated. Clinicians should be aware of the aortic complications that may progress under special circumstances, such as anthracycline use or immunodeficiency. Careful observation is mandatory for patients with aortic disease.

Keywords

Penetrating atherosclerotic ulcer • Aortic aneurysm • Aortic dissection • Leukaemia • Tuberculosis • Case report

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Learning points

- Penetrating aortic ulcer progression could lead to a saccular aortic aneurysm (SAA).
- Aortic plaques and pre-existing aortic aneurysms should be carefully evaluated because aortic lesions may progress to life-threatening conditions due to anthracycline use and concomitant infections.
- In case of uninfected aneurysms, surgical approaches such as thoracic endovascular aortic repair should be promptly considered because a progressive SAA can often rupture.

Introduction

A penetrating atherosclerotic ulcer (PAU) is an ulcerating lesion that penetrates the internal elastic lamina and allows haematoma formation within the aortic medial wall.¹ PAUs occur in advanced atherosclerotic lesions; therefore, they are more common in elderly individuals with increased cardiovascular risk. Their clinical course is variable and can be complicated by intramural haematomas, dissection, and pseudoaneurysms. If an ulcerative lesion breaks through the adventitia, it might lead to aortic rupture² and a life-threatening condition; therefore, PAUs should be managed carefully.

We describe a case of PAU that rapidly developed into a saccular aortic aneurysm (SAA). The aortic lesion progressed during chemotherapy for leukaemia and was finally complicated by Stanford type A acute aortic dissection (AAD).

Timeline

10 months before	1st hospitalization Diagnosis of acute myeloid leukaemia (AML) with an M0-FAB classification (Figure 1A) Remission induction therapy with cytarabine and idarubicin (Figure 1B and C)
8 months before	2nd hospitalization Consolidation therapy with high-dose cytarabine (Figure 1D)
6 months before	3rd hospitalization Cord blood stem cell transplantation (Figure 1E)
4 months before	End of a series of AML treatments
0 days	4th hospitalization Admission due to miliary tuberculosis (Figure 1F)
Day 6 of hospitalization	Onset of type A acute aortic dissection with cardiac tamponade (Figure 1G and H) Sequelae of hypoxic encephalopathy Conservative treatment
10 months later	End of anti-tuberculosis treatment
2 years later	Death due to unknown causes

Case presentation

Ten months prior to the most recent presentation, a 68-year-old woman with pulmonary tuberculosis diagnosed during childhood,

diabetes mellitus, and a heavy smoking habit presented to our hospital with a high fever (39.0°C) and sore throat. Physical examination revealed pharyngeal redness and multiple enlarged lymph nodes in the neck. Detailed examinations revealed acute myeloid leukaemia (AML) of French-American-British subtype M0. Pre-treatment computed tomography (CT) revealed enlarged cervical and mediastinal lymph nodes that were suggestive of extramedullary involvement, and a PAU-like lesion in the distal aortic arch (Figure 1A). She received remission induction therapy with cytarabine and idarubicin and was discharged. However, just before discharge, CT revealed that while the enlarged lymph nodes seemed to have shrunk, the aortic lesion appeared to have eroded deeper into the aortic wall (Figure 1B and C).

Eight months prior, the patient was hospitalized again for consolidation therapy with high-dose cytarabine. At admission, unenhanced CT revealed that the aortic lesion had begun to form a convex surface against the outside, thereby developing into SAA (Figure 1D). Six months prior, she was hospitalized for a third time for cord blood stem cell transplantation. Pre-transplant CT revealed further SAA enlargement (Figure 1E); however, no symptoms associated with the aortic lesion were observed during the clinical course.

Four months ago, she completed a series of AML treatments. After discharge, few inflammatory markers were noted occasionally, but no symptoms were associated with them, and they did not worsen (Supplementary material online, Figure S1). Furthermore, multi-disciplinary team review for therapeutic interventions for SAA was postponed because of severely diminished physical strength.

At the most recent presentation, the patient complained of headache and lumbar pain lasting for 1 week. Disorientation and nuchal rigidity were observed immediately after admission; therefore, a lumbar puncture was performed. Chest CT revealed miliary nodules throughout the lung fields (Figure 2), and SAA had enlarged to 12.8 × 12.1 × 11.0 mm (Figure 1F). On day 6 of hospitalization, the patient experienced sudden cardiopulmonary arrest (CPA); therefore, cardiopulmonary resuscitation was initiated, and 10 min later, she showed return of spontaneous circulation (ROSC). CT after ROSC revealed a Stanford type A AAD with a patent false lumen from the aortic root to the infrarenal abdominal aorta. Additionally, cardiac tamponade was considered to be the cause of CPA due to the accumulation of a large amount of bloody pericardial fluid (Figures 1G and 3, Videos 1 and 2). Thereafter, spontaneous circulation was maintained without invasive approaches such as pericardial drainage. Although SAA grew rapidly, previous CT findings revealed no PAU-associated complications such as intramural haematoma, peri-aortic tissue involvement, or haemorrhage. Additionally, based on the CT findings, we could not determine whether SAA was the 'entry' point of AAD.

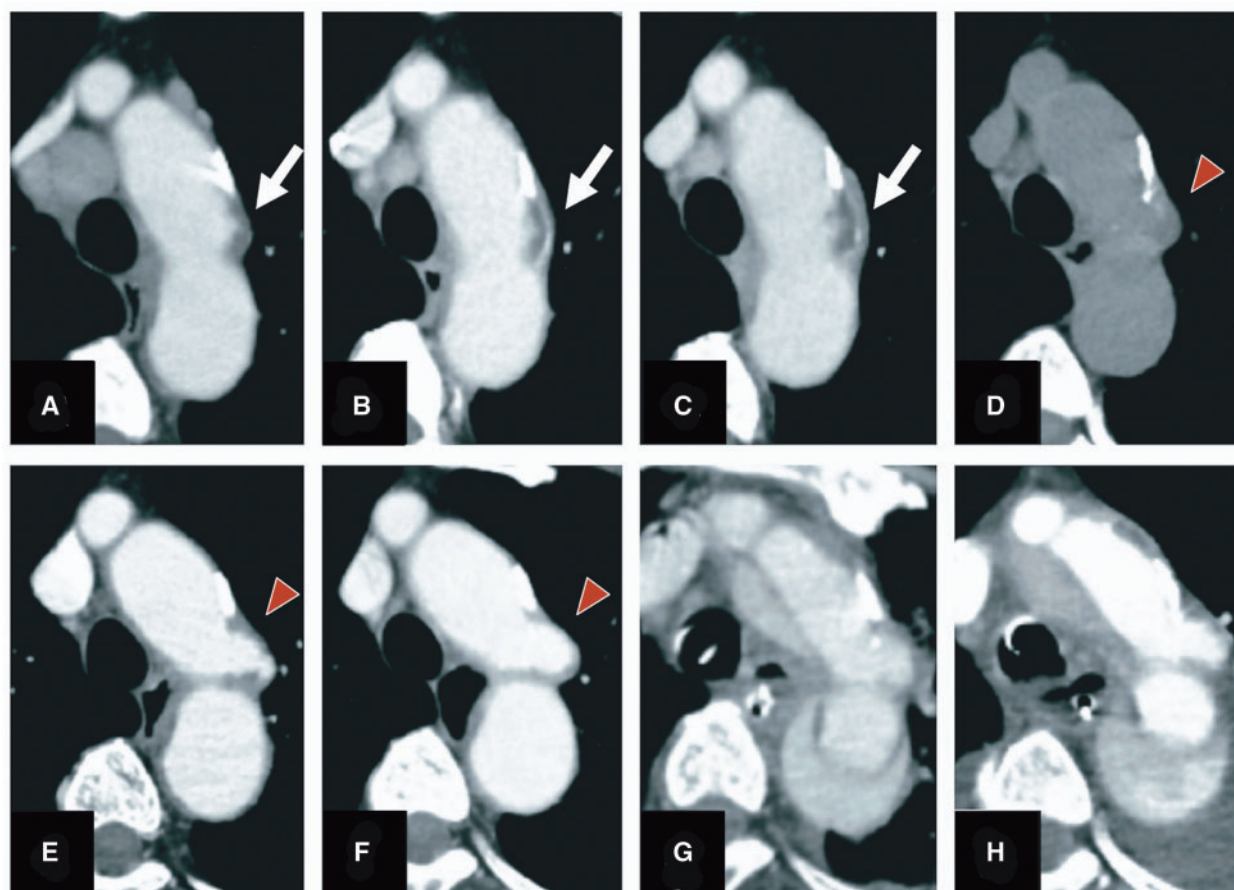


Figure 1 Axial computed tomography scans illustrating the progression of the lesion from a penetrating atherosclerotic ulcer to a saccular aneurysm in the distal aortic arch at the following time points: (A) 10 months ago (first visit), (B) 9 months ago (after remission induction therapy), (C) 8.5 months ago (at first discharge), (D) 8 months ago (before consolidation therapy), (E) 6 months ago (before cord blood stem cell transplantation), (F) 5 days before the onset of acute aortic dissection, (G) on the day of acute aortic dissection onset, and (H) 20 days after the onset of acute aortic dissection. The penetrating atherosclerotic ulcer (A–C, white arrow) in the distal aortic arch rapidly enlarged during the leukaemia treatment and formed a small saccular aortic aneurysm (D–F, red arrowhead). Thereafter, a type A acute aortic dissection (G, H) developed during disseminated tuberculosis. Computed tomography scan obtained 5 days before the onset of acute aortic dissection shows that the size of the saccular aortic aneurysm had enlarged to 12.8 mm × 12.1 mm × 11.0 mm. Iodine contrast-enhanced computed tomography scans in the arterial phase (A–C, E, F, and H) and the delayed phase (G) and an unenhanced computed tomography scan (D).

AAD was treated conservatively because her family denied emergency surgery. On the day of CPA, cerebrospinal fluid samples confirmed tuberculosis, and anti-tuberculosis treatment was initiated. During the anti-tuberculosis treatment, the patient never regained consciousness due to severe hypoxic encephalopathy. Thereafter, she was transferred to another hospital and died of unknown causes approximately 2 years after AAD onset.

Discussion

PAU is the most frequent cause of SAAs.³ In our case, chronological changes in the atherosclerotic lesion could be clearly observed because CT was performed repeatedly until just before AAD onset.

While CT findings suggested that PAU was the underlying cause of SAA, the rapid growth of the aortic lesion may have been facilitated by unique leukaemia-related circumstances.

The first of these circumstances involves the effects of immunodeficiency. In haematological malignancies, the malignancy itself, chemotherapy, and pre-treatment with haematopoietic stem cell transplantation may result in decreased macrophages and neutrophils, limiting cellular immunity. Therefore, these patients may be immunocompromised and prone to various bacterial and viral infections.⁴ Our patient had tuberculosis during childhood, and the AML itself as well as the subsequent treatment may have contributed to its recurrence, leading to miliary tuberculosis and even a tuberculous aneurysm of the aorta. Several mechanisms have been proposed to explain tuberculosis in aortic aneurysm pathogenesis, including the



Figure 2 Computed tomography scan of the chest lung window indicating miliary nodules throughout both lung fields.



Video 1 Iodine contrast-enhanced computed tomography scans of the delayed phase indicating a classic type A acute aortic dissection with a large amount of bloody pericardial fluid (axial view).

following: (i) erosion of the aortic wall by a contiguous focus, (ii) seeding of the aortic media or adventitia through the vasa vasorum or lymphatics, and (iii) direct seeding of the intima in patients with miliary tuberculosis.⁵ Additionally, the risk of infected aortic aneurysms generated by direct infection of arteriosclerotic plaques increases with age.⁶ In our case, *Mycobacterium tuberculosis* may have infected the atherosclerotic lesion, subsequently promoting SAA formation.

The second circumstance involves the effect of anthracyclines on the arterial wall. Some reports have shown that after anthracycline administration, arterial remodelling parameters (aortic distensibility, intima-media thickness, and pulse wave velocity) are affected early through the following mechanisms: (i) anthracyclines increase the formation of reactive oxygen species and induce oxidative stress, thereby increasing arterial stiffness by causing structural changes within the vascular matrix and interfering with the endothelial regulation of vascular smooth muscle tone; (ii) vascular endothelial damage diminishes



Video 2 Iodine contrast-enhanced computed tomography scans of the delayed phase indicating a classic type A acute aortic dissection with a large amount of bloody pericardial fluid (coronal view).

nitric oxide synthesis and promotes endothelial cell dysfunction, thereby increasing vascular stiffness; and (iii) anthracyclines promote inflammatory cytokine overexpression, which can cause endothelial injury.⁷⁻⁹ Therefore, in this case, idarubicin treatment during remission induction therapy may have contributed to SAA progression.

A histological diagnosis could not be established because this was a non-surgical case. Although the exact pathological condition of the aorta was unknown, the mechanisms described above could have promoted SAA formation, which then rapidly progressed during AML treatment and eventually formed a Stanford type A AAD with massive pericardial effusion. AAD can develop at the site of PAU caused by atherosclerosis; however, this is infrequent, because an association between atherosclerosis and AAD development is uncommon.¹⁰ Moreover, we could not find any report on AAD wherein SAA became the 'entry' point without an extravascular rupture. In our case, it is unknown whether SAA was the 'entry' point of AAD and whether aggressive SAA treatment, such as thoracic endovascular aortic repair, could have prevented AAD formation. However, in the absence of an aneurysm infection, such surgical approaches should be considered immediately because a progressive SAA might rupture. Notably, despite the need for a multidisciplinary team review for SAA in this case, the review was postponed due to her physical exhaustion.

In conclusion, clinicians should be aware of aortic complications that may progress under special circumstances, such as anthracycline use or immunodeficiency conditions. Careful observation is mandatory for patients with aortic lesions, such as aortic plaques or pre-existing aortic aneurysms. Greater insights into these types of cases may help improve their outcomes.

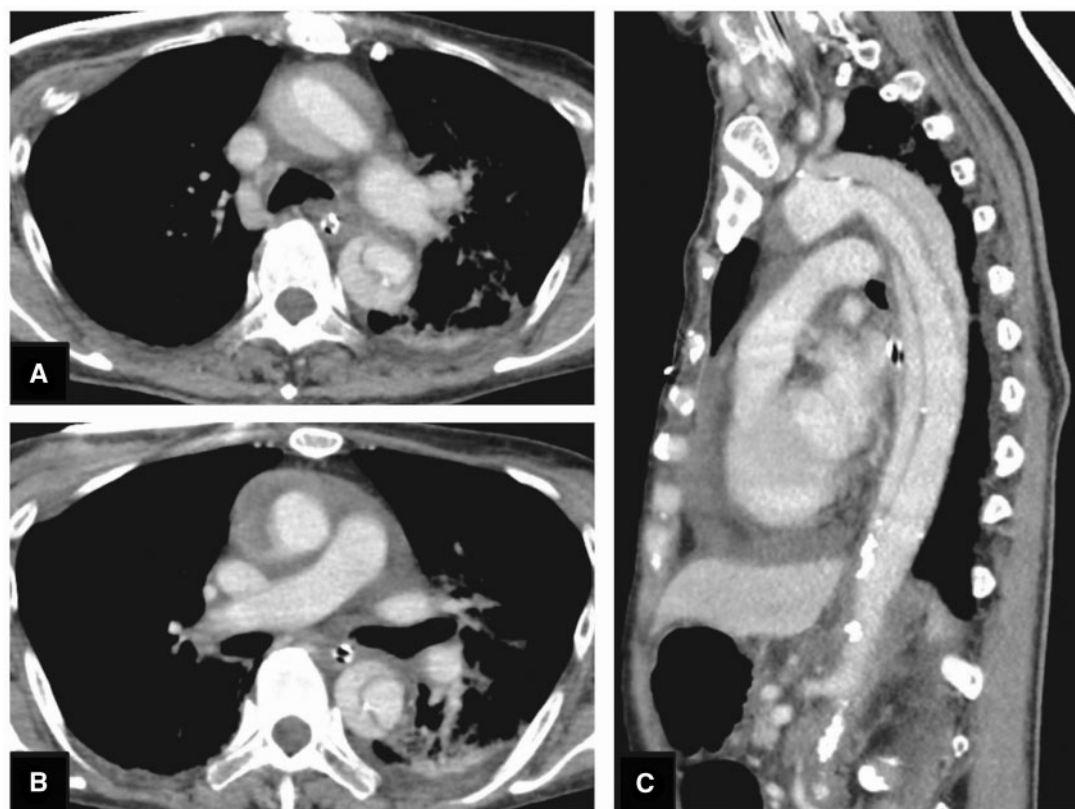


Figure 3 Iodine contrast-enhanced computed tomography scans of the delayed phase indicating a classic type A acute aortic dissection with a large amount of bloody pericardial fluid (A, B: axial view; C: sagittal view).

Lead author biography



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Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient's next-of-kin in line with COPE guidance.

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