Fatal Thoracic Aortic Aneurysm in a Patient with Childhood-onset Vasculo-Behçet's Disease: An Autopsy Report

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Abstract

A 33-year-old man died following sudden unexpected rupture of a saccular thoracic aortic aneurysm. The patient had been treated as suspicious Behçet's disease (BD) for 9 years, however, the medication was discontinued at the age of 24. Autopsy disclosed multiple aneurysms at the descending thoracic and abdominal aorta. Histopathologically, infiltration of inflammatory cells and destruction with loss of elastic and muscle fibers of the aortic medial wall were seen. Taking the clinical course into account, all the postmortem findings were compatible with those of vasculo-BD. It is important that medical follow-up should be implemented even for childhood-onset patients who do not satisfy criteria of BD.

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Key words: sudden death, post-mortem examination, aortitis, vasculitis, insidious progression

Introduction

Behçet's disease (BD) is a multisystem disease characterized by recurrent oral and genital ulcers, relapsing uveitis, mucocutaneous, articular, neurological, urogenital, vascular, intestinal and pulmonary manifestations (1). Large artery involvement is infrequent, i.e., 1.5–2.2% of all patients with BD (2), however, the specificity of vascular involvement in BD is as high as that of eye or skin lesions (3). Recently, Schirmer et al (3) suggested that failure to diagnose a BD patient with vascular manifestations could be critical for the patient's outcome and that the current criteria of BD by the International Study Group (4) may not be sufficient to support this aspect. Here we report an unfortunate patient with juvenile-onset vasculo-BD who had a recognized but untreated aneurysm in spite of the initial adequate speculation in childhood.

Case Report

A 33-year-old man was transferred to our hospital because of sudden cardiopulmonary arrest suffered at work. Twenty minutes after the onset, advanced cardiopulmonary resuscitation was commenced at our emergency department, but it was not effective.

At the age of 11, the patient complained of continuous general fatigue with low grade fever, relapsing oral aphtha, systemic arthralgia and eye discomfort. Laboratory tests showed elevated white blood cell (WBC) count, erythrocyte sedimentation rate and C-reactive protein. The symptoms fluctuated and continued. From the age of 16, the patient was treated with non-steroidal anti-inflammatory drugs for 9 years based on the tentative diagnosis of BD at the Institute of Rheumatology, Tokyo Women's University Hospital. During this period, neither ophthalmologic abnormality nor genital ulcer had been identified, and pathergy testing was negative throughout the patient's history. The criteria for BD (1) were not fulfilled at this stage. At the age of 24, the medication and medical follow-up were discontinued due to persistent improvement of symptoms and the blood inflammatory markers without any steroid treatment. Subsequently, the patient had apparently been well, and an abnormality of the descending aorta in the chest X-ray photograph (CXP) (Fig. 1A) was first pointed out at his company's physical checkup at the age of 30. Further examination for CXP abnormality had never been performed in spite of the cautions given him annually. Although the patient had reported having intermittent back pain to his family approximately one year before his death, he did not visit any hospital for further examination. The patient was a highly-skilled worker and performed his job up until the time of his death.

Autopsy was performed 17 hours after death. Massive hemorrhage of 2.6 l was found in the left pleural space, and the left lung was completely collapsed. The origin of the hemorrhage was a ruptured saccular aneurysm of the thoracic descending aorta (Fig. 1B). The maximal length and diameter of the thoracic aneurysm were 19 and 8 cm, respectively. A protruding dome-like formation was seen at the site of the aneurysm (white

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A

B

Figure 1. Chest X-ray (A) and gross photographs of autopsied heart and thoracic aorta (B). A: This image was obtained one year before death. Shadow of the descending aorta is obviously protruding into the left mid-lung field. B: The thoracic aneurysm is identified from the top of the arch to 19 cm distal (black arrows) to the descending thoracic aorta with a maximum diameter of 8 cm. There is a ruptured slit on the top of dome-like protrusion of the aneurysm (white arrows). Another aneurysm is identified at the abdominal aorta (asterisk). The intima of the entire aorta is rough-surfaced, irregularly thickened and wrinkled.

arrows in Fig. 1B), and a torn slit was identified at the top of the dome. Another saccular aneurysm was additionally identified at the abdominal aorta just below the diaphragm, and it was anatomically apart from the thoracic aorta (skipped lesion) (asterisk in Fig. 1B). The aneurysm was filled with a thick thrombus showing a lamellar structure on sectioning. The intimal surface of the entire aorta was rough and wrinkled indicating scarred aortitis. Histopathologically, nonspecific chronic mesoaortitis was the general feature; mild to moderate lymphocytic infiltrate was mainly seen in the outer media and the adventitia, especially around the vasa vasora and it resulted in destruction of the medial elastic lamina and smooth muscle cells (Fig. 2A). Severe medial destruction was likely the cause of aneurysm formation. Fibrous thickening of the adventitia was marked. The intima showed irregular fibrous thickening with hyalinization and foci of atherosclerotic change. Focally,

more active aortitis was diagnosed due to the intense infiltration of lymphocytes and neutrophils and the presence in the outer media of granulomatous inflammation, where collections of multinucleated giant cells were noticed (Fig. 2B, C, D).

In the tissues of the kidneys, heart, hepatic artery branches and the intima of the aorta, amyloidotic deposition was identified. Since the amyloid protein was sensitive for KMnO_4 pretreatment, it was considered to be secondary amyloidosis.

Discussion

The histopathological characteristics in the present patient were compatible with an earlier study of vasculo-BD (5). Taking the clinical course and autopsy findings into account, the patient was diagnosed as vasculo-BD with childhood-onset, although granulomatous aortitis with giant cells of the present

Figure 2. Histopathology of the aorta. A: Low magnification of chronic aortitis. Fibrous thickening with wrinkles of the intima (I), irregular patchy loss of the elastic lamina of the media (M) and marked fibrosis of the adventitia (A) are noted ($\times 5$). B–D: Chronic active aortitis. Note intense chronic inflammatory infiltrate mainly in the media and adventitia. Several foci of granulomatous inflammation are noticed accompanied by destruction of elastic fibers of the media. A multinucleated giant cell is shown (D, arrow). All images are stained with Victoria Blue-Hematoxylin Eosin. I: intima, M: media, A: adventitia.

patient was histologically indistinguishable from Takayasu's aortitis. The unfortunate course of the present patient highlights several important problems. Recently, Krause et al (6) discussed the clinical features of BD in childhood-onset in comparison with adult-onset disease. Their study showed that the genital ulcers and uveitis were less common among major symptoms in childhood-onset BD than in adult-onset, as was the case with the present patient. All the patients analyzed in their study (6) fulfilled the conventional criteria (1), and patients with childhood-onset BD in the general population may not be immediately diagnosed due to incompleteness of criteria. By evaluating the severity scales in childhood- and adult-onset disease, it was concluded that the children with BD had a significantly lower activity index of disease compared with adults (6). In contrast, Yazici et al (7) evaluated the clinical disease activity in patients with BD, and the authors stated that young males

(disease onset, i.e. under 25 years old) were associated with more severe symptoms. Furthermore, vascular involvement in BD usually develops insidiously in both adults and children, and the insidious course leads to a delayed diagnosis (8). These lines of evidence certainly suggest the difficulty of diagnosis and management of BD especially with childhood onset. As for the present patient, medical follow-up was discontinued at the age of 24 without any advisory explanation regarding recurrence despite the initial thorough diagnosis. The present patient and his parents were not aware of the recurrence of disease despite cautions by doctors for CXP screening at his company's physical. Vascular involvement progressed insidiously. Amyloid deposition in the kidneys and other organs likely indicates persistent subclinical inflammatory activity (9). A different outcome may have been expected if an adequate explanation about recurrence had been given when his medica-

tion was discontinued. In 1999, Schirmer et al (3) proposed the need for additional criteria to establish an early diagnosis of BD in order to adequately survey the patients with large vessel disease such as the present patient. Mignogna et al (10) also described three atypical patients with minor symptoms of BD who did not fulfil the ISG criteria, and the authors suggested a revised criteria for BD with more focus on the minor symptoms. Clinical evaluation of this issue is necessary as previously proposed (11), and all clinical physicians should be reminded of the difficulty diagnosing and managing BD. Even when improvement of the symptoms and laboratory data are seen, careful explanation of the possible recurrence of disease activity is necessary.

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