—Case Reports—

Acute Aortic Dissection Associated with Cystic Medial Necrosis of Unknown Etiology

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Abstract

A 61-year-old man without a Marfan-like phenotype was admitted to the hospital because of acute Stanford type A aortic dissection. The patient underwent surgical repair with total arch replacement. Histological examination of the excised aorta showed a connective tissue abnormality, which could have contributed to the development of aortic dissection. The cause of the connective tissue abnormality could not be determined through physical examination. Recently, however, many novel gene mutations have been found to be related to aortic diseases that do not always produce physical signs and symptoms. In this case, unknown causes of connective tissue abnormalities might be existed.
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Key words: aortic dissection, connective tissue abnormality, gene mutations

Introduction

Although the exact cause of acute aortic dissection has not yet been determined, several predisposing factors are known. Aortic dissection is one of a known manifestation of connective tissue disorders (CTDs). CTDs are associated with connective tissue abnormalities, such as cystic medial necrosis (CMN) and elastic fiber degeneration; Marfan syndrome and Ehlers-Danlos syndrome are well known CTDs. Recently, the causes of CTDs have been further elucidated as genetic analysis has improved. However, all causes of CTD are not known, and novel gene mutations are often nonsyndromic. Here we report on a patient with acute aortic dissection and aortic CMN of unknown cause.

Case Report

A 61-year-old man was brought to the emergency department because of acute Stanford type A aortic dissection. He had undergone surgical removal of the

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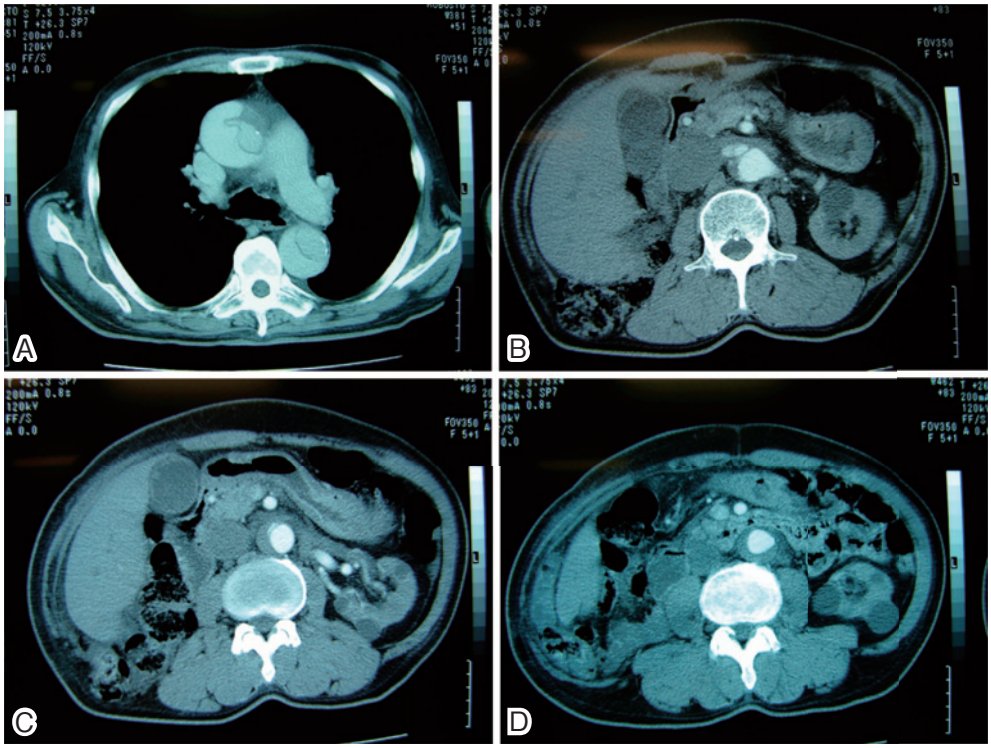

Fig. 1 **A**: CT on admission showed acute type A aortic dissection extending from the aortic root to the level of the infrarenal arteries. **B–D**: CT also revealed 5 or more cysts in the left kidney.

right kidney because of renal tumors at age 52 years, and had a 3-year history of hemodialysis and a 13-year history of hypertension that had been treated with multiple medications but had recently been well controlled. There was no documented family history of aortic or renal disease. Two days before admission, he had complained to his physician of severe back pain of sudden onset and had been given nonsteroidal antiinflammatory drugs. The back pain was alleviated, but he had returned to find its cause and underwent a computed tomography (CT). A CT scan showed acute type A aortic dissection extending from the aortic root to the level of the infrarenal arteries (**Fig. 1A**). CT also revealed at least 5 cysts in the left kidney (**Fig. 1B–D**). Although autosomal dominant polycystic kidney disease (ADPKD) was suspected, it could not be diagnosed on the basis the ultrasonographic diagnostic criteria[1], because the CT performed before the right kidney was removed had shown only 2 cysts in each kidney.

At presentation, the patient had no pain but had hypertension (blood pressure: 180/100 mmHg). He had not had a Marfan-like phenotype, hypertelorism, bifid uvula, or aortic branch aneurysm, which are characteristics of Loeys-Dietz syndrome[2]. Sleep apnea was not detected during hospitalization. Five days after the onset of aortic dissection when the pain started, the patients underwent surgical repair with total arch replacement. However, the patient

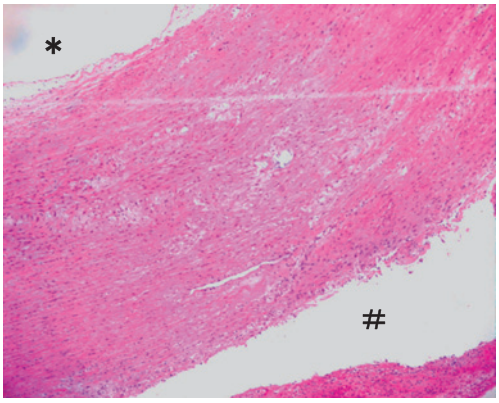

Fig. 2 Low-power view of dissected aorta with hematoxylin and eosin stain. Note the absence of intimal atherosclerosis. (*: Aortic true lumen. #: Dissected pseudolumen. magnification ×4)

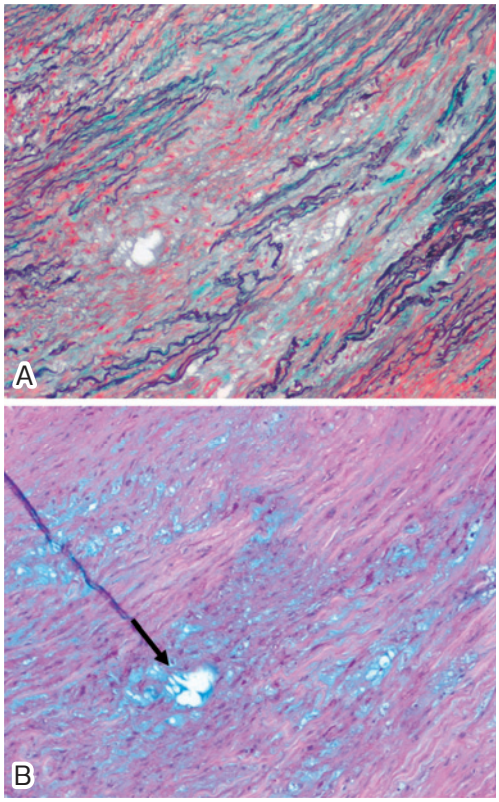

Fig. 3 (A) High-power view of the section shown in Figure 2 with Elastica-Masson Goldner stain. Elastic fibers of the aortic media are torn or degraded (magnification ×10); (B) CMN. The same view as in (A) with Alcian-blue periodic acid-Schiff stain showing mucoid degeneration and small cystic changes **(arrow)**. (magnification ×10)

died of poor control of bleeding 6 days after the onset of aortic dissection. Histological examination of the excised tissue from the dissected aorta showed connective tissue abnormality characterized by elastic fiber discontinuity with mucoid degeneration and sparse distribution of smooth muscle cells without obvious atherosclerosis, which is termed CMN **(Fig. 2, 3)**.

Discussion

The mechanism of acute aortic dissection is poorly understood. In general, some factors related to the development of aortic dissection are known and can be divided into 3 groups: (1) chronic diseases or conditions, (2) diseases based on a specific pathological background, and (3) trauma or iatrogenic factors. The chronic diseases and conditions include hypertension, obstructive sleep apnea, pregnancy, collagen disease, and steroid use, aging with atherosclerosis, and aortic aneurysm. Diseases based on a specific pathological background include CTDs such as Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome, ADPKD, Takayasu arteritis, Behcet's disease, and giant cell arteritis. Conditions causing acute aortic dissections are shown in **Table 1**.

Table 1 Conditions causing aortic dissection

Chronic disease or condition
Hypertension
Obstructive sleep apnea
Pregnancy
Aging/Atherosclerosis
Coexisting aortic aneurysms
Collagen disease
Steroid use
Cocaine abuse/Amphetamine abuse
Diseases based on a specific pathological background
Marfan syndrome
Ehlers-Danlos syndrome
Loeys-Dietz syndrome
Bicuspid aortic valve
Autosomal dominant polycystic kidney
Renal cysts
Takayasu arteritis
Giant cell arteritis
Behcet's disease
Trauma or iatrogenic factors

The etiology of CTD has been elucidated by advances in genetic analysis. Mutations in *FBN1* have been known since 1991 to cause Marfan syndrome[3]. Loeys-Dietz syndrome was first called Marfan syndrome type II in 2004[4], and the responsible gene mutations were finally determined in 2005 to be associated with *TGRBR1* and *TGFBR2*[2]. Subsequently, other novel gene mutations related to aortic diseases were found and have included *ACTA2*[5], *MYH11*[6], and *SLC2A10*[7]. However, not all gene mutations causing CTD have been identified. ADPKD is also caused by gene mutations and is reportedly rarely complicated by aortic dissection accompanied by CMN[8].

In the present case, the patient had a 13-year history of hypertension, which was suspected to be associated with the development of the aortic dissection. Obvious physical signs reminiscent of

Marfan syndrome or a Marfan-like disease were not found in the present case; however, latent gene mutations cannot be suspected solely on the basis of physical examination because patients with gene mutations related to aortic diseases such as Marfan syndrome, Loeys-Dietz syndrome, and vascular type Ehlers-Danlos syndrome do not always have a clear syndrome. Because we detected multiple renal cysts with CT, we suspected ADPKD, which can cause aortic dissection; however, this suspicion was not supported by the previous CT findings. Nevertheless, simple renal cysts were recently reported to be associated with aortic dissection[9].

CMN was first described by Ehrdin in 1929. Classically, CMN has been regarded as the cause of aortic dissection. Recently, CMN is reportedly observed in only 8% to 19% of cases of aortic dissection in patients without Marfan syndrome and in 40% to 82% of cases in patients with Marfan syndrome[10,11]. In contrast, one study has found that 65% of patients without Marfan syndrome who have type A aortic dissection have CMN[12], suggesting that CMN may not be limited to patients with Marfan syndrome. These differences may depend on the definition of CMN. In this context, CMN is a finding that is not specific to Marfan syndrome but a finding by which we could suspect genetic abnormalities causing connective tissue abnormalities.

The possible etiology of aortic dissection in this patient could be limited to hypertension, multiple renal cysts, and the fact that the excised aorta showed connective tissue abnormalities, such as fragmented elastic fibers, mucoid degeneration, and cystic changes without obvious atherosclerosis in the medial layer, which are often observed in patients with Marfan syndrome. However, the presence of hypertension and multiple simple renal cysts are not sufficient cause for the observed pathological abnormalities. Therefore, the etiology of the connective tissue abnormality was undetermined, and genetic analysis might have shown gene mutations to be the cause of the connective tissue abnormality in this patient. However, because the patient died, and no tissue is available, genetic analysis could not be performed. We suspect that there are many patients with aortic dissection whose cause cannot be determined.

We have reported a case of acute aortic dissection with connective tissue abnormality of unknown etiology. Genetic mutations which cause connective tissue abnormalities might be existed.

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