Ann Vasc Dis Vol. 12, No. 2; 2019; pp 236–239

Online April 10, 2019
doi: 10.3400/avd.cr.19-00003

Case Report

Hypereosinophilia and Multisite Vasculopathy of Fibromuscular Dysplasia: A Case Report

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The impact of blood disorders on fibromuscular dysplasia is unknown, and cardiovascular surgery results are also unclear. Furthermore, there are only a few case reports about the association between fibromuscular dysplasia and blood disorders. We report a case of a coronary bypass surgery and an aortic root replacement for a patient who is hypereosinophilic with multisite vasculopathy of fibromuscular dysplasia, including that of the coronary artery and saphenous vein, which was diagnosed by a histopathologic examination after an autopsy was performed 5 months after surgery. The outcome of cardiovascular surgery can be unfavorable for fibromuscular dysplasia. Blood disorders may also have an impact on the outcome.

Keywords: fibromuscular dysplasia, hypereosinophilia, TGF-β

Introduction

Fibromuscular dysplasia (FMD) usually affects the renal and extracranial cerebrovascular arteries, and FMD of the internal thoracic artery, sinus of Valsalva, and saphenous vein (SV) are rare.[1–3)]

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Received: January 7, 2019; Accepted: February 8, 2019
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The impact of a blood disorder on FMD and the results of cardiovascular surgery are unclear. We report a case of an aortic root replacement and a coronary bypass surgery using SV grafts (SVGs) in a patient with hypereosinophilia and multisite FMD.

Case Report

A 41-year-old Japanese woman was referred to the cardiology department because of chest pain and ST depression in lead II, III, aVf, and V4-6 on electrocardiography. An emergency coronary angiography revealed triple-vessel disease with aneurysms in the left anterior descending artery and sinuses of Valsalva (**Fig. 1**).

Her medical history included hypereosinophilia and elevated serum immunoglobulin E (IgE), without any asthma symptoms. Twelve years ago, blood tests showed an eosinophil count of 11,000 cells/μL and an IgE of 1,217 IU/mL. The hematologist diagnosed her with idiopathic hypereosinophilic syndrome by close examination and initiated treatment using steroids and anti-allergic agents without anticancer therapy. She had been taking prednisolone and suplatast tosilate. The eosinophil count and serum IgE levels remained high during the present admission.

Preoperative examination showed the involvement of multiple systemic arteries, which were mostly affected

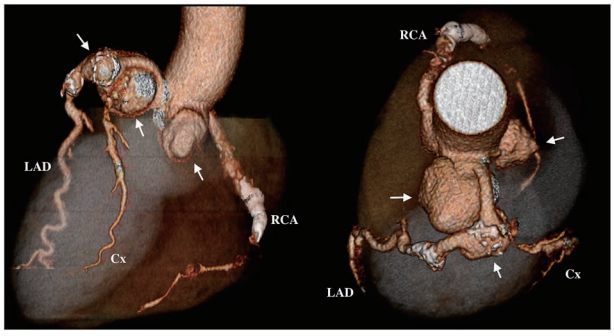

Fig. 1 Computed tomography shows aneurysms of the proximal left anterior descending artery and the Valsalva sinuses of the left coronary and non-coronary cusps (white arrows). The left anterior descending artery shows tortuosity.

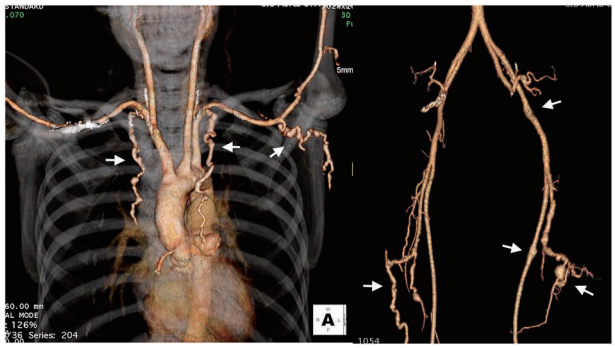

Fig. 2 A computed tomographic scan shows multiple peripheral arteries, including the internal thoracic, subscapular, external iliac, superficial femoral, and profundal femoris artery involved in the pathological change (white arrows).

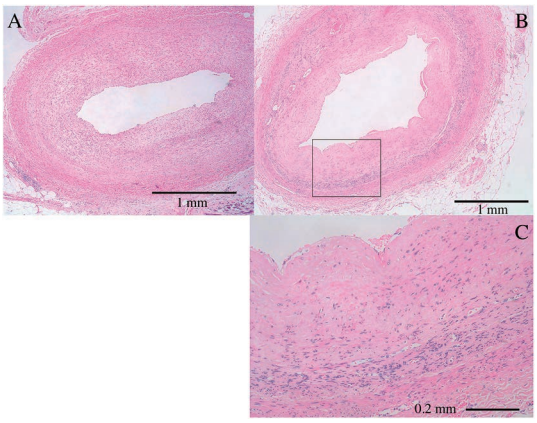

Fig. 3 Microscopic findings of the circumflex artery and saphenous vein graft showing smooth muscle cell and fibroblast proliferation without any infiltration of foam cells or inflammatory cells. Panel **A** shows the saphenous vein graft. Panel **B** shows the circumflex artery. Panel **C** shows a magnified picture of the circumflex arterial wall.

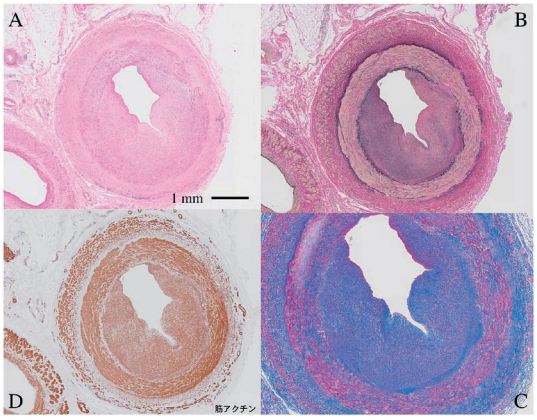

Fig. 4 Microscopic finding of the small artery near the common iliac artery. Panel **A**, hematoxylin and eosin staining; Panel **B**, Elastica van Gieson staining; Panel **C**, Masson staining; Panel **D**, immunostaining for smooth muscle actin.

bilaterally, including the internal thoracic, radial, subscapular, iliac, femoral, popliteal, and hepatic arteries (**Fig. 2**). The renal or cervical arteries were not involved. Most of the affected arteries showed multiple stenosis or aneurysms. Skin biopsy demonstrated no evidence of vasculitis, although vasculitis was suspected based on the clinical features.

She received an aortic root replacement with a composite mechanical valve graft and coronary bypass surgery with SVGs to the left anterior descending artery (LAD), diagonal branch, posterolateral branch, and posterior descending artery (PD). The SVG was abnormally thin. All the bypass grafts were patent on postoperative computed tomography (CT).

One-month post-surgery, she developed chest pain. Cardiac ultrasonography showed hypokinesis of the left anterior ventricular wall. CT showed SVG obstruction to the LAD and PD. Percutaneous coronary intervention was not considered because of the aneurysm of the LAD. Five months post-surgery, she was transferred to our hospital because of cardiopulmonary arrest. A CT scan showed widespread consolidation of both lungs and an absence of pericardial effusion. She died despite resuscitation attempts. An autopsy was performed after informed consent so that the vasculopathy could be diagnosed.

Macroscopically, both ventricles were severely dilated, and both lungs were heavy and congestive. The posterior wall of the left ventricle revealed scar tissue. The SVG to the circumflex artery was patent; however, SVGs to the LAD and PD were occluded. Microscopically, small fresh myocardial infarction was scattered in the endocardium. Small myocardial infarction, which was not acute but relatively new, was noted at the anterior and posterior walls of the left ventricle. We clinically and pathologically diagnosed the cause of death as acute heart failure due to severe myocardial ischemia. Histopathologic findings revealed smooth muscle cell and fibroblast proliferation in the intima and media of the circumflex, hepatic, other arteries, and SVG, without any infiltration of foam cells or inflammatory cells, including eosinophils (**Fig. 3**). Elastic and collagen fibers increased (**Fig. 4**). By monism, we diagnosed multisite vasculopathy due to FMD.

Discussion

Leadbetter and colleagues first reported FMD in a 5-year-old boy with hypertension and renal artery occlusion in 1938.[2] FMD is more common in young women, and Asians are less frequently affected than Caucasians.[1]

Olin et al. showed that the renal or carotid artery is affected in about three-quarters of cases, with hypertension or headaches as its most common presenting signs. Chest pain and dyspnea are found in 16.1% of cases.[2] In our

patient, preoperative examination did not show renal and carotid artery disease or angiographic findings of beading, which are characteristic of FMD. Our patient also suffered from hypereosinophilia. Accordingly, FMD was not considered, despite reduced age and absence of risk factors for coronary artery disease.

About 60% of patients with renal or cerebrovascular FMD had multisite FMD and were older than those with single-site FMD.[4] The number of affected arterial beds can increase with age and close systemic evaluation is required, especially in adult cases.

Less commonly affected arteries were involved in our patient. Olin et al. reported that the involvement of the aorta and coronary artery was 19.7% and 3.4%, respectively.[2] The radial and internal thoracic arteries, which were excluded in their report, were also affected in the present case. FMD of the internal thoracic artery has been shown in only a few case series.[3] Identification of determinants of arterial bed involvement is important for future research.[2] Such determinants may help elucidate patient-specific features of affected arterial distribution. These determinants may help us prevent organ dysfunction due to FMD, and it also may be valuable to treat patients with FMD.

Coronary bypass surgery outcomes for FMD are unclear. FMD prevalence with spontaneous coronary artery dissection (SCAD) is reported in 72–86% cases.[5] Tweet et al. reported the outcome of coronary bypass surgery for SCAD,[6] with early mortality in 1 of 20 patients and target vessel revascularization required in 6 of 20 patients. Another study reported that, of 15 bypass grafts, 11 became occluded (including 6 internal thoracic arteries and 5 vein grafts).[7] Therefore, coronary bypass surgery may not be protective. Moreover, considering the possibility of an increasing number of affected vascular beds with age and its possible genetic nature, FMD can occur de novo in arterial grafts during post-surgery.

A few case reports on the association between FMD and blood disorders are available. Odero et al. reported a 77-year-old man with infrarenal aortic FMD and monoclonal gammopathy.[8] To the best of our knowledge, this is the first case report of FMD and hypereosinophilia. The association between the pathogenesis of these diseases is unclear, although the genetic abnormality may be assumed to be one of the important factors between these diseases.

Transforming growth factor beta (TGF-β) can promote migration of smooth muscle cells and fibroblasts and accumulation of extracellular matrix.[9,10] TGF-β receptor gene mutation is reportedly associated with FMD.[2,11]

Variants of the TGF-β receptor gene may be considered to have a functional significance, and the signaling pathway of this receptor may become overactive. Eosinophils of patients with blood eosinophilia can produce TGF-β.[12] TGF-β overproduction due to hypereosinophilia and overactivation of the signaling pathway of the TGF-β receptor by mutation may have affected the poor outcome and multisite FMD, including unusual vessel involvement, although we unfortunately could not examine the TGF-β and TGF-β receptor gene. This means blocking agents of TGF-β signaling, including losartan, can be an additive therapy for patients with FMD and hypereosinophilia and might improve the clinical course of the patient.[13]

Slovut and Olin reported that FMD had been identified in the venous system, indicating a possibility of FMD occurrence in the SV.[14] Two of three SVGs in our patient were occluded during an early stage, possibly because of FMD of the SVG.

Coronary bypass surgery should be considered for patients with coronary FMD, which is amenable to other treatment options, although a suboptimal surgical outcome might be predicted.

Conclusion

The outcome of cardiovascular surgery can be unfavorable for patients with fibromuscular dysplasia. Blood disorders may also have an impact on the outcome.

Disclosure Statement

All authors declare that there is no conflict of interest.

Author Contributions

Study conception: MT
Data collection: MT
Analysis: MT
Investigation: MT
Writing: MT
Funding acquisition: none
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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