Multimodality assessment of left ventricular dysfunction in Takayasu arteritis and familial hypercholesterolaemia

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Abstract

Although left ventricular (LV) systolic dysfunction in patients suffering from Takayasu arteritis (TA) has been reported, little is known regarding the development of heart failure (HF) in these patients. We report a novel finding of active TA and familial hypercholesterolaemia presenting with severe LV dysfunction through multimodality assessments of LV systolic dysfunction.

Keywords Dilated cardiomyopathy; Takayasu arteritis; Familial hypercholesterolaemia; Vascular inflammation

Introduction

Some previous reports suggest presences of left ventricular (LV) systolic dysfunction in patients suffering from Takayasu arteritis (TA). However, little is known regarding the development of heart failure (HF) in these patients. We describe a young female patient with active TA presenting with severe LV dysfunction and HF.

Case report

A 15-year-old girl with an unremarkable prior medical history was admitted to our hospital for progressive dyspnoea and orthopnoea. She presented with hypertension (blood pressure: 159/125 mmHg) and sinus tachycardia (heart rate: 115 b.p.m.). Echocardiography showed dilated LV with a reduced ejection fraction of 15% without significant aortic valve abnormalities (Figure 1A). Right heart catheterization on admission revealed mean pulmonary capillary wedge pressure of 30 mmHg, mean pulmonary artery pressure of 40 mmHg, mean right atrial pressure of 9 mmHg, cardiac index of 1.93 L/min/m², and elevated systemic vascular resistance (SVR) of 46.8 Wood units. She was also noted to be febrile with an erythrocyte sedimentation rate (ESR) of 91 mm/h and had bilateral thickening of the Achilles tendons with an extremely high low density lipoprotein (LDL) cholesterol level of 297 mg/dL. Fluorodeoxyglucose-positron emission tomography (FDG-PET) after an 18-h fast showed high uptake in the aortic arch, right subclavian artery, and bilateral carotid arteries as well as diffuse uptake in the myocardium (Figure 1B). Uptake of fluorodeoxyglucose (FDG) was clearly distributed on the vessel walls of the aorta, which was highly suggestive of the presence of inflammation of the vessel walls (Figure 1C). Endomyocardial biopsy showed no evidence of either inflammatory cell infiltration or myocarditis, revealing only...
moderately hypertrophic myocytes and mild interstitial fibrosis (Figure 3A). Three-Tesla cardiac magnetic resonance (CMR) showed no late gadolinium enhancement, nor was there any evidence of myocardial oedema on the T2 weighted image, however, revealed a prolonged native T1 time and increased extracellular volume fraction indicating the presence of diffuse interstitial fibrosis (Figure 3B,C). No significant coronary artery involvement was detected by coronary angiography.

We diagnosed active TA according to her magnetic resonance angiography findings and elevated inflammatory markers. In addition to standard HF treatment including three anti-hypertensive medications, we started immunosuppressive therapy (prednisolone, 50 mg). Genetic analysis of the LDL receptor gene showed a deletion mutation (c.310_312delTGT/p.C104del) in Exon 3, and the same gene mutation was also detected in her mother who had hypercholesterolaemia. Therefore, we diagnosed familial hypercholesterolaemia (FH) in addition to TA and initiated aggressive statin therapy. ESR normalized after 3 months of treatment, and her LV ejection fraction gradually improved to 45% during a 12-month follow-up.

Discussion

We describe a young female patient with active TA and FH presenting with severe LV dysfunction. In addition to

Figure 1 Multimodality cardiovascular imaging. (A) Echocardiography showing left ventricular dilatation and reduced ejection fraction. (B) Fluorodeoxyglucose-positron emission tomography showing significant uptake in the aortic arch, right subclavian artery, and bilateral carotid arteries (red arrows) as well as diffuse uptake in the myocardium. (C) Magnetic resonance angiography showing dilation of the right subclavian artery and diffuse narrowing of the abdominal aorta (red arrows).

Figure 2 Fluorodeoxyglucose-positron emission tomography (FDG-PET; A) or computed tomography (CT; B) images and their merged image (C) are shown in this figure. Uptake of fluorodeoxyglucose was distributed on the vessel walls of the aorta.
standard HF treatment, immune suppression for TA and statin therapy for FH led to compensation of her HF, and subsequently, her LV systolic function was moderately improved. Both pathology and CMR detected mild interstitial fibrosis in her LV without evidence of myocarditis.

Although diffuse uptake of FDG was observed in this case, negative inflammatory cell infiltration in endomyocardial biopsy raises a possibility of non-specific uptake in the heart, suggesting a lower probability of cardiac inflammation. One possible speculation of LV dysfunction in this case is that a chronic vascular inflammation had contributed to chronically elevated afterload resulting in LV systolic dysfunction. Although previous classical symptoms of TA (fever, arthralgia, malaise, and body weight loss) were not presented, advanced vascular lesions suggest the presence of a long standing history of TA, and we also observed a marked elevation in SVR (46.8 wood units) and systemic hypertension, as previously reported in patients with TA. Mild cardiac fibrosis detected by both endomyocardial biopsy and CMR was also consistent with chronically pressure overloaded heart.

In patients with FH, lipid-driven inflammatory disorder of arterial wall is widely known. Lipid accumulation in vessel
walls provokes a local inflammatory response by oxidized lipoproteins and activated macrophages.\(^2\) Furthermore, recent studies have demonstrated that the lipid lowering therapy attenuate the degree of arterial wall inflammation,\(^3\) which is associated with decreases in inflammatory markers as C-reactive protein.\(^4\) These findings suggest the direct link between lipid accumulation and induction of local inflammation of vessel walls in patients with FH. Considering these pathological background factors and the findings in our present case, there is a possibility that chronic vascular inflammation in hypercholesterolaemia\(^5,6\) might modify disease state of TA as a trigger or as an exacerbating factor including elevation in vascular resistance. Etiologies of TA are still not fully understood, and further investigation is warranted to address the precise disease mechanism(s) and potential therapeutic targets in patients with TA complicated HF. Additionally, the fact that we could not perform the pathological analysis to confirm vascular inflammation is a limitation of this case report. Further pathological studies will be warranted to address this matter.

Additionally, prevalence of LV dysfunction in TA has not been clarified. Observational studies have reported relatively high prevalence of LV dysfunction in TA of 15–50%,\(^1,7,8\) including non-hypertensive dilated cardiomyopathies in 4–6%.\(^1,9\) Since HF symptoms may often be masked in TA patients,\(^10\) allowing underestimation of HF prevalence in TA, further larger scale clinical studies are warranted for these patients.

While multiple factors such as valvular regurgitation or coronary artery involvement are known to be related to LV dysfunction in TA, vascular inflammation resulting in chronically elevated vascular resistance may be one of the underlying pathogenesis of LV dysfunction. Elevation of vascular resistance should be considered as a possible and reversible cause of LV dysfunction in TA without myocarditis, coronary artery involvement, or valvular regurgitation. Importantly, in patients with TA, both cardiac involvement and development of HF were significant mortality predictors.\(^11,12\) The evaluation for LV function, aortic regurgitation, coronary arterial involvements, and the degree of HF should require the use of echocardiography, laboratory testing including B-type natriuretic peptide, and other conventional modalities. In patients who present HF symptoms or LV systolic dysfunction, it is also necessary to evaluate the degree of cardiac damage. Imaging by magnetic resonance may provide useful information not only about the anatomy of the aorta and major vessels without radiation exposure but also about myocardial trait in TA.\(^13\) On the other hand, it is necessary to evaluate the presence of cardiovascular inflammation for a diagnosis of TA. From this perspective, FDG-PET is a useful tool for a diagnosis of active TA and may be more sensitive than magnetic resonance in detecting segmental arterial inflammation.\(^14\) Taken together, it is worth considering multimodality assessments in cases of patients who present the development of HF and/or presence of LV systolic dysfunction even when considering their costs. Further, endomyocardial biopsy is the gold standard for diagnosing myocarditis in TA, which may yield important candidates for immunosuppression.\(^15\) Thus, multimodality assessments may provide beneficial information for patients at high risk for developing HF. However, it is difficult to confirm the protocol of multimodality assessments of TA through only one case; further large scale clinical investigations are necessary to confirm it.

**Conflict of interest**

None declared.

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