Takotsubo (Ampulla-shaped) Cardiomyopathy Associated with Microscopic Polyangiitis

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Abstract

Recently, a cardiac disorder characterized by ballooning and hypokinesis at the apex has been described as takotsubo (ampulla-shaped) cardiomyopathy. We encountered a patient with a rare case of takotsubo cardiomyopathy associated with microscopic polyangiitis. A 70-year-old woman suddenly presented with ventricular dysfunction during the active phase of microscopic polyangiitis. The findings on echocardiograms and electrocardiograms were consistent with those of takotsubo cardiomyopathy. The ventricular dysfunction completely resolved after treatment with 40 mg/day of prednisolone and methylprednisolone pulse therapy. This unique type of cardiomyopathy can be a complication of microscopic polyangiitis.

Key words: inverted T wave, microscopic polyangiitis, myeloperoxidase-antineutrophil cytoplasmic antibody, myocardial injury, takotsubo cardiomyopathy, ventricular dysfunction

Introduction

A form of ampulla-shaped ventricular dysfunction characterized by apical ballooning and hypokinesis of the left ventricle is described as takotsubo cardiomyopathy (1, 2). Its manifestations closely resemble those of acute myocardial infarction; however, it differs from acute myocardial infarction in that the coronary arteriogram of patients with takotsubo cardiomyopathy is normal, and that this ventricular dysfunction usually resolves without any specific treatment. At present, its precise cause remains yet determined.

Microscopic polyangiitis (MPA) is characterized by necrotizing vasculitis of small vessels and internal organ damage such as alveolar hemorrhage and necrotizing glomerulonephritis (3). Cardiovascular diseases rarely develop in patients with MPA (4). We describe herein a case of takotsubo cardiomyopathy associated with MPA. We consider that this unique type of cardiomyopathy can be a complication of microscopic polyangiitis.

Case Report

A 70-year-old woman had a temperature of 38°C and felt pain in her legs from April 2003. She was admitted to our hospital on May 24, 2003 due to the sudden development of numbness and palsy in her legs. On admission, she had normal vital signs as determined by general examinations. On auscultation, fine crackles were audible in the left lower lung field. Muscle weakness of both lower legs was noted. Asymmetrical sensory disturbance was noted in both legs and in her right hand fingers. Patellar tendon reflexes were present, but Achilles tendon reflexes were absent in both legs. These neurological findings were compatible with those of mononeuritis multiplex. Moreover, she had livedo reticularis on her legs.

Laboratory results were as follows: The total leukocyte count was 8.2×10⁹ cells/l. The serum liver transaminase level was normal. The C-reactive protein level was 4.1 mg/dl (normal range, 0 to 0.4) and the erythrocyte sedimentation rate was 72 mm/hour (normal range, 3 to 15). The serum creatinine level was 0.6 mg/dl (normal range, 0.5 to 1.2). The creatinine phosphokinase (CPK) level was 207 IU/l (normal range, 24 to 192).
range, 20 to 150). The myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA) level was 507 EU (normal range, 0 to 10). Urinalysis results were normal. A chest roentgenogram and computed tomography scan showed ground-glass opacifications and honeycombing in the lower lung fields. Nerve conduction studies showed that motor and sensory nerve action potentials were not elicited in the lower extremities. The results of electrocardiography were normal on admission (Fig. 1A).

On the 19th day of hospitalization, palpable purpura on the legs and palsy of the right fingers suddenly developed. The skin biopsy of the purpura showed vasculitis of small vessels, leukocytoclasis around small vessels, and extravasation of red blood cells (Fig. 2). MPA was diagnosed (5),

![Figure 1. Electrocardiogram on admission, showing a normal pattern (A). Electrocardiogram on the 20th day of hospitalization, showing extensive inverted T waves (B).](image1)

![Figure 2. Histopathology of skin biopsy specimen, showing vasculitis of small vessels, leukocytoclasis around small vessels, and extravasation of red blood cells (arrow) (HE stain, ×100).](image2)

![Figure 3. An echocardiogram in the apical view showing ballooning and hypokinesis at the apex at the time of diagnosis of takotsubo cardiomyopathy (A, diastolic; B, systolic). The wall motion of the left ventricle became normal after treatment with 40 mg/day of prednisolone and methylprednisolone pulse therapy (C, diastolic; D, systolic).](image3)
and prednisolone therapy at a dose of 40 mg/day (1 mg/kg body weight/day) was started. The announcement of the diagnosis appeared to have emotionally stressed the patient intensely. On the next day, the CPK level increased to 2,535 IU/l, although she showed no symptoms. Inverted T waves in her electrocardiogram were observed (Fig. 1B). The CPK isoenzyme MB level was 12 IU/l (normal range, 0 to 19), but the myosin light chain-1 level was 23.0 ng/ml (normal range, 0 to 2.5), and the test for troponin T revealed a positive result. An echocardiogram in the apical view showed ballooning and hypokinesis at the apex (Fig. 3A, B). The ejection fraction measured using the Simpson formula and fractional shortening at the apical region were 24% and 11%, respectively. The contractions of the basal segment of the ventricle were normal. From the 21st day of hospitalization, 1,000 mg of methylprednisolone was administered intravenously for three days. On the 31st day of hospitalization, the ejection fraction and fractional shortening recovered to 78% and 31%, respectively. On the 38th day of hospitalization, 500 mg of cyclophosphamide was administered intravenously. During this course, the patient received no additional specific treatment for the cardiovascular system. The MPO-ANCA level decreased to 54 EU, and the CRP level normalized. Ground-glass opacifications in the lower lung fields disappeared. The wall motion at the apex became normal (Fig. 3C, D), and inverted T waves in the electrocardiogram gradually normalized (Fig. 4). The patient’s neurological symptoms gradually improved. A dose of 40 mg/day of prednisolone was administered for one month, then the prednisolone dose was successfully tapered at a rate of 10% every two weeks (Fig. 5).

**Discussion**

We describe a case of ampulla-shaped ventricular dysfunction that developed during the course of MPA. Takotsubo cardiomyopathy was diagnosed because the clinical and laboratory findings and echocardiographic findings, such as ballooning and hypokinesis at the apex and reversibility of ventricular dysfunction, were consistent with this type of cardiomyopathy (1). The levels of cardiac enzymes do not usually increase, but a case of takotsubo cardiomyopathy with increased cardiac enzyme levels was reported (6). Strictly speaking, coronary angiography should have been performed to rule out acute myocardial infarction. However, we ruled out myocardial infarction because it could not explain the ampulla-shaped ventricular dysfunction, inverted T waves in the electrocardiogram, and the complete recovery without any specific treatment for the cardiovascular system.

To date, there is no consensus as to the cause of takotsubo
cardiomyopathy. A stunned myocardium induced by ischemia due to vasospasms, high levels of catecholamines, myocardial injuries, such as the infiltration of inflammatory cells or fibrosis of myocardium, and alcohol withdrawal, have been described in some cases as the causes of this dysfunction (7–10).

MPA was the underlying disease of takotsubo cardiomyopathy in the present case. Although the exact relationship between MPA and takotsubo cardiomyopathy could not be clarified, we speculated myocardial injury due to MPA as the cause of takotsubo cardiomyopathy, because its development coincided with the active phase of MPA. In addition, elevated serum CPK level, elevated myosin light chain-1 level, and positivity for troponin T suggested myocardial injury. A biopsy of ventricular muscles would have proved angiitis or myocardial injury. The recovery of our patient may be explained by the possibility that the cardiomyopathy was due to the myocardial injury caused by MPA; therefore, our patient responded to the immunosuppressive therapy including 40 mg/day of prednisolone and methylprednisolone pulse therapy. In addition to myocardial injury due to MPA, emotional stress may have played a role in the development of myocardial dysfunction (11). It was not confirmed whether the patient had high levels of catecholamines because these were not measured.

Diffuse ventricular hypokinesis was described in cases of MPA or polyarteritis nodosa (PN) (12, 13). The incidences of heart failure were reported to be 17.6% in patients with MPA and 61% in those with PN (3, 14), suggesting that ventricular dysfunction is not uncommon in patients with MPA or PN. The level of CPK can be normal (11), and diffuse ventricular hypokinesis is sometimes completely reversible following immunosuppressive therapy (15). We speculate that takotsubo cardiomyopathy can develop in patients with MPA or PN because the features of cardiomyopathy associated with MPA or PN such as ventricular hypokinesis and reversibility agree with those of takotsubo cardiomyopathy. However, there are no reports on takotsubo cardiomyopathy associated with vasculitic syndrome. The reason for this may be that takotsubo cardiomyopathy has been described only recently and it is not yet well known.

In the present case, the cause of apical wall motion abnormality remains to be identified. It may be explained by myocardial injury due to MPA, a myocardial perfusion defect (16), cardiac sympathetic hyperactivity (17, 18), or an impaired myocardial fatty acid metabolism (19) in the apical myocardial wall. The pathological examinations of myocardial muscle and the scintigraphic studies of myocardial per-
fusion, cardiac sympathetic activity, and fat metabolism will elucidate its cause in MPA or PN in the future.

In conclusion, we described a case of takotsubo cardiomyopathy that developed during the active phase of MPA. Although the association between these two disorders has not yet been described, this unique type of cardiomyopathy can be a complication of MPA. Further examinations will elucidate such an association.

References