Acromegaly with Multiple Cardiovascular Complications —Cardiomyopathy, Chordae Rupture of Mitral Valve, Myocardial Infarction and Sick Sinus Syndrome

Tadahiko YAMAMOTO, Hajime NAKAMURA, Tatsuya OGAWA*, Toshihiko SAGA* and Kinji ISHIKAWA

Abstract

A 62-year-old woman had acromegaly and developed congestive heart failure with cardiomyopathy, mitral regurgitation due to chordae rupture, coronary artery disease and sick sinus syndrome. Since congestive heart failure was resistant to medical therapy, mitral valve replacement, aortocoronary bypass surgery and implantation of permanent pacemaker were performed one month after her admission. Although acromegalic patients with cardiomyopathy are usually resistant to therapy, we successfully treated the patient by the surgeries. It appears that all these diseases resulted from an elevated plasma concentration of growth hormone. Untreated acromegaly for more than ten years may contribute to multiple complications such as those in the present patient.

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Key words: acromegaly, congestive heart failure, cardiomyopathy, coronary artery disease, mitral regurgitation; sick sinus syndrome

Introduction

Acromegaly is often associated with cardiovascular morbidity and its complications play a prominent role in worsening the prognosis of this disease. The patient we present here had congestive heart failure with cardiomyopathy, coronary artery disease, valvular heart disease and sick sinus syndrome, and no acromegalic cases with such a wide variety of cardiovascular complications had been previously described. Although acromegalic patients with cardiomyopathy are usually resistant to therapy, we successfully treated the patient by mitral valve repair, aortocoronary bypass surgery and implantation of permanent pacemaker.

Case Report

A 62-year-old woman was referred to the hospital with worsening shortness of breath. Around the age of 50, the patient had noticed a coarsening of facial features and had become aware of increased finger size. She had been diagnosed as heart failure with progressive dyspnea on exertion 6 years previously, and since that time she had been taking diuretics and angiotensin-converting enzyme inhibitors. On admission, her height was 157 cm, weight 58 kg, blood pressure 96/58 mmHg and pulse rate 45 beats/min with a regular rhythm. She had the characteristic acromegalic appearance of hands, feet and facial features. A grade 3/6 holosystolic murmur at the lower left sternal border and a diastolic blowing murmur at the higher left sternal border were audible. A dry rale was heard at the bilateral lower lung fields. She had hepatomegaly but no edema, goiter or visual disturbance was observed. Laboratory tests revealed hyperlipidemia (total cholesterol; 248 mg/dl), hyperglycemia (glucose; 174 mg/dl) and an elevated plasma concentration of brain natriuretic peptide (829 pg/ml). Both the plasma levels of growth hormone and insulin-like growth factor I were elevated (GH; 56.1 ng/ml, IGF-I; 486 ng/ml) and they were not inhibited after glucose ingestion. The plasma concentrations of thyroid hormones and other pituitary hormones were normal. Diabetes mellitus was confirmed by 75 g oral glucose tolerance test. Oral administration of octreotide lowered the plasma growth hormone level from 62.8 ng/ml to 19.5 ng/ml.

The chest X-ray showed cardiomegaly with dilatation of the pulmonary artery and pulmonary congestion. The electrocardiogram showed sinus bradycardia, first degree of atrioventricular block and left ventricular hypertrophy with
Acromegaly with Cardiovascular Complications

Figure 1. The electrocardiogram showed sinus bradycardia, first degree of atrioventricular block and left ventricular hypertrophy (A). The ambulatory electrocardiogram monitoring revealed 22 times of sinus pause with maximal R-R interval for 4.8 seconds (B).

premature ventricular contractions and premature supraventricular contractions (Fig. 1A). The ambulatory electrocardiogram monitoring revealed a decrease in total heart beats (72,265 beats/day) and 22 times of sinus pause including maximal R-R interval for 4.8 seconds (Fig. 1B). The skull X-ray revealed an enlargement of the sella turcica and the magnetic resonance imaging of the brain showed a pituitary microadenoma (2.1x1.6 mm) without compression of the optic nerve.

The echocardiography showed dilatation of the both ventricles and atriums (Fig. 2 and Table 1). Wall motion of the left ventricle was diffusely reduced with akinesis of the inferior wall. Severe mitral regurgitation, mild aortic regurgitation and severe pulmonary regurgitation were shown. Prolapse of the anterior mitral leaflet with torn chordae was recorded by transesophageal echocardiography (Fig. 3).

Coronary angiography revealed a triple vessel disease of the coronary artery with total occlusion of the left circumflex artery and good collateral flow from the diagonal artery to the left circumflex artery. Thallium-201 myocardial perfusion scintigraphy revealed a perfusion defect of the inferior

Figure 2. Dilatation of the left ventricle and left atrium was shown. Wall motion of the left ventricle was diffusely reduced with akinesis of the inferior wall. LV: left ventricle, RV: right ventricle, LA: left atrium, Ao: aorta.
Table 1. Time Course of Echocardiographic Parameters

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>LV end-diastolic diameter</td>
<td>80 mm</td>
<td>70 mm</td>
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<tr>
<td>LV end-systolic diameter</td>
<td>67 mm</td>
<td>62 mm</td>
</tr>
<tr>
<td>Fractional shortening</td>
<td>16%</td>
<td>11%</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>38%</td>
<td>31%</td>
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<tr>
<td>Left atrium diameter</td>
<td>58 mm</td>
<td>49 mm</td>
</tr>
<tr>
<td>LV E/A</td>
<td>4.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Mitral Regurgitation</td>
<td>severe</td>
<td>mild transvalvular leak</td>
</tr>
<tr>
<td>Tricuspid Regurgitation</td>
<td>trivial</td>
<td>mild (PG=21 mmHg)</td>
</tr>
<tr>
<td>Aortic Regurgitation</td>
<td>mild</td>
<td>mild</td>
</tr>
<tr>
<td>Pulmonary Regurgitation</td>
<td>severe</td>
<td>moderate</td>
</tr>
<tr>
<td>LV asynergy</td>
<td>General hypokinesis with inferior akinesis</td>
<td>General hypokinesis with inferior akinesis</td>
</tr>
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LV: Left ventricular, PG: pressure gradient.

Figure 3. Severe mitral regurgitation was shown in the apical four-chamber view (Left). Prolapse of the anterior mitral leaflet with torn chordae (arrow) was recorded by transesophageal echocardiography (Right). LV: left ventricle, RV: right ventricle, LA: left atrium.

Discussion

This patient had acromegaly with congestive heart failure, mitral regurgitation due to chordae rupture, myocardial infarction and sick sinus syndrome; she also underwent mitral valve replacement, coronary artery bypass surgery and cardiac pacemaker implantation. It appears that all of these diseases resulted from an elevated plasma concentration of growth hormone. Growth hormone excess deteriorates glucose tolerance and arteriosclerosis, leading to myocardial infarction and cardiomyopathy, which contribute to mitral regurgitation and sick sinus syndrome. Both direct and indirect effects of the growth hormone excess may lead to multiple cardiovascular complications of the present patient.

In the initial stage of acromegaly, growth hormone increases myocardial contractility and cardiac output. Subsequently, ventricular hypertrophy becomes evident and diastolic function slowly deteriorates (1). If the disease is untreated, cardiac function deteriorates further and eventually congestive heart failure with dilated cardiomyopathy develops, which is known as acromegalic cardiomyopathy. Acromegalic cardiomyopathy is more closely correlated with duration of the disease than with growth hormone levels (2). Left ventricular hypertrophy and cardiac dysfunction can be improved after effective treatment in the early stage of acromegaly (3, 4). Histologic appearance of acromegalic heart shows hypertrophied myocardial fiber, interstitial fibrosis and mucopolysaccharide deposits (5). Such findings were seen in the myocardium from the intraoperative biopsy of the present patient, suggesting that she had an advanced acromegalic cardiomyopathy.

Mitral and aortic valvular disease are observed in the late stage of acromegaly. An autopsy study performed at the Mayo Clinic noted that the prevalence of valvular pathology was 19% in patients with acromegaly (5). Cable et al (6) performed valvular surgery in 10 acromegalic patients and suggested that it can be performed safely even in active endocrinopathy. Ohtsuka et al (7) reported a series of 5 patients who underwent valvular replacement and described that valve replacement was better than plasty because of degeneration and fragility of the valvular rings.

Ischemic heart disease is often observed in association with acromegaly. Atherosclerosis in acromegalic patients is due to coexisting coronary risk factors such as hypertension,
diabetes mellitus and dyslipidemia rather than to a direct effect of growth hormone (8, 9). The present patient had an occluded left circumflex coronary artery and a fixed defect of the inferior wall in the thallium-201 myocardial perfusion scintigraphy, suggesting that she had suffered from old myocardial infarction. She underwent aortocoronary bypass surgery simultaneously with mitral valve repair. Mitral regurgitation was the major cause for heart failure, because her symptoms were improved without improvement of left ventricular wall motion and ejection fraction after the surgery.

It is known that the cardiac conduction system as well as myocardium, is affected in the patients with an excess of growth hormone. Rossi et al (10) reported a case of acromegaly with sick sinus syndrome who suffered sudden death. Yamanaka et al (11) performed implantation of permanent pacemaker in an acromegalic patient with complete atrioventricular block, but their patient died during sleep one year after the implantation. Both papers documented that an histological examination in the conduction system indicated inflammatory infiltration and myofibrillar degeneration, these are probably due to the effect of growth hormone on collagen synthesis. Although bradycardia in the patient was asymptomatic, we decided to implant a pacemaker, because sick sinus syndrome was progressive and bradycardia could deteriorate hemodynamics.

Untreated acromegaly for more than ten years may have contributed such multiple complications of the present patient. Normalization of growth hormone secretion in the early stage of acromegaly is needed for improvement of prognosis.

References