lagic acidやgingerolにはこのような問題が無いことが期待される。

心不全の薬物治療では、心筋そのものの収縮性を改善するというよりはむしろangiotensin系阻害薬等を用いて循環系全体の特性を長期的に改善する治療を目指す傾向にあるのが現状である。SERCA機能を増大させる薬物により心臓の拡張機能を直接改善させることが出来れば、拡張機能不全を原因とする心不全に対する新たな治療戦略を構築することが可能となる。今回の研究で見出されたellagic acidやgingerol等の化合物がそのための出発点になることを期待する。

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[III]

研究成果の刊行に関する一覧表

別紙４

研究成果の刊行に関する一覧表

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[IV]

研究成果の刊行物・別刷

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CASE REPORT

A case of giant coronary artery aneurysm and literature review

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KEYWORDS
Coronary artery aneurysm;
Kawasaki disease

Summary A 40-year-old man was referred to our hospital because of an abnormal shadow on the left cardiac border on the chest roentgenogram at the regular medical health examination without any symptoms. A giant coronary artery aneurysm of left anterior descending artery with a maximum diameter of approximately 50 mm was detected with computed tomography and coronary angiography. The patient was treated and followed up medically. Four years later, the size of the coronary artery aneurysm became larger. Then resection of the coronary artery aneurysm and coronary artery bypass grafting were successfully performed. Coronary artery aneurysms are rare in adults and are usually found in association with Kawasaki disease, coronary atherosclerosis, and so on. We also review the literature of giant coronary artery aneurysms exceeding 50 mm in diameter.

Introduction

Coronary artery aneurysms are rare lesions. They are caused by Kawasaki disease (mucocutaneous lymphnode syndrome), coronary atherosclerosis,

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trauma (including percutaneous coronary intervention), autoimmune diseases (polyarteritis nodosa, systemic lupus erythematosus, scleroderma), coronary artery dissection, and so on. In Kawasaki disease, coronary artery aneurysms are not rare complications. However, giant coronary artery aneurysms are rare. We treated a case with a giant coronary artery aneurysm, the size of which is about 50 mm in diameter, and report here with a literature review.

Case presentation

A 40-year-old man was referred to our hospital for the evaluation of an abnormal shadow on the left cardiac border on the chest X-ray film at the regular medical health examination. The abnormal shadow on the left cardiac border was not pointed out at the previous regular medical examination. He did not experience angina-like chest pain. He had no history of Kawasaki disease or chest trauma. However, he had been admitted to hospital because of high fever and cervical lymphadenopathy and had had tonsillectomy at the age of 12.

On physical examination, his blood pressure was 110/76 mmHg and pulse rate was 72/min. Precordial auscultation disclosed no abnormalities. Physical examination results were normal. The results of blood test were normal. The chest roentgenogram showed an abnormal shadow on the left cardiac border. Electrocardiogram showed normal and no Q waves. Treadmill exercise testing was negative.

Computed tomography (CT) of the chest showed a 50 mm round mass with calcification beside the aorta (Fig. 1A). Intravenous contrast medium injection revealed a large cavity inside the mass. Cardiac magnetic resonance imaging (MRI) with gadolinium enhancement demonstrated a 50-mm mass adjacent to the left ventricle.

Coronary angiography and left ventriculography were performed. Right coronary artery (RCA) was totally occluded at the proximal portion with well-developed collateral artery from left circumflex artery to distal RCA. Oval calcification was identified at the distal portion of RCA and it was thought to be a coronary artery aneurysm. Proximal left anterior descending artery (LAD) opened into a large spherical cavity that was filled with contrast medium in a swirling fashion with slow opacification of distal LAD, confirming the diagnosis of a giant coronary artery aneurysm. Diagonal branch had 75% stenosis at the outlet of the aneurysm. Left ventriculogram revealed no asynergy, and ejection fraction was 77%. The anterobasal portion of left ventricle was compressed by the aneurysm. Stress myocardial perfusion imaging showed mild ischemia at diagonal branch area and inferior wall without any symptoms. Coronary artery bypass grafting (CABG) with coronary artery aneurysm resection was first considered. However, he was asymptomatic with good exercise capacity, and had no significant stenosis and ischemia in the LAD. Because the management of patients with coronary artery aneurysms is somewhat controversial, we decided to treat him medically with a low dose of aspirin and followed him carefully with periodical CT and MRI examinations; this was what he wished also.

The size of the coronary artery aneurysm remained unchanged for 3 years. He had no symptoms. However, 4 years later, the size of the aneurysm started to increase and reached 60 mm × 53 mm on the CT (Fig. 1B, C, and D). Coronary angiography was performed again (Fig. 2A and B), which showed similar results to the previous study except for the progression to 75% stenosis at the ostium of LAD aneurysm. Therefore, he underwent surgery. Median sternotomy was performed. Giant LAD aneurysm (Fig. 3) and small (approximately 1 cm in diameter) distal RCA aneurysm were identified. Two venous cannulae were inserted into superior and inferior vena cava via right atrium, and arterial cannula was inserted into ascending aorta. After cardiopulmonary bypass was initiated, the aorta was cross-clamped. Free gastroepiploic artery (GEA) graft was anastmosed to the posterolateral branch of the RCA. When coronary aneurysmal sac was opened, yellow fluid was released and the remaining part of the sac was filled with organized thrombi. The organized thrombi were removed. The inlet of the aneurysm was the proximal LAD, and the outlets were the distal LAD and diagonal branch. Proximal LAD was ligated at the ostium of the aneurysm, and distal LAD and diagonal branch were ligated at the ostia. The aneurysmal sac was excised. Free radial artery (RA) graft was anastmosed to diagonal branch. Left internal thoracic artery (LITA) was anastmosed to distal LAD. The proximal ends of the free GEA and RA were anastmosed to ascending aorta. The resected aneurysm was atheromatous, and histological examination of the coronary artery aneurysm wall revealed marked wall thickening with calcification and hyalinization of the media. Hemosiderosis was also observed, but no evidence of active vasculitis was observed. The postoperative course was uncomplicated. Coronary angiograms after CABG showed patent grafts without stenoses (Fig. 4A–D). Proximal septal branches

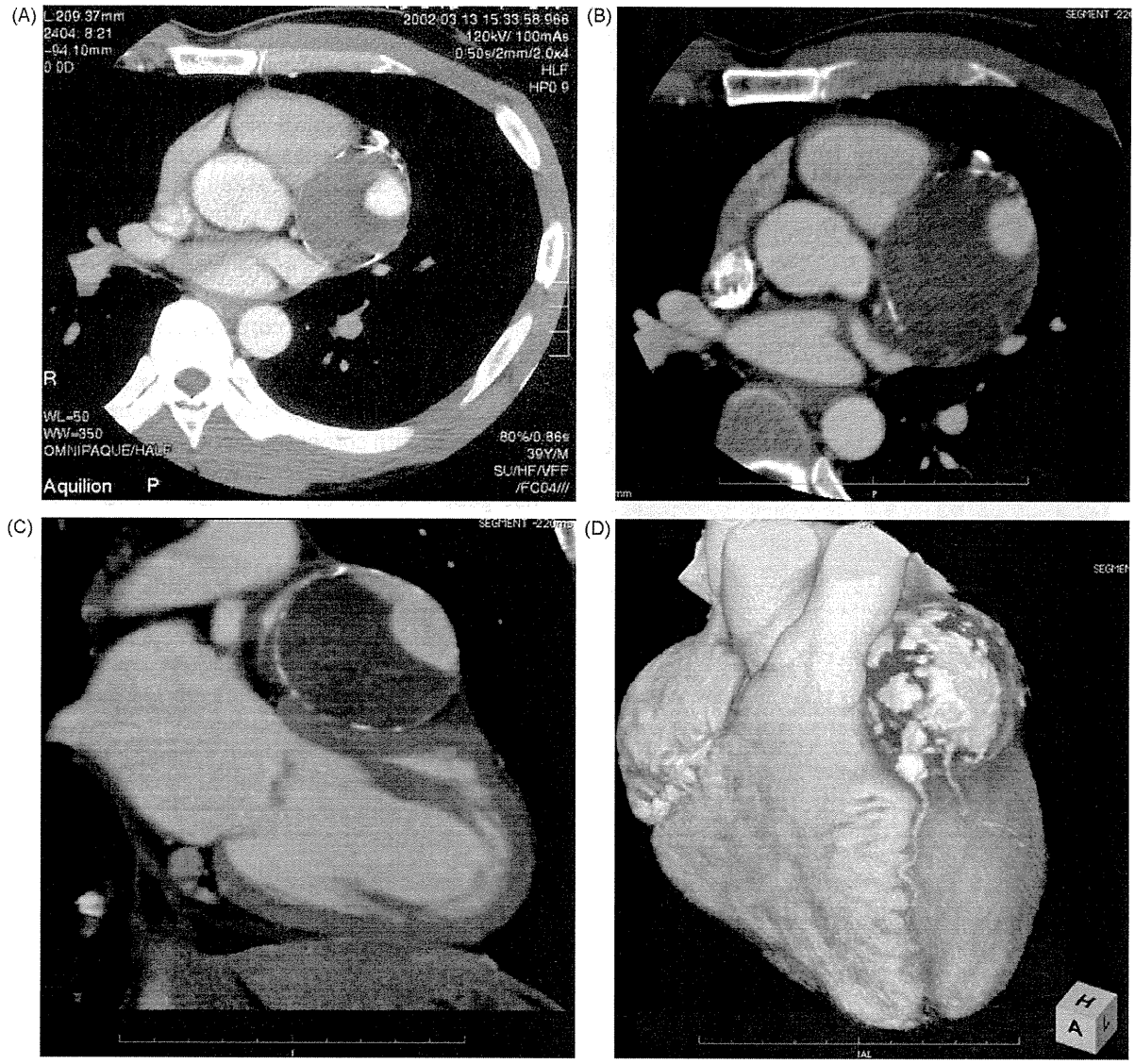

Figure 1 Enhanced computed tomography. (A) At the initial examination. An approximately 50 mm round mass with calcification is shown. Partial enhancement beside the aorta is also shown. (B and C) Four years later. The size of the coronary artery aneurysm became 60 mm × 53 mm. (D) Three dimensional reconstruction of the follow-up CT.

of the LAD were filled by collaterals from the posterior descending branch of the RCA.

Discussion

Coronary artery aneurysms are detected in 1.2—4.9% of patients undergoing coronary angiography and are reportedly present in 1.4% of post-mortem examinations. They occur in males more frequently than females. The most affected coronary artery is the RCA. They are frequently asymptomatic. In symptomatic cases, it is usually caused by myocardial ischemia. The causes of coronary artery aneurysms are Kawasaki disease (mucocutaneous lymph node syndrome), atherosclerosis, autoimmune diseases (polyarteritis nodosa, systemic lupus erythematosus, scleroderma), trauma (including coronary angioplasty), coronary artery dissection, rheumatic, mycotic coronary emboli, syphilis, and so on [1]. Kawasaki disease was initially described by Kawasaki in 1967 in Japan [2]. It is a generalized vasculitis of unknown etiology and occurs in children. Coronary artery abnormalities develop in approximately 20% of children with untreated Kawasaki disease. Abnormalities of coronary arteries include ectasia or aneurysms that may be

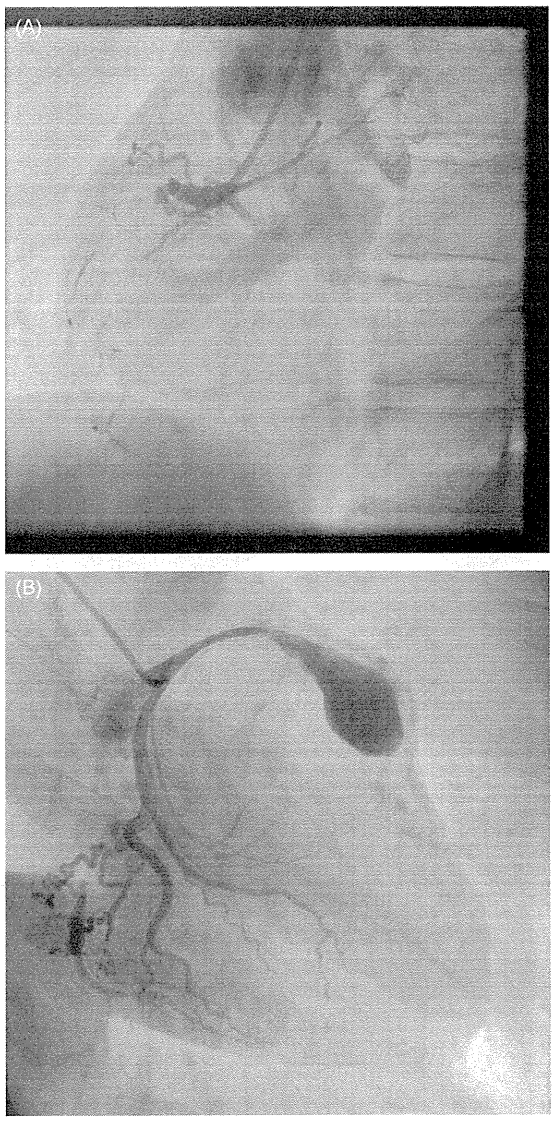

Figure 2 Coronary angiograms. (A) Right coronary artery was occluded at the proximal portion, and oval calcification was identified at the distal portion of right coronary artery. (B) Giant coronary artery aneurysm of left anterior descending artery.

fusiform or saccular [3,4]. Burns et al. described the sequelae of Kawasaki disease in adolescents and young adults [5]. Of Seventy-four patients, who were identified with presumed late sequelae of Kawasaki disease at the mean age of 24.7 years, 93.2% had coronary artery aneurysms and 66.1% coronary artery occlusion. A striking radiographic finding of the ring calcification representing calcium deposition in the walls of the coronary artery aneurysms was noted in about 36% of patients.

In the present case, Kawasaki disease was not diagnosed in childhood. However, he had been admitted to hospital because of high fever and cervical lymphadenopathy at the age of 12. The possibility of Kawasaki disease cannot be ruled out, even though the age of 12 was somewhat older for the onset of Kawasaki disease. The findings of CAG and CT showed coronary artery aneurysms in two coronary arteries, calcification, and occlusion without coronary risk factors. These findings suggest the possibility of the consequence of Kawasaki disease. Because the size of the aneurysm was already 50 mm, and there was some risk of rupture of the aneurysm, CABG with coronary artery aneurysm resection was considered. Most of the cases with giant coronary artery aneurysm in previous reports were surgically treated. However, the management of patients with coronary artery aneurysms is somewhat controversial [6,7]. He was asymptomatic and had good exercise capacity. Also he had no significant stenosis and ischemia in the LAD. Therefore, he was treated medically with a low dose of aspirin, and was followed carefully. Multislice CT is useful for diagnosis and follow-up in this situation. However, 4 years later after the initial examination, the size of the coronary artery aneurysm became larger, and the LAD had significant stenosis. Therefore, we performed surgery including resection of the aneurysm and CABG. Histological findings did not show evidence of vasculitis. The inflammation had been already resolved, and only atheromatous change remained.

Giant coronary artery aneurysm, especially with a diameter exceeding 50 mm, is extremely rare. Table 1 shows a summary of giant coronary artery aneurysms with a diameter of 50 mm or more without fistula, which were described in a previous report [8] and others [9–39]. There is no sex predomination. The most affected coronary

Figure 3 Coronary aneurysm during surgery. Giant left anterior descending artery aneurysm is shown.

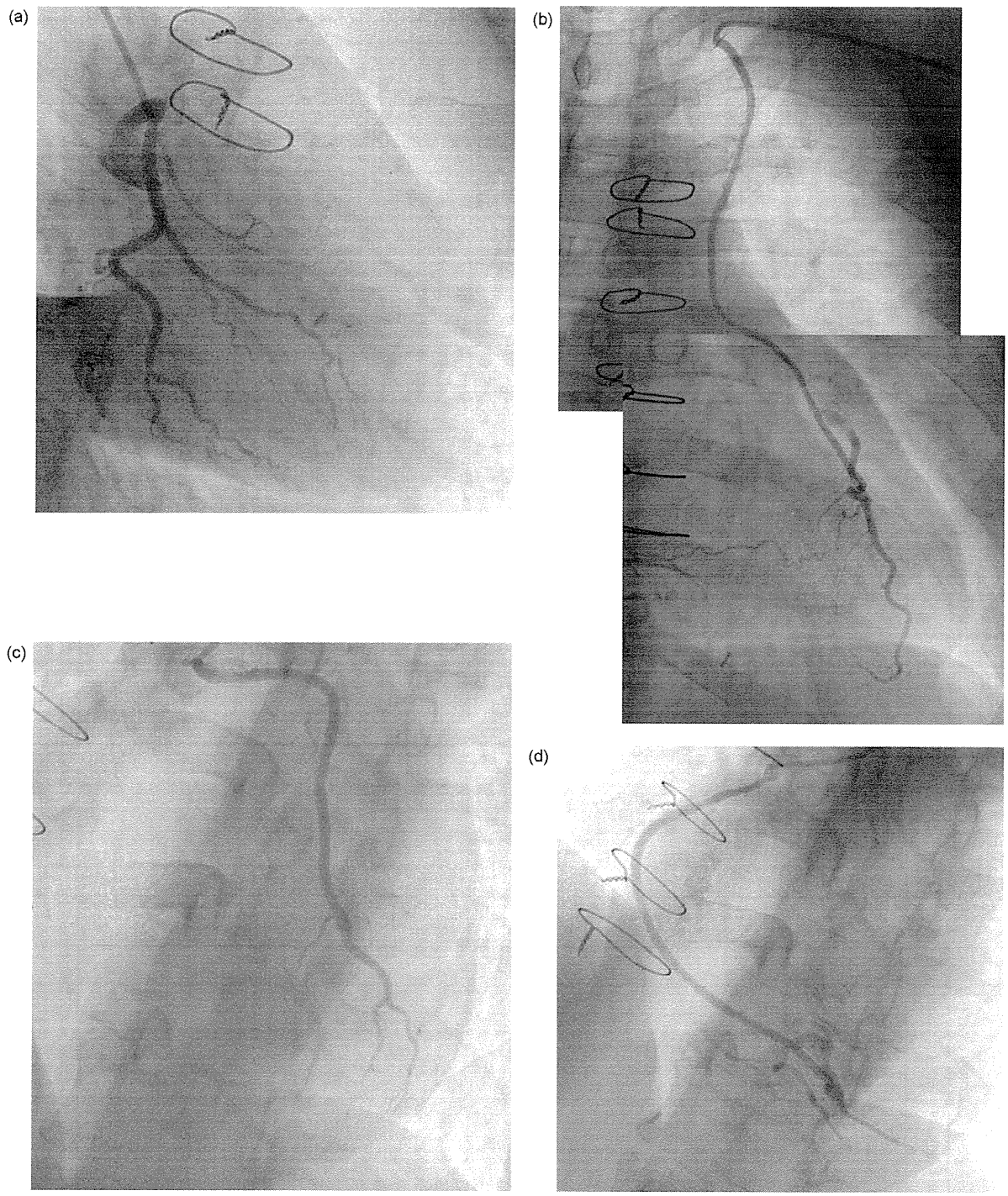

Figure 4 Coronary angiograms after CABG. (A) Left anterior descending artery was occluded at the ostium. (B) Left internal thoracic artery to left anterior ascending artery was patent without stenosis. (C) Radial artery graft to diagonal branch was patent without stenosis. (D) Gastroepiploic artery graft to distal right coronary artery was patent without stenosis.