Increased Interleukin-6 Activity in Cardiac Myxoma with Mediastinal Lymphadenopathy

Shigetaka Kuroki, Keiko Naitoh, Osamu Katoh, Hozumi Yamada and Tsuyoshi Itoh*

We report a case of cardiac myxoma with mediastinal lymphadenopathy which seems to be a very rare feature. Laboratory examination revealed high level of interleukin-6 (IL-6) activity in serum. Interestingly, after removal of cardiac myxoma, mediastinal lymphadenopathy disappeared on the chest CT and the level of serum IL-6 was decreased. These findings suggest that IL-6 which was probably derived from myxoma, may have played an important role in the development of lymphadenopathy.

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Key words: IL-6, Cardiac myxoma, lymphadenopathy, Castleman’s disease

Introduction

Cardiac myxoma is a rare disease, but it is the most common condition as a primary cardiac tumor. Patients of cardiac myxoma present various clinical manifestations, such as easy fatigability, weight loss, arthralgia, and low grade fever, accompanied by laboratory abnormalities such as accelerated erythrocyte sedimentation rate (ESR), anemia, polycythemia, and increased immunoglobulin levels (1). In addition to these features, the present patient revealed mediastinal lymphadenopathy which was thought to be a very rare manifestation of cardiac myxoma.

Recently, it has become known that IL-6, originally established as one of the B cell stimulatory factors, has multiple biological functions, and also may be associated with the pathomechanism of some diseases (2), one of which is cardiac myxoma. We report here a case of cardiac myxoma with mediastinal lymphadenopathy, revealing a high level of IL-6 activity in the serum.

Case Report

A 60-year-old woman was admitted to the Hospital of Saga Medical School with complaints of dyspnea on May 17, 1989. Cardiopulmonary examinations showed crepitant rales at the base of both lungs, 3rd cardiac sound at the apex and a systolic murmur at the left sternal border of the 4th intercostal space. Laboratory examinations showed hemoglobin of 10.9 g/dl, alkaline phosphatase level of 292 IU/l (normal 86–218), IgG 2,451 mg/dl, IgM 332 mg/dl. C-reactive protein (CRP) was 7.4 mg/dl and ESR was 102 mm per hour. A chest film on admission showed cardiomegaly, moderate increase of peribronchial markings over the lower lung fields, and bilateral pleural effusions. Echocardiogram revealed the presence of a round mass, 47 × 31 mm in size, arising from the interatrial septum. Chest CT scan showed a cardiac mass in the left atrium (Fig. 1a) and also numerous enlarged mediastinal lymphnodes (Fig. 1b).

Two days after admission, operation was performed as follows. After median sternotomy, the left atrium was longitudinally incised and the foramen ovale was resected to which the pedicle of the cardiac tumor was attached. Then, patch closure of the defect of interatrial septum was performed by prolene continuous suture. In addition, a paratracheal lymph node was removed. Histology of the cardiac tumor showed appearance of a typical cardiac tumor, including a loose stroma with various shapes of multinucleated cells scattered throughout the tumor, small vessels lined with plump endothelial cells, and foci of lymphocytes. Histology of the lymph node revealed accumulation of sinus histiocytes which phagocytized coal pigment and hemosiderin, an enlarged germinal center, and a small number of plasma cells in the interfollicular area (Fig. 2). Immunohistochemical analysis using monoclonal antibody such as UCHL-1 (CD45RO) and L-26 (CD20) disclosed that the distribution of T and B cells was almost normal.
Fig. 1. CT scan image. a) On admission, cardiac myxoma was seen in the left atrium. b) On admission, many mediastinal lymph nodes were enlarged. c) After excision of cardiac myxoma, all of the enlarged mediastinal lymph nodes were no longer visible.

These findings were compatible to sinus histiocytosis.

IL-6 activity in the serum before and one and two months after operation was 1.188, 0.445 and 0.396, respectively (control: 0.228 ± 0.06 n = 6). IL-6 activity was measured by [3H]-thymidine uptake using IL-6 dependent murine hybridoma clone, MH60 (3). The IL-6 activity was extremely high before removal of the cardiac myxoma (1.188 U/ml) as compared to normal control (0.228 ± 0.06 U/ml) and then it decreased after removal of the cardiac myxoma.

Postoperatively, mediastinal lymphadenopathy spontaneously disappeared as shown in Fig. 1c, and also clinical and laboratory abnormalities improved subsequently.

Discussion

In general, the various clinical manifestations and laboratory abnormalities which accompany cardiac myxoma disappear after removal of myxoma. Previous reports have suggested that IL-6 might play an important role in the development of various manifestations in cardiac myxoma, because cultured supernatant of myxoma showed increased activity of IL-6 (4). Recently, IL-6 was demonstrated to have numerous biological functions, including stimulation and differentiation of lymphocytes (5).

The present case had an additional feature, mediastinal lymphadenopathy, which seemed to be a very rare condition associated with cardiac myxoma. In fact, we could not obtain a description of any patient with mediastinal lymphadenopathy in myxoma in the literature. However, it may well be speculated that persistent exposure to lymphokine-like IL-6 results in sinus histiocytosis. If a chest CT is performed routinely in patients with cardiac myxoma, mediastinal lymphadenopathy may more likely be found.

Another disease showing an increased serum IL-6 level is Castleman’s disease which is mainly described as a localized hyperplastic lymphoid process of the mediastinum (6). The plasma cell type of Castleman’s disease presents with systemic manifestation such as fever and weight loss and B cell hyperreactivity, and
the histopathology shows an architecturally recognizable lymph node with solid sheets of plasma cells in the interfollicular area. Another type of Castleman's disease is a hyaline-vascular type which features an abnormal architecture showing hypervascular lymphoid tissue with burnt out germinal centers; this type is usually characterized by a slowly progressive mass with an asymptomatic condition. Although the present case required the differentiation of multicentric mediastinal lymph node swelling from Castleman's disease, the lymph node histology was not compatible with the finding of this disease.

In the present case, after removal of the myxoma, lymphadenopathy as well as clinical and laboratory abnormalities promptly improved. In parallel with these changes, the serum IL-6 level, which had been increased before excision of myxoma, returned to a nearly normal level postoperatively. These events suggest that IL-6 probably released from the cardiac myxoma may have been responsible for the development of mediastinal lymphadenopathy as well as for other systemic and laboratory abnormalities seen in this patient.

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**References**