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**A CASE OF LEFT ATRIAL MYXOMA ACCOMPANIED
BY PANCYTOPENIA AND PATHOLOGICAL
FINDINGS SUGGESTIVE OF PULMONARY
HYPERTENSION**

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Abstract: A case of left atrial myxoma accompanied by peculiar symptoms is reported. A 15-year old boy had progressive congestive heart failure and three episodes of acute attacks of pancytopenia. The anemia was accompanied by helmet-shaped, broken red blood cells, erythroid hyperplasia and elevation of indirect bilirubin. The thrombocytopenia gave rise to hemorrhagic tendency of the skin and mucous membrane. The leukocytopenia was seen at the same time. The patient also had general constitutional disturbances showing generalized malaise, persistent fever, elevation of erythrocyte sedimentation rate, positive C-reactive protein, pulmonary infection and anginal attacks. Postmortem examinations revealed a left atrial myxoma and intricated pulmonary changes. There was obliterative endarteritis of the left coronary branch and pulmonary arteries. The interstitial pulmonary fibrosis was also prominent. The pancytopenia should have been induced by the mechanical damage of circulating blood cells by the left atrial myxoma. The pathological findings of the lungs were highly suggestive of pulmonary hypertension, which was assumed to be due to mitral block caused by the atrial myxoma.

Benign primary cardiac tumors are rare and about half of these is myxoma. They usually occur in the atria and are approximately 75 per cent in the left atrium. Diagnosis of cardiac myxomas is often difficult because of confused array of signs and symptoms, which may simulate mitral stenosis or subacute bacterial endocarditis. GOODWIN (1) divided clinical manifestations of cardiac tumors into four groups; hemodynamic disturbances, mechanical hemolysis, biochemical effects and constitutional symptoms.

In the case presented here, of special interest is that attacks of hemolytic anemia, thrombocytopenia and leukocytopenia occurred in a patient with the clinical picture of far advanced congestive heart failure, accompanied by remittent fever and jaundice. Postmortem examination revealed a left atrial myxoma and the changes that suggested pulmonary hypertension.

CASE REPORT

The patient was a 15-year old school boy and had always felt well until March 1969, when he was first noticed of systolic murmur at the apex of his heart on the physical examination. In the morning of August 8, 1969, he developed a sudden onset of abdominal pain and coldness of his right lower leg and foot. He was admitted to the Surgical Department of Okayama University Hospital for an anticoagulant therapy for the embolism of the right femoral artery and further evaluation of the cardiac condition. During the hospitalization, he had a persistent low grade of fever. As a result of a cardiac catheterization, he was diagnosed as possible mitral stenosis with subacute bacterial endocarditis. The patient was discharged from the surgical ward in September 1969. But his cardiac condition gradually worsened, with developing generalized malaise, palpitation, dyspnea and swelling of the liver. He was readmitted to the surgical ward of the University Hospital on January 8, 1970. Physical examination showed a remarkably dilated heart with grade II diastolic rumbling murmur at the apex of the heart and the markedly enlarged liver. Erythrocyte sedimentation rate was 5 mm/h, ASLO 12 units, CRP 3+. Hematological data revealed red blood cells (RBC) 464×10^4 /cmm, hemoglobin (Hb) 9.4 g/dl, white blood cells (WBC) 12,500/cmm, hematocrit (Ht) 31%. Total bilirubin was 1.57 mg/dl, direct bilirubin 0.67 mg/dl, SGOT 21 units and SGPT 77 units. In the beginning of February, the patient had the right pleural effusion and moderate pitting edema on his legs. This congestive heart failure responded poorly to digitalis and diuretics. And he became more anemic and icteric.

He was transferred to the medical ward on March 18, 1970 for a further medical treatment. Physical examination on admission revealed a thin, pale and icteric boy with signs of far advanced congestive heart failure. The radial pulse was rapid but regular. Arterial blood pressure was 102/52 mmHg. The jugular veins were distended. The heart was markedly dilated bilaterally; 5 cm to the right and 8 cm to the left, with a grade III systolic murmur at the apex. There was dullness in the right chest. The liver extended by about 17 cm below the right costal margin. The spleen was not palpable. He had ankle edema. His temperature was 36.7°C.

Laboratory Findings: The erythrocyte sedimentation rate showed 1 mm/h and 4 mm/2h. The hematological data on admission and during the subsequent hospitalization (Table 1 and Fig. 1) indicated that the patient had attacks of severe anemia with reticulocytosis, thrombocytopenia and leukocytopenia with relative neutrophilia at the same time. Study of sternal bone marrow showed a marked erythroid hyperplasia and a normal amount of

megakartocytes. Total serum bilirubin was 4.12 mg/dl and indirect bilirubin 1.66 mg/dl (Table 1 and Fig. 1). The SGOT was 37 units, and SGPT

TABLE 1 HEMATOLOGICAL DATA AND SERUM BILIRUBIN LEVELS DURING THE HOSPITALIZATION.

	3-18-70 (on admission)	4-30-70 (1st attack)	5-18-70	6-9-70 (2nd attack)	8-24-70	9-5-70 (3rd attack)
RBC ($\times 10$)	370	144	365	149	302	190
Hb (%)	—	20	—	28	—	37
Ht (%)	—	18	—	—	28	21
Reticulocyte (%)	—	27	—	7	6	1
Platelet ($\times 10^4$)	5.35	4.8	8.76	2.38	20.0	0.57
WBC	10200	5040	9600	3600	6800	1100
Neutrophil (%)	51	69	—	67	87	86
Lymphocyte (%)	45	31	—	27	3	12
Total bilirubin (mg/dl)	4.12	5.68	6.07	6.31	1.78	1.71
Indirect bilirubin (mg/dl)	1.66	2.30	2.40	2.85	0.71	0.47

32 units. The colloidal reactions were within normal limits. The serum iron level was 23 $\mu\text{g}/\text{dl}$, serum Na 120 mEq/l, K 5.0 mEq/l. The total serum protein was 5.0 g/dl with 70 per cent of albumin, 4 per cent α_1 -, 6 per cent α_2 -, 8.5 per cent β -, 11.5 per cent γ -globulin, A/G ratio 2.33. ASLO was 100 units (Todd), RA test and antinuclear factor negative, serum complement titer (CH50) 22.5. The chest roentgenogram (Fig. 2) showed a marked cardiomegaly, with pulmonary congestion and right pleural effusion. The electrocardiogram revealed sinus tachycardia and non-specific ST-T changes, that showed depressed ST and diphasic or inverted T waves.*

Hospital Course: The patient was put on digitalization and diuretic therapy, which responded poorly on him. In the end of March 1970, he developed low grade of fever. On April 30, 1970, he looked very tired and his lips were markedly pale. His skin became more icteric. The hematological data showed acute attack of hemolysis. The smear of the blood cells showed helmet-shaped erythrocytes. Direct and indirect Coombs' tests were negative. The osmotic fragility test of erythrocyte ranged from 0.42 to 0.30 per cent. After he was transfused 1,200 ml of fresh whole blood, his general condition improved in spite of temperature elevation. In the beginning of June, he experienced the second attack of the severe anemia accompanied by the thrombocytopenia and moderate leukocytopenia. The bleeding time was prolonged more than 10 minutes. The occult blood of stool was positive.

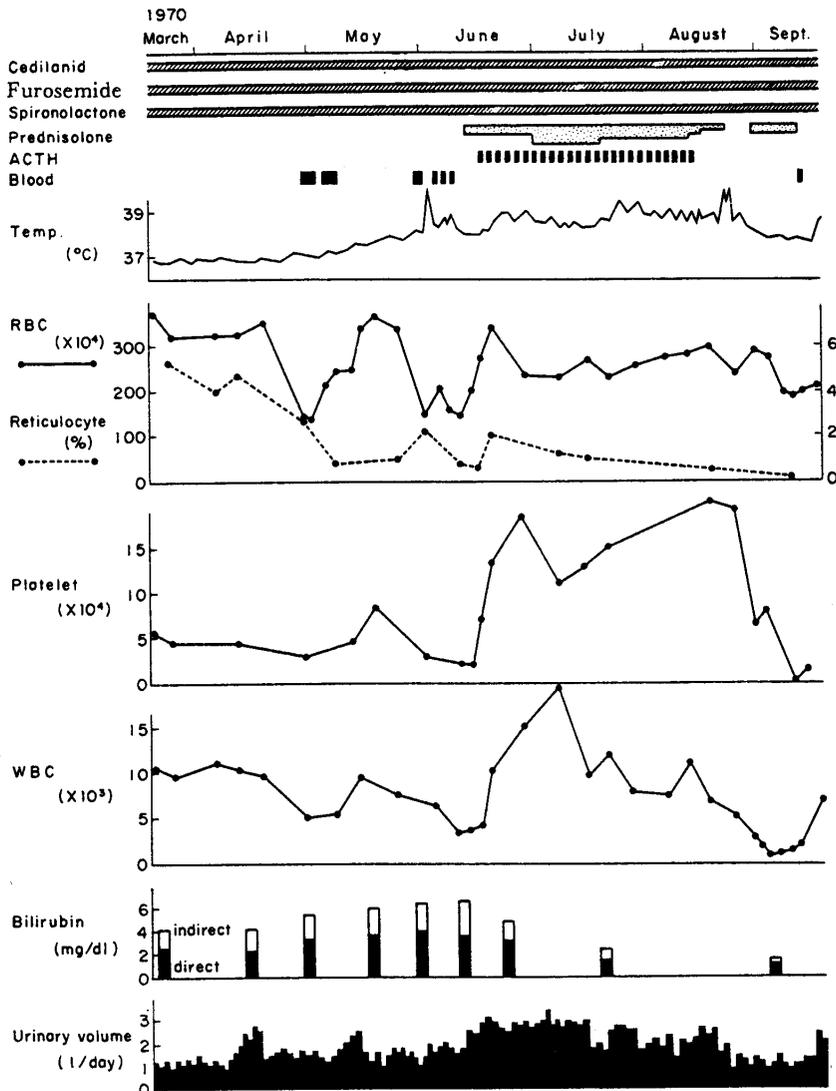


Fig. 1. Hospital course.

Numerous petechiae were seen on the skin and mucous membrane. He was given 800 ml of whole blood and 200 ml of thrombocyte suspension blood. Also he was administered 10 mg of prednisolone daily and 0.25 to 0.5 mg ACTH twice a week for 8 weeks. With the steroid administration, his urinary output increased up to 3,000 ml per day and the right pleural effusion was disappeared. The ascites and pitting edema of the extremities were decreased. The size of the liver became smaller. The cardiac silhouette on

x-ray film was reduced in size. But his temperature remained remittent, showing the highest of 40°C. Several laboratory studies were carried out; arterial blood culture showed no organism, Widal, Weil-Felix and Paul-Bunnell test were negative. Repeated Coombs' tests were entirely negative.



Fig. 2. Chest X-ray on admission to the medical ward. There were prominent enlargement of cardiac silhouette and right pleural effusion.

Fig. 3. Autopsy finding of the heart. Upper arrow indicates a left atrial myxoma, which was attached to the posterior wall of the atrium with a pedicle. Lower arrow indicates multiple infarct scars of the anterior wall.

Immunoglobulins of the blood were IgG 700 mg/dl, IgA 107 mg/dl, IgM 22 mg/dl. The chest roentgenogram on August 8, 1970, showed diffuse small miliary nodular infiltrations throughout both lungs. Culture of the sputum revealed *Neisseria*, *Klebsiella* and *Candida*, but no tubercle bacillus. The erythrocyte sedimentation rate was 62 mm/h, CRP 6+. The remittent fever responded poorly to steroid and antibiotics administration. However, in the end of August, the temperature fell to normal ranges spontaneously. The chest x-ray showed no definite infiltrations any more. Electrocardiograms revealed tall and peaked P waves, without any remarkable ST-T changes. In the beginning of September, the patient suffered the third attack of the anemia, marked thrombocytopenia and leukocytopenia accompanied by hemorrhagic tendency at the same time. He was given 200 ml of whole blood transfusion, but his general condition rapidly deteriorated and on September 15, 1970, he died of the right pneumothorax.

Main Autopsy Findings :

Heart (Fig. 3): Weighed 340 g. In the left atrium, a pedunculated gelatinous tumor in the size of $6 \times 4 \times 3.5$ cm was found. It was attached to the posterior wall of the atrium with a pedicle laying its apex within the mitral valve cusps. Grossly and microscopically, the tumor was a myxoma. The left atrium and ventricle were dilated and the left ventricle was hypertrophied. There were obliterative endarteritis of the descending branch of the left coronary artery (Fig. 4) and multiple infarct scars of the anterior wall.

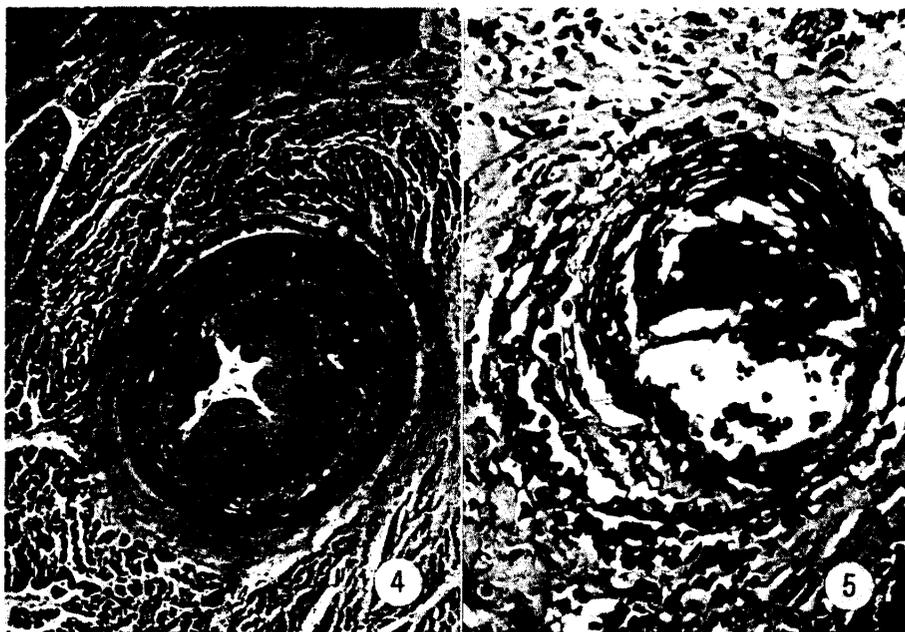


Fig. 4. Transverse section of the descending branch of the left coronary artery. The vessel is markedly narrowed, both by prominent intimal proliferation and organization. $\times 100$.

Fig. 5. Transverse section of a small pulmonary artery in the areas of interstitial fibrosis. There are medial hypertrophy and intimal proliferation accompanied by thrombus formation. $\times 400$.

Lungs: There were left fibrinoid pleuritis and right spontaneous pneumothorax. Microscopic observation showed interstitial fibrosis, hemorrhagic infarctions and pneumonia with partially organized fibrinous exudation of the bilateral lungs. Cytomegalic inclusion bodies were seen in the right middle lobe. In the areas of interstitial fibrosis the small and medium sized pulmonary arteries were often markedly narrowed. Histologically, this was obliterative thrombotic endarteritis (Fig. 5).

The liver weighed 1560 g. There were fatty infiltration, bleeding and fibrinoid necrosis of the central areas.

DISCUSSION

The case presented above was a typical case of the left atrial myxoma, and satisfied almost all of the symptoms of diagnostic criteria for cardiac tumors described by GOODWIN (1). However, the most interesting features of this case were the associated attacks of severe pancytopenic syndrome and obliterative endarteritis of the cardiopulmonary system.

Anemia is often mentioned among the systemic manifestations of atrial myxoma. But the anemia accompanying left atrial myxoma is occasionally caused also by mechanical hemolysis (1). It is said about this symptom that very similar pathologic abnormalities of red blood cells are seen in patients with heavily calcified aortic valves (2) and prosthetic valves (3). The red cells are destroyed in excessive numbers by the damaging effect of the moving tumor. VUOPIO and NIKKILÄ (4) reported a case of left atrial myxoma associated with mitral stenosis which developed profuse hemolytic anemia with increased level of serum indirect bilirubin and thrombocytopenia giving rise to petechial bleedings. Morphologic observation indicated this hemolytic anemia was induced by the intense erythropoiesis. They suggested that both red blood cells and platelets were destroyed or injured in the intracardiac blood whirls.

An additional interesting feature of this case was leukocytopenia, which might have been produced also by mechanical leukocytolysis. Three attacks of the pancytopenia seemed to occur when the red cell counts exceeded $300 \times 10^4/\text{cmm}$.

In cases of left atrial myxoma, general constitutional disturbances may be seen (1, 5, 6, 7). These are cachexia, fever, anorexia, malaise, high erythrocyte sedimentation rate, abnormal serum proteins, anemia and positive C-reactive protein. The symptoms may mimic the collagen diseases. The etiology of the general constitutional symptoms is unknown, but there have been described some immunological speculations, which include systemic reaction due to hemorrhage or necrosis of the tumor (5), immune response to fragments of tumor released into circulation (8), and autoimmune state analogous to that seen after cardiotomy or myocardial infarction (9). The case of atrial myxoma described by GATT and his associates (10) responded to steroid. Administration of steroid in our case increased urinary output followed by improvement of congestive heart failure.

Autopsy findings in our case of the obliterative endarteritis of the pulmonary arteries and the hemorrhagic infarctions with intricate pulmonary

changes might have been caused by pulmonary hypertension, which was assumed to be due to mitral block caused by atrial myxoma. In the left atrial tumor, the pulmonary hypertension develops by the same mechanism as in mitral stenosis (11). Here the pulmonary vascular changes are very similar to those found in mitral stenosis, with medial hypertrophy of muscular pulmonary arteries and exudative changes with pulmonary congestions and hemosiderosis with interstitial fibrosis. The cases of left atrial myxoma reported by SOLOMON (12) and HARVEY (6) showed interstitial pulmonary fibrosis secondary to pulmonary venous hypertension. ANDREWS' case (13) showed interstitial pulmonary fibrosis and obliterative endarteritis of the lung. It is considered that these changes can be placed in the category of pulmo cardialis (14). It is assumed that the obliterative endarteritis of the left coronary branch in our case might cause multiple infarctions of the anterior wall of the left ventricle. The possibility of thrombotic thrombocytopenic purpura was excluded by the absence of platelet thrombosis at autopsy. In addition to these changes, bacterial or viral infections per se and additional allergic inflammations caused by the infections seemed to have caused complicated pulmonary changes.

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