A Case with the Primary Hemangio-fibrosarcoma of the Left Atrium

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The case was a female patient 56 years of age, admitted with chief complaints of the palpitating heart and dyspnea. She frequently had seizures of acute pulmonary edema with occasional febrile condition. She was suspected of the mitral valvular disease or bacterial endocarditis.

A diagnosis of the tumor of the left atrium of the heart was also under consideration in view of the fact of changing quality of the heart murmur with respect to posture was observed, and with further chest X-ray evidences of abnormally expansive cardiac shadow as well as pronounced configuration, supported by successive increase in the cardiac silhouette. The diagnosis was conclusively made by angiocardiology.

The patient became progressively worse and died of acute pulmonary edema 14 months after the onset of symptoms. In the terminal stage, a metastatic tumor was found in her trunk of the left femur.

The autopsy revealed a huge tumor in the left atrium of the heart which practically occluded the enlarged heart chamber. Microscopic diagnosis of the hemangio-fibrosarcoma was made.

THE CASE

Patient: Fifty-six years of age; female, married.

Chief complaints: Dyspnea and palpitation on effort.

Family history: Five brothers, one died of pulmonary tuberculosis.

Past history: Always in good health and never had rheumatic fever nor any other infectious disease. Mantoux's test was positive.

Present illness: On about the middle of January, 1962, the patient had an attack of sudden heart palpitation during sleep and she was able to control the symptoms by keeping quiet. However, the condition got progressively worse, slight exertion caused frequent attacks of palpitation, cold sweat and dyspnea. In the middle of May, 1962, the patient fever up to 37° to 38°C and became weaker. Febrile condition was under control upon treatment, but cardiorespiratory attacks continued and had 4 to 5 spells per month. In September, 1962, the symptoms and signs relapsed with recurrent fevers and aggravated. In October, 1962, the patient was admitted to Kobe Medical College Hospital, and diagnosis of mitral valvular disease was made. Her condition then was fair, having normal appetite and slept better. Prior to admission the patient had no habit of smoking or alcoholic drinks.

Condition on admission: Present status—Height 156.2 cm. Weight 51.5 kgs. Her mental condition was clear. The skin was moist and slight pallor of face observed. Blepharconjunctiva showed anemia. Both pupils were equal in size and reacted light and accommodation. The throat and tonsils were negative. The rate of respiration was 20 per minute and with normal breathing. Temperature was 37.2°C. No lymphadenopathy or enlarged thyroid noticed. Thorax was in normal in shape. Cardiac dullness was enlarged to both sides, the right side

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was within the sternal edge, while the left extended a fingerbreadth from the left nipple line. Systolic cardiac murmurs were heard over the apex, accompanied by diastolic rumbling, though it was rather feeble. Accentuation of the second pulmonic valve sounds was noted. Percussion and auscultation of the chest cavity were normal. The abdomen was flat. Knee reflexes were normal and no abnormal reflexes were found.

Laboratory findings: Erythrocytes sedimentation rate, Westergren method (E.S.R.) was 103 mm. in an hour and 123 mm. in two hour. Elbow venous pressure 132 mm H₂O. Circulation time (by Dehicol) was 13.1 seconds. Red blood cells were 357×10^4 per cu. mm. Hemoglobin 10.0 gm/dl. Hematocrit value 25 per cent. White blood cells 7,200 per cu. mm. Blood platelets 156,000 per cu. mm. White blood cell differential count showed 68 neutrophils, 6 monocytes, 22 lymphocytes. A slight anemia was observed. Serum protein 6.8 gm/dl., serum urea nitrogen 15.4 gm/dl. Bromsulphalein Excretion Test 12.5 per cent (value at 45 minutes), C.C.F. (—). Serum G.O.T. 29 Karmen unit, serum G.P.T. 18 Karmen unit. Serum iron 80.6 γ per cent, serum copper 206.3 γ per cent. Fraction of serum protein, total protein 6.8 gm/dl., albumin 35.2 per cent, α_1 -globulin 7.8 per cent, α_2 -globulin 11.8 per cent, β -glob-

ulin 18.9 per cent, γ -globulin 26.3 per cent, and A/G ratio was 0.54. Serologic tests for rheumatoid arthritis (Latex) (—), serum anti-streptolysin O titer 125 Todd unit. C reactive protein test (—), serologic test for syphilis were negative. Phenolsulfophthalein Excretion Test 15' 23.6 per cent, 120' 62 per cent, Urinalysis showed protein (—), glucose (—), urobilinogen normal and no abnormal finding of the sediment. Fecal examination showed parasite egg (—) and occult blood reaction (—).

Bacterial culture of arterial blood was negative. Sputum culture was normal. In the function test of lungs percentage of observed per predicted vital capacity 65 per cent, percentage of forced expiratory volume per fast vital capacity 63 per cent, basal metabolic rate 18 per cent, arterial blood oxygen saturation 79.5 per cent, chest X-ray film showed the expansions of the heart, particularly the left 2nd arch was abnormally expanded (Fig. 1). No anomalous

Fig. 1. Chest X-ray.

Fig. 2. Electrocardiographic findings in the early and late stage of hospitalization; Lowering of QRS and occasional atrial fibrillation seen in the left column.

shadow was observed in the lung fields. Electrocardiography (ECG) indicated the findings of sinus tachycardia with the right axis deviation (Fig. 2).

Clinical course: Febrile condition continued with increased red blood cell sedimentation rate and cardiopulmonary condition also persisted. Antibiotic course of therapy was given several times. The results of bacterial culture of arterial blood were always negative.

Although remittent fever continued to appear, E.S.R. had improved slightly to 24 mm. in an hour and 52 mm. in 2 hour. The patient still had frequent complaints of palpitation and suffered from coughs, and expectoration with mild dyspnea. Sputum were usually mucoid and

white in color but contained blood at times. Systolic murmurs were audible over the apex. Sometimes the murmurs become louder but diastolic murmurs were also heard. In early week of December, 1962, injection of aminophylline was seemed to be effective when ushered with dyspnea, while the patient complained of loss of appetite, disturbed sleep and general weakness.

From the middle of December, 1962, dyspneic attacks became more frequent with accompanying cyanosis, orthopnea, sweats, rise in blood pressure, cough, expectoration and the findings of rales in the lungs. At first it was considered as the case of pulmonary edema caused by mitral valvular disease, however, di-

Fig. 3. Angiocardiographic findings; Delayed visualization of the left pulmonary arteries, showing obstruction of its trunk. (a). Engorged pulmonary veins in the right side and downward deviated left atrium. (b).

Fig. 4. Effective trial of intravenous administration of 10 mg. Regitine to dyspnoeic episode due to pulmonary edema characterized by the high blood pressure.

agnosis of the heart tumor in the left atrium was made following the angiocardigraphy (Fig. 3). Administration of regitine at times showed relief for dyspnea (Fig. 4). When cyanosis appeared with dyspneic condition, intermittent positive pressure breathing (I. P. P. B.) was tried for relief. Digitalization with Lanatoside C and Digitoxin was given for treatment which was found to be effective (Fig. 5). February, 1963, chest examination revealed no signs of breath sound audible, while rales were heard clearly in the lower field of the right lung. Hydrothorax of the left side was found. Thoracentesis revealed light yellowish transudate which was found to contain no malignant cells. By this time, E.C.G. showed the lower voltage, comparing with the time of admission (Fig. 2). A month before this time, January 1963, a tumor on the left thigh which had developed to a size of fist was discovered. The roentgenogram of the femur revealed abnormal osteogenesis (Fig. 6). By March, 1963, the patient became gravely embarrassed with breathing distress with

cyanotic appearance which had occurred several times a day. Intermittent positive pressure breathing and cardiotonics were the means of getting over critical condition. In the morning of March 20th, the patient went into a fatal shock when she tried to urinate and never recovered from the condition despite various emergency medications attempted.

Autopsy Findings: post mortem the heart was remarkably enlarged, weighing 830g. This enlargement was due to a large grayish white tumor mass of irregularly bumpy surface, apparently arising from the posterior wall of the left auricle. The tissue of the enlarged tumor

Fig. 5. Clinical features in course of digitalization.

Fig. 6. The metastatic tumor to the femur of the left side.

Fig. 7. Autopsy findings of the heart: The tumor grayish white in color with the uneven bumpy surface covering the entire left atrial wall extending to the posterior of the left ventricle.

had on the one side, extended into the posterior wall of the left ventricle, and on the other side had protruded into the left atrium chamber occupying one half of the left auricular cavity, moreover, not only had it brought forth stenosis of the orifices of pulmonary vein but a small pedunculated tumorous mass had extended into the mitral valvular region (Fig. 7 and 8). Other than unusually large tumor in the left auricle, there were several small tumors in the left ventricular wall. The aortic, mitral and pulmonary valves themselves showed no significant pathologic changes. In the pericardial cavity there was roughly 50ml. of clear yellowish fluid, while the left thoracic cavity contained about 1000ml of similar fluid.

Excepting the metastatic tumor of fist great in the shaft of the left femur, which shows similar structural nature with the tumor of the heart, both macroscopically and microscopically, there was no existence of metastatic tumor tissue and cell in the other organs.

Microscopic Findings: Histological examination of the cardiac neoplastic tissue was made on the several different parts, and each sections showed various histological features. That is; in one part, the section consisted of abundant fibrous spindle cell elements, in an conspicuously irregular arrangement, with the marked atypical nuclei of irregular shape and of abundant chromatin contents. These cells, in some parts, frequently arrange in line and form a lumen

Fig. 8. Autopsy findings of the heart: The tumor protruded into the left atrial chamber occupying one half its cavity, resulting in the occlusion of many pulmonary veins. An accessory tumor, one of the small pedunculated mass contributed to the postural obstruction of the mitral valvular area.

structure, which can easily be taken for the endothelial cells (Fig. 9). By silver impregnation staining, there were apparently the formation of capillary vessels (Fig. 9). In another parts, there were occasionally some larger cells, which contain a bit larger and chromatin rich nuclei, and at the same time, the irregularly structured eosinophilic cytoplasm, indicating of possibility of myogenic neoplastic cells (Fig. 9). However, the peculiar striation structure could not be proved by any staining method. In the several sections, particularly in the middle of neoplastic tissue, the lesions became remarkably edematous and were scanty of cell elements. In this area, the special substances such as lipids or glycogen were not identified, therefore, it assumed reasonably to be a sort of myxomatous degenerated changes. Examination of the tumor in the shaft of femur showed identical histological findings with as those in the heart, these cells were mainly of spindle cells and in some part the capillary formation was observed.

From the above mentioned point of view, the neoplastic tissue originating from the left atrium of the heart was diagnosed pathohistologically as "hemangio-fibrosarcoma".

The other postmortem findings were the atelectasis of the left lung, and pulmonary edema of the right lung. Hepatic cells presented marked atrophy throughout the organ. The liver, spleen and kidneys were all congested. No significant pathologic changes were observed in the other organs.

DISCUSSION AND SUMMARY

The primary tumor of the heart is found to be comparatively rare, as RAVID¹ (1943) found only 0.05 per cent among all primary tumors. STRAUS and MERLISS² (1945) reported only 8 cases, viz. 0.0017 per cent against 480,331 autopsy cases found in available statistics from 1938 to 1942. The primary tumors of heart usually comprised of myxomas, sarcomas, hemangiomas, fibroma, rhabdomyosarcoma and hamartoma, of these the myxoma takes the greatest number and sarcoma is in the next place. PRICHARD³ (1951) reported that 113 sarcomas were found in 915 tumors of the heart, while CHENG and SUTTON⁴ (1955) picked up

134 sarcomas and JANAS⁵ (1963) 181 sarcomas. Of 113 cases of sarcomas, PRICHARD found 62 in the right atrium, and metastasis to the lung, lymphatic glands, liver, kidney, pericardium and pancreas have been observed with ratio more than 30 per cent. It is said that "Spindle-cell" sarcoma including fibrosarcoma, fibromyxosarcoma, myxosarcoma and leiomyosarcoma have occupied the majority of the primary sarcoma of the heart, followed by the "round cell" sarcoma like lymphsarcoma, reticulumsarcoma and occasional deformities of the angiosarcoma or rhabdomyosarcoma. Present case appeared more like the fibrosarcomatous tissue mixed with angiosarcoma.

Classification seemed indefinite but it should be named hemangiofibrosarcoma. BORMAN and REIN⁶ reported an example of "Primäre fibro-

angioplastische Geschwulst in linken Herzvorhof", which he classified as the fibrosarcoma, presenting no malignant tissue findings but reported involvement of metastasis in bone and brain. WOLL and VICKERY⁷ reported a case with bone metastasis of the heart fibrosarcoma, while MCNAELLY⁸ collected the angiocardio-sarcomas and found an example of bone metastasis. It is quite reasonable to diagnose this case the primary hemangiofibrosarcoma of the heart for the following reasons that the tumor was fairly large which had metastasized into the myocardium and marked bone involvement was found a long after the symptoms of heart failure complained. PRICHARD reported that of 146 cases of metastatic heart tumors, the sarcomas were 26 cases, and only 2 cases of metastasis from primary bone sarcoma. Primary tumor of the heart

(a)

(b)

(c)

a) shows the fibrosarcomatous pattern.
(Hematoxylin-eosin staining $\times 40$)

b) & c) higher power photomicrograph of Fig. a.
The cells arranged irregularly with nuclei
of the various form rich in the chromatin.
(Hematoxylin-eosin staining $\times 100$a
 $\times 400$b)

Fig. 9. Microscopic findings of the neoplastic tissues in the heart and femur;
a)-f): Sections from various parts of the cardiac tumor.

is rarely diagnosed before death, and the percentage is as well as 2.7 per cent. Integrated correlation of clinical symptoms, chest X-ray film, cytohistological study, angiocardiology and intracardiac catheterization is the effective means to diagnose the primary tumor of the heart. With reference to the clinical symptoms, YATER⁹, GOODWIN¹⁰, and GRIFFITHS¹¹ explained them in details.

The occurrence of primary tumor of the heart, both in the left or in the right atrium, accompanies dyspnea on effort, the general fatigue, cyanosis, syncope, vertigo, chest pain, fever and hepatomegaly. GOODWIN explained the clinical

features of the heart tumor in the left atrium with three points, namely obstructive, embolic and constitutional effects. For obstructive effect, enumerated the pulmonary hypertension, dyspnea, shifting mitral murmur, auscultation of mitral opening snap, syncope and vertigo. For embolic effects, mention was made of embolic phenomena and fever, increased rate of red blood cell sedimentation, abnormal condition of serum protein, decrease in weight and anemia have been referred as the constitutional effect. He explained that the combination of the above three effects will be an important key for the differentiation of the mitral disease particularly

(d)

(e)

(f)

(g)

- d) the nuclei are a bit larger and of the abundant chromatin with the eosinophilic cytoplasm, but no striation structure in cytoplasm.
(Hematoxylin-eosin staining $\times 400$)
- e) shows the tendency of the capillary formation, which can be also taken for the endothelial cells.
(Hematoxylin-eosin staining $\times 400$)
- f) the same tissue as previous figure, showing the pattern of capillary vessels outlined by argyrophile fibrils.
(Silber staining $\times 400$)
- g) the histological picture taken from the tumor in the left femur shows the varieties of features identical with those in the heart.
(Hematoxylin-eosin staining $\times 40$)

mitral stenosis from tumor of the heart.

At the time of admission, there were some doubt as to mitral disease or endocarditis. Angiocardiology was tried because of suspect of whether the abnormal enlargement of the mediastinal shadow was originated from the tumor of the chest or the heart (Fig. 3). As the results, we diagnosed the case as tumor in the left atrium for the following three facts, viz. (1) the left pulmonary arterial trunk was narrower in comparison with the right pulmonary trunk, (2) the left pulmonary vein shadow could not be visualized yet when the aorta could be seen and (3) the left atrium had deviated to the right and downward, and tumor shadow pressing the left pulmonary artery and the left ventricle. Angiocardiology, in case of tumor of the heart, is quite essential in diagnosis as STEINBERG et al.¹² stated. It is indispensable not only when the heart shadow becomes widened due to the unexplicable causes, in other words, in cases suspected of enlarged pericardial sac, formation of the cyst adjacent to the heart or the mediastinal tumor or pulmonary tumor, but also when shifting cardiac murmur of the tricuspid stenosis or mitral stenosis were detected. Retention of the pericardial fluid is often a sign of the tumor of heart. TACKETT et al. had observed tumor cell in the fluid, though we failed to observe.

There were no pathologic electrocardiographic finding made at the time of admission, but as the disease progressed low voltage and absolute arrhythmia appeared (Fig. 2). No attempt was made of intracardiac catheterization because of the grave condition, however, detection of pulmonary hypertension is a diagnostic corroboration. Observation was made of A/G ratio 0.54 signifying decreased albumin and increased globulin, which may serve to offer some guide in diagnosis. With antibiotic therapy, fever was controled and red blood cell sedimentation rate showed some improvement. Because of slow response, Chromomycin A3, an antitumor agent was combined. Bacterial infection seemed to be apparent because of a short remission. The patient developed acute pulmonary edema with the symptoms of substernal oppression, blood pressure elevation during respiratory distress, tachypnea, tachycardia and

orthopnea. Physical signs of cold sweats, cyanosis and rales became noticeable as pulmonary edema advanced. Occurrence of pulmonary edema is probably due to pulmonary capillary congestion as the result of pressure of the tumor as explained as "obstructive effects" by GOODWIN. In view of the fact that pulmonary edema occurred and disappeared incidentally with the postural change pulmonary edema may be developed acutely. Consequently obstructive effect can definitely cause nervous reflex and influence progressively the pulmonary congestion. Pulmonary process are well explained by the effectiveness of regitine. It is true that pulmonary edema had been reasonably controlled by Lanatoside C, so the left ventricular failure was possible cause of the pulmonary episode though no hypertrophy or dilatation of the left ventricle could be found in the autopsy.

Death ensued eventually following of weeks of marked period of dyspnea, cyanosis and comatous condition.

Death is attributed to advanced anoxemia due to circulatory interference following 14 months of protracted illness.

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