Refractory Pleuropericardial Effusion, Cardiac Tamponade and Congestive Heart Failure as the Initial and Major Manifestation in the Lymphosarcoma

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THE MALIGNANT LYMPHOMAS are known to involve the heart as frequently as the cancer of the breast, lungs and melanoma^{3,6,9,10,13,14,18,24,25,29}. However, cardiac involvement invariably occurs during the terminal phase of lymphoma or the phase of general dissemination, and its clinical manifestation is relatively rare. This situation led us to report an unusual case of lymphosarcoma which was initiated with refractory pleuropericardial effusion and cardiac tamponade preceding any detectable lymphoadenopathy.

CASE REPORT

First Admission

The patient is a 31 year-old gas station service man transferred from another hospital on November 6, 1963, because of refractory pleuropericardial effusion and congestive heart failure.

He had been well until early August, when noted the onset of occasional precordial pain not associated with exertion. Subsequently upper abdominal distension and anorexia developed. His wife noticed that his jugular vein pulsated and distended more than previously. In the mid August he experienced palpitation, shortness of breath and excessive sweating on exertion. On the 23rd of August he was caught by acute pleuritic pain in the left back and visited a hospital where x-ray film of the chest revealed a minor left lower pleuritic change and definite enlargement of cardiac silhouette (Fig. 1). In early September he always lied on the left side. No lymphnode enlargement was noted.

On September he was admitted to another

hospital. The x-ray film of the chest revealed massive left pleural effusion dislocating the heart and mediastinum to the right. The electrocardiogram demonstrated low voltage in limb leads and left precordial leads. Left thoracentesis yielded yellow clear fluid which was Rivalta-positive. The sputum as well pleural fluid was negative for acid fast bacilli. He was put on isoniazid and streptomycin. He required numerous sedatives and narcotics for dyspnea and cough attack. He coughed up bloody sputum frequently. Thoracentesis gave almost no re-

Fig. 1. Film of the chest showing enlargement of cardiac silhouette (compare with Figure 6) and minor pleuritic change in left lower lung field.

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lief; the fluid became hemorrhagic. He was put on digitoxin, chlorothiazide and prednisolon. However, dyspnea, cyanosis, engorged jugular vein, and generalized edema developed progressively and he became lethargic and confused. He was transferred on the 51st hospital day.

Appendectomy was performed at the age of 25. He had peptic ulcer five years ago. A tuberculin skin test became positive two years ago. Family history was not contributory.

Physical examination revealed a moderately developed, markedly edematous, delirious, and restless young man lying on the left side and complaining of dyspnea and distension in the upper abdomen. The pulse rate was 120 per min. being weak especially on inspiration; the blood pressure was 110 systolic and 90 diastolic with 15 mmHg of pulsus paradoxus; the respiration rate 20; the temperature was normal. The lips and finger nail beds were slightly cyanotic. The skin was dried; the generalized edema was present especially on the left side; eyelids were very puffy allowing only scanty palpebral fissures; there were fluid wave at the left chest, and marked pitting edema on the extremities. There were few small lymphnodes palpable in the bilateral inguinal region. The palpebral conjunctiva was anemic. The pupils and fundi were normal. The jugular vein was distended tensely. The left chest was consistent

with pneumohydrothorax; the right border of the heart extended two finger breadths from the right sternal border. The apical impulse was not palpable; the heart sounds were distant; no murmurs or extrasounds were audible. The lung-liver border was sixth interspace. The blunted liver edge was palpable four finger breadths below the right costal margin. The spleen was not palpable. The prostate was normal. The neurological examination was within normal limits.

The hemoglobin was 15.0g per dl; the hematocrit 49; the red-cell count 491×10^4 ; the platelet count 21×10^4 ; the white-cell count 4200 with 73% neutrophils, 2% band forms, 2% monocytes and 23% lymphocytes. The urine specimen gave trace reaction for protein; the sediment contained one red-cell per high power field. A stool specimen gave positive guaiac test. The serum total protein was 5.7g per dl; A-G ratio 1.0; the urea nitrogen 16mg, the total cholesterol 275mg, the uric acid 4.2mg per dl. The sodium was 124 milliequiv., the potassium 4.2 milliequiv., and the chloride 85 milliequiv. per liter. The alkaline phosphatase was 2.8 Bessy units, the icterus index 7, the thymol turbidity 2. The C reactive protein was 3 + positive. The erythrocyte sedimentation rate was 5 mm in an hour. A tuberculin skin test was 1 + positive. A serum elec-

Fig. 2. Electrocardiogram revealing electrical alternans in right and mid precordial leads.

trophoretic pattern revealed increased α_2 and β globulin. An electrocardiogram revealed low voltage, and electrical alternans in the right and mid precordial leads (Fig. 2). The pericardiocentesis yielded yellow serous effusion with fibrin exsudates; the total protein was 4.0 g per dl; the cell block revealed innumerable scattered basophilic fairly uniform lymphoid cells; the nuclei varied somewhat in size and shape, and contained rich chromatin. (Fig. 3). The pleural fluid was moderately hemorrhagic; the total protein was 2.8 g per dl; the cell block disclosed similar atypical lymphoid cells. Cultures were negative.

Cedilanid and hydrochlorothiazide were

given paraenterally and diuresis of about 1000 ml per day was obtained with slight regression of edema. On the fifth hospital day massive hemoptysis developed, and dullness and course and fine rales were elicited over the right lung base; the x-ray film of the chest revealed new

Fig. 3. Sediment of pericardial aspirate revealing multiple atypical lymphoid cells.

Fig. 4. Film of the chest showing enlargement of cardiac silhouette, left pneumohydrothorax and new diffuse density in right lower lung field.

Fig. 5. Biopsy specimen of supraclavicular lymphnode revealing infiltrated capsule and atypical lymphoid pattern (right with low magnification, left with high magnification).

densities at lower lung field, enlarged cardiac silhouette and left pneumohydrothorax. (Fig. 4) On next day a lymphnode, 2 cm in diameter, was palpable in the left supraclavicular region, and was biopsied; the normal lymphnode architecture was replaced by atypical lymphoid pattern similar to that seen in the pericardial and pleural effusion (Fig. 5). Irradiation of 2200 roentgen was performed to the heart. All signs of congestive heart failure, cardiac tamponade and pleural effusion dramatically disappeared. Electrocardiograms became normal. The serial x-ray studies of the chest revealed moderate left pneumothorax with minimum effusion and slow resorption of right lower densities (Fig. 6); no mediastinal mass or lymphnode enlargement were demonstrated; the heart was small and pulsated well on fluoroscopy. During admission bilateral tonsils enlarged with granulomatous appearance and ulceration which were successfully treated with irradiation of 1300 roentgen. The patient was discharged on the 105th hospital day.

Second Admission

After discharge he had had palpitation on walking but otherwise had been doing well with

bed rest. On March 7 persistent cough developed, followed by facial edema, distension in the upper abdomen and loss of appetite. He would lie on the right and was confined to bed because of palpitation and dyspnea on slight exertion. He was readmitted on March 22, 1964.

Physical examination revealed a chronically ill young man lying on right lateral half recumbent position. The right lung base was dull and few inspiratory rales were audible. The liver was two finger breadths palpable below the right costal margin. There were few moderately enlarged lymphnodes at bilateral axillar, left supraclavicular and posterior cervical region.

The blood count was negative except for moderate hypochromic anemia. The blood biochemistry revealed increased uric acid. The x-ray film of the chest revealed pericardial effusion, right pleural effusion and enlarged right hilar lymphnodes (Fig. 7); linear pericardial silhouette was observed on lateral projection. An electrocardiogram was unremarkable.

Irradiation of 1200 roentgen was successful to prevent cardiac tamponade, but was ineffective for continued right pleural effusion. The systemic lymphnodes enlarged, and Endoxan and predonisolon were given with temporary

Fig. 6. Film of the chest revealing left pneumothorax with minimum effusion and decreased density in right lower lung field.

Fig. 7. Film of the chest showing recurrent enlargement of cardiac silhouette and right pleural effusion.

effect. The white-cell count increased 164000 with 94 % atypical lymphoid cells. The patient deteriorated progressively and died on the 62nd hospital day, May 22, 1964.

Autopsy

There were generalized reddish brown 1.5–1.0cm size ubiquitous conglomerated lymphnodes at submandibular, cervical, supraclavicular, axillary, paraaortic, retroperitoneal and inguinal region sparing tracheobronchial region where the irradiation was performed. There were hemorrhagic pleural effusion 2150ml right and 200ml left. The left pleura adhered loosely and the right firmly with the diaphragma; the bilateral lower lobe of the lungs were hypostatic and atelectatic. The pericardium was thickened and moderately adhered with the epicardium at the posterior aspect of the heart. There were 20ml of yellow transparent fluid in the pericardial space. The heart weighed 260g; the myocardium, endocardium and valves was normal. The peritoneal cavity was not significant. The liver (1580g), spleen (100g) and kidneys (180g left, 170g right) were congested moderately. The pituitary gland, thyroid, adrenals and testes were normal. The brain (1430g) was grossly normal. The bone marrow was markedly friable and hemorrhagic. The histologic pattern of the lymphnodes was consistent with lymphocytic cell sarcoma. The pericardium and epicardium were infiltrated in a spotty manner; there were calcium deposits in the pericardium. Diffuse infiltration was seen in the Glisson's sheath of the liver, spleen, small intestine and bone marrow. There was one mesenterial lymphnode which revealed total necrosis with scattered tubercle foci.

DISCUSSION

The incidence of cardiac involvement by malignant lymphoma in several autopsy series varies around 20 per cent^{3, 6, 9, 10, 11, 13, 14, 18, 21, 24, 25, 26, 29}. Generally they rarely occur without the presence of wide spread metastases; cases of solitary metastasis to the heart are extremely rare; the cardiac involvement is a part of general dissemination of the primary tumor. Authors emphasized that the antemortem diagnosis or clinical manifestations of cardiac involvement

are relatively rare. The following signs and symptoms are listed as suggestive of cardiac involvement of the malignant lymphoma as well as of the other malignant tumors: refractory congestive heart failure, signs of superior or inferior vena cava obstruction, pericardial rub and effusion, signs of constrictive pericarditis, inexplicable tachycardia, arrhythmia, conduction disturbance, electrical alternans, infarction-like EKG, irregular or unusual heart border, ball valve syndrome, syndrome of subacute bacterial endocarditis, and sudden death. However, the results of an attempt to correlate autopsy data with clinical manifestations are rather disappointing^{19, 21}. In most cases cardiac lesions represented incidental autopsy findings and were not responsible for major manifestations during life. Clinical findings suggestive of heart failure which were not improved by adequate digitalization of the patients were observed in patients who died of disseminated lymphoma without cardiac involvement, as well as in some patients with such involvement. Electrocardiograms of patients with cardiac involvement were not strikingly different from those of patients who were found not to have cardiac involvement at autopsy. Among the more reliable signs are pericardial friction rub, pericardial effusion, electrical alternans. Electrical alternans is an alteration of the form of the electrocardiographic complexes in the presence of regular rhythm²⁰. It may be incidental to a paroxysmal tachycardia, or it may occur with a heart near normal as a sign of severe myocardial disorder. In addition there have been reports of a small number of cases, usually of malignant pericardial disease, in which electrical alternans was caused by severe tamponade and was quickly relieved by pericardicentesis.

Despite the facts that clinical manifestation of cardiac involvement of previously known malignant lymphoma is relatively rare, or against the general rule that the cardiac involvement rarely occurs without the presence of wide spread metastases, there are several reports in which the initial manifestations of the lymphomatous process are those of cardiac involvement. In 1953 NABARRO²¹ reported a case of reticulosarcoma with congestive heart failure as the presenting symptom and he reviewed the litera-

authors	year	clinical symptoms	diagnosis
KEAT and TWYMAN ¹⁵	1955	congestive heart failure	lymphosarcoma
KISSIN and EISINGER ¹⁶	1962	pericarditis	reticulosarcoma
SCHACHTER et al. ²⁸	1962	paroxysmal tachycardia	lymphosarcoma
CASTLEMAN ⁷	1963	congestive heart failure	reticulosarcoma
CASTLEMAN ⁸	1964	pericarditis	reticulosarcoma

ture collecting nine such cases by malignant lymphoma which were manifested by the cardiac symptom initially. We could find the other five cases.

Since the heart and pericardium are mesodermal in origin, the lymphoma which is mesoblastic origin, definitely develops within the heart primarily and there have been reported at least 46 cases of primary cardiac malignant lymphoma. In comprehensive reviews by WHORTON³², OBRUCKER and GLASSY⁵, and SOMERS and LOTHE³⁰ until 1960 there were 178 cases of the malignant primary neoplasms of the heart. They include 20 "round cell" sarcoma, 6 lymphosarcoma, and 12 reticulosarcoma, although some of which are doubtful of their primarity in the heart³⁰. We could find the other eight cases of primary malignant lymphoma of the heart^{1, 2, 4, 12, 17, 22, 23, 27}. Signs and symptoms of primary cardiac tumors are the same with the secondary tumors of the heart as listed previously, and the absence of clinical signs and symptoms or difficulty in antemortem diagnosis are noteworthy as well.

There are no definite difference between primary and secondary cardiac neoplasm as to the clinical signs and symptoms, when the initial clinical manifestation is those of cardiac one. With the radiation or chemotherapy the course will be altered as to obliterate the anatomical conditions and the primary site will not be demonstrated on autopsy. As to the primary site of our case, there are no conclusive evidence whether it arose from the heart and pericardium, or adjacent lymphnodes, since the patient survived the first critical stage of congestive heart failure and cardiac tamponade by irradiation, however, thereby obliterating the anatomical situation which is conclusive for the determination of the primary site. Multicentric origin is the third possibility. Actually lymphosarcoma is a systemic disease, and from the clinical point of view the establishment of diagnosis of tumor and early appropriate therapy is of prime importance. In this respect cases of a long survival of malignant lymphoma with cardiac initial symptoms are more desirable than primary cardiac lymphoma which was found incidentally at autopsy.

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SUMMARY

A case of lymphosarcoma which was primarily manifested as cardiac tamponade, and congestive heart failure is presented. Irradiation caused dramatic recovery and later the patient succumbed due to systemic dissemination. The primary site was undetermined at autopsy. A discussion of primary cardiac malignant lymphoma versus secondary one is given with review of the literature.

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