VEGETATIVE ENDOCARDITIS DUE TO HISTOPLASMA CAPSULATUM

Report of a Case

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HISTOPLASMA capsulatum was first recognized by Darling[1] in 1906 as being pathogenic for man. The organism most commonly causes a benign pulmonary infection which is not accompanied by symptoms and progresses to healing with calcification. Generalized infection occurs at times, however, and in these instances the fungus usually affects the reticuloendothelial system predominantly. Involvement of the heart is of rare occurrence, 9 cases having been reported to date.[2,3,4,5,6,7,8,9,10] In 6 cases the pathologic lesions were those of an infective endocarditis, and in 2 the organisms were present only in the myocardium. In one the exact site of involvement was not mentioned. An additional case of vegetative endocarditis due to Histoplasma capsulatum is recorded in this report.

Report of Case

A white, married woman, 55 years of age, was admitted to the hospital on November 18, 1949 because of intermittent fever, a mildly productive cough, anorexia and weakness of 2 months' duration. Periods of palpitation had been experienced for several months, but there had been no symptoms of myocardial failure. She had been receiving digitalis for 3½ weeks. There was a past history of rheumatic fever at the age of 8 years.

Physical examination revealed a poorly nourished patient in no acute distress. The temperature was 99 F., the heart rate 60 per minute, and the blood pressure 128 mm. systolic and 80 mm. diastolic. There were no petechiae, and no enlarged lymph glands were noted. The lungs were clear on percussion and auscultation. The area of relative cardiac dullness extended 10 cm. to the left of the midsternum in the fifth intercostal space. Auricular fibrillation was present. A blowing systolic and rumbling diastolic murmur of moderate intensity was audible at the apex. The liver was not enlarged or tender but the tip of the spleen was palpable just below the costal margin. There was no peripheral edema.

The urinalysis and blood count revealed no abnormalities except for a slight increase in the percentage of polymorphonuclear neutrophils in the differential count. The Wassermann reaction of the blood was negative. The erythrocyte sedimentation rate was normal. X-ray examination of the chest revealed moderate enlargement of the heart with prominence of the pulmonary artery and, in the right oblique view, enlargement of the left auricle. The lung fields were clear. An electrocardiogram confirmed the pres-

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ence of auricular fibrillation and showed depression of the RS-T segments in the standard limb leads and precordial leads.

During the first 4 days in the hospital the temperature did not exceed 99.6 F. but on the fifth day it rose abruptly to 103.2 F. From then until the patient's discharge to her home on January 4, 1950, an irregular fever of 100.4 F. to 102.4 F. occurred almost daily. Five blood cultures failed to yield organisms. The leukocyte count ranged from 4,800 per cu. mm. to 6,900 per cu. mm. Repeated measurements of the erythrocyte sedimentation rate gave normal results. A smear of sternal bone marrow revealed no abnormal cells and no organisms. Three specimens of sputum were examined and all were negative for tubercle bacilli and fungi. Intensive antibiotic therapy with penicillin, streptomycin and aureomycin had no effect upon the fever.

Further roentgenograms of the chest on the eleventh day in the hospital showed irregular infiltration in the middle and lower lobes of the right lung. There had been no change in the severity of the cough, no pain and no hemoptysis. The x-ray findings cleared gradually during the following 2 weeks.

The patient was discharged to her home unimproved 47 days after admission. During hospitalization her weight had decreased from 94 pounds to 88 pounds. After being home 5 weeks she was readmitted to the hospital in a mentally confused state and complaining of pain in the lower left quadrant of the abdomen and left flank which had developed 2 days earlier. During the time at home the low grade fever, anorexia and cough had continued, and the patient had become progressively weaker.

Physical examination revealed a cachectic, dehydrated, irrational and stuporous patient. The temperature was 101.8 F., the heart rate 104 per minute, the respiratory rate 20 per minute, and the blood pressure 100 mm. systolic and 80 mm. diastolic. There was a generalized light brown pigmentation of the skin which did not involve the mucous membranes of the mouth. No petechiae were present, and there was no lymphadenopathy. The cardiac findings were unchanged, and the lungs were clear on percussion and auscultation. The spleen was palpable as before. The erythrocyte count was 5,470,000 per cu. mm., and the hemoglobin content of the blood was 14.5 Gm. The white blood cell count was 15,400, and differential counts showed 87 per cent polymorphonuclear neutrophils. The urine contained one plus albumin, an occasional pus cell and a rare red blood cell.

The daily administration of fluids by intravenous injection resulted in improvement in the mental state but the patient's condition otherwise remained unchanged. On the fifth day in the hospital, she experienced sudden severe pain in the precordial area accompanied by increased weakness and the appearance of numerous medium rales over the base of both lungs. Twenty-four hours later severe pain recurred, this time in the substernal region. Profound shock developed almost immediately, and the patient died within a few minutes.

Necropsy. The heart weighed 490 Gm. The leaflets of the mitral valve were fused, thickened and extensively calcified, and the orifice of the valve was greatly reduced and of the "fish-mouth" type. The chordae tendineae were thickened, fused and shortened. On the auricular surface of the valve there was an irregular, flattened, somewhat granular, firm but friable, brownish-yellow vegetation which measured nearly 2 cm. in diameter (fig. 1). All other valves were normal. A small mural thrombus was present in the right ventricle. There was a small fresh infarct in the lower lobe of the left lung. The spleen weighed 450 Gm. and contained one large and several small infarcts. Several recent infarcts, ranging up to 1.4 cm. in diameter, were present in both kidneys. The adrenal gland appeared normal on inspection but microscopic examination showed small foci in which the cortical cells were replaced by histiocytes, lymphocytes and rather large oxyphilic cells.

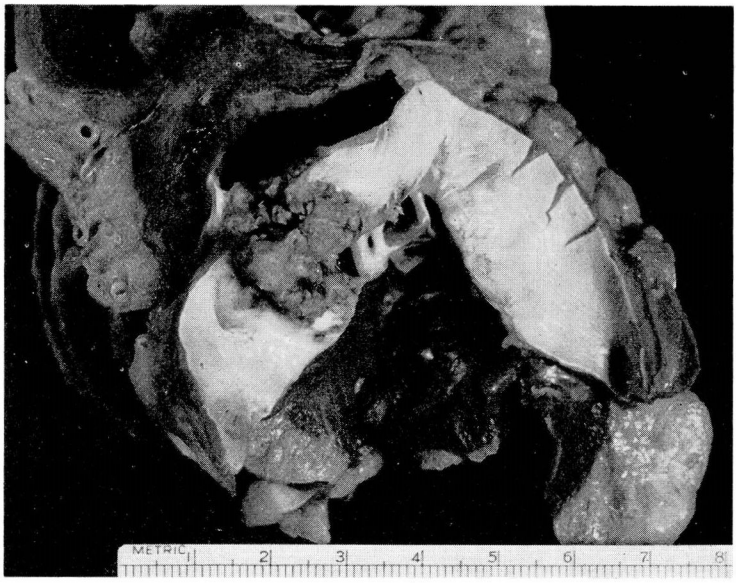

FIG. 1. Vegetative endocarditis due to Histoplasma capsulatum showing the vegetation on the auricular surface of the thickened, stenosed mitral valve.

In one of four sections of the vegetation on the mitral valve, microscopic examination revealed small collections of histiocytes containing many round, sharply outlined bodies, measuring approximately 3 microns in diameter (fig. 2). These bodies were amphophilic with Gram-Weigert stain and were readily identified as Histoplasma capsulatum. Similar bodies could not be found in the lungs, liver, spleen or adrenal glands.

Cultures of the heart blood and from the vegetation remained sterile.

The pathologic diagnosis was (1) rheumatic heart disease with mitral stenosis, and (2) vegetative endocarditis due to Histoplasma capsulatum.

Discussion

Although it was suspected early in the clinical course that the patient might be suffering from subacute bacterial endocarditis, this diagnosis was discarded because of the consistently negative blood cultures and the lack of response to antibiotic therapy. A definite conclusion as to the cause of the fever was not arrived at during the patients's life. After the postmortem discovery of vegetative endocarditis, the failure to culture organisms from the heart blood and vegetation left the etiology of the infection still in doubt. It was only after the demonstration of Histoplasma capsulatum in the section from the vegetation that the cause of the illness was established. It is to be regretted that the possibility of histoplasmosis was not considered in the differential diagnosis so that a complement fixation test and histoplasmin skin test might have been done. Christie and his associates[11] have reported encouraging results from use of the ethyl ester of

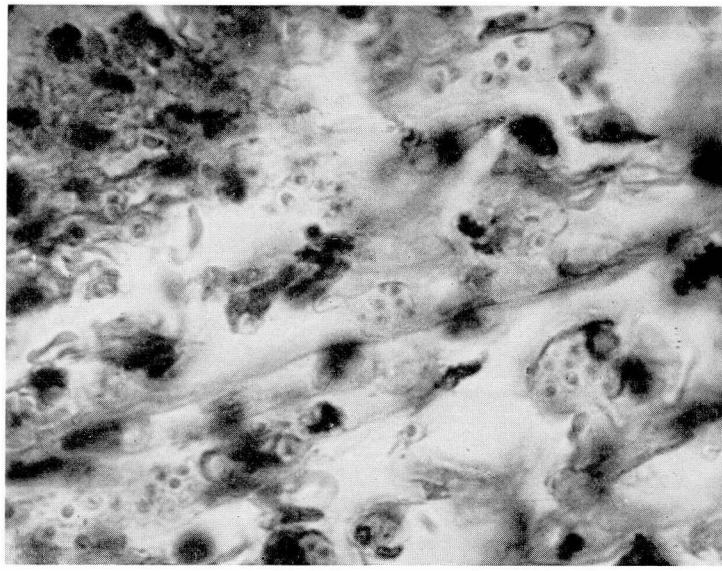

FIG. 2. Histologic section of the vegetation on the mitral valve showing histiocytes containing Histoplasma capsulatum (x850).

vanillic acid in the treatment of histoplasmosis, and it would have been of interest to have employed the preparation in this instance.

The purpose of the present report is to emphasize again that Histoplasma capsulatum is a rare cause of vegetative endocarditis. The possibility of an infection of this type should be considered whenever a case of probable subacute bacterial endocarditis fails to yield positive blood cultures and does not respond to antibiotic therapy.

Summary

A case of vegetative endocarditis due to Histoplasma capsulatum is reported in a patient who had chronic rheumatic heart disease with mitral stenosis and insufficiency.

The possibility of an infection of this type should be considered whenever a case of probable subacute bacterial endocarditis fails to yield positive blood cultures and does not respond to antibiotic therapy.

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