Coincidence of Mycotic (Histoplasma capsulatum) Vegetative Endocarditis of the Mitral Valve and the Lutembacher Syndrome

Report of a Case

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VEGETATIVE endocarditis caused by Histoplasma capsulatum is rare, although cases are being reported with increasing frequency.1, 2 What constitutes the Lutembacher syndrome is controversial.3 Usually, however, it is regarded as a combination of an atrial septal defect and mitral stenosis.4 Because of the concurrence in this instance of mycotic (Histoplasma capsulatum) endocarditis and the Lutembacher syndrome, each of which is rare, this case is reported.

Clinical Summary

A 50-year-old white man was admitted to University Hospitals March 2, 1964, because of weakness, anorexia, and loss of approximately 60 pounds of weight during the 8 months before admission. In June 1963 and in December 1962 dental work had been done without the administration of antibiotics. In December 1963 low-grade fever and progressively severe weakness suggested the possibility of subacute bacterial endocarditis, although blood cultures were sterile. There was no history of orthopnea, dyspnea, edema, or rheumatic fever, but he was known to have had a cardiac murmur since youth.

His mother and her 12 brothers and sisters were said to have died of heart attacks.

The patient appeared chronically ill and weighed only 130 pounds. The oral temperature was 101.4 F. There were no petechiae, enlargement of lymph nodes, or edema. Mild distention of the cervical veins when the head was elevated 30° and moderate degree of clubbing of the fingers were noted. The lungs were normal. The right and left ventricles were enlarged. The pulmonic second sound was increased in intensity. A loud, rough systolic murmur was heard best at the apex, and a faint opening snap was heard. A rumbling diastolic murmur was sharply localized at the apex. The liver was slightly tender and enlarged. The spleen was slightly enlarged.

Initial laboratory examination revealed anemia and leukopenia. Skin tests for histoplasmosis, blastomycosis, coccidioidomycosis, and tuberculosis were negative. Roentgenograms showed prominence of the pulmonary arteries, cardiomegaly, and perihilar interstitial edema. An electrocardiogram showed first-degree AV block, P-wave changes indicating atrial disease, right ventricular hypertrophy, and digitalis effect. Six blood cultures, done shortly after admission, and cultures of the spinal fluid and bone marrow were sterile. The blood pressure averaged 98/62 mm. Hg. Administration of penicillin and streptomycin was started; despite large doses, the patient's temperature rose intermittently to 103 F.

After 20 days of treatment with penicillin and streptomycin the patient continued to have fever and was lethargic. The antibiotics were changed to large doses of oxacillin and colistimethate sodium (Colistin). The patient had been treated since admission with digoxin, chlorothiazide, potassium, and a low-salt diet.

On March 14 a solitary petechia was found in the right palpebral conjunctiva. On March 22 many petechiae suddenly appeared in the skin of both legs. In the morning of March 28 the patient developed congestive heart failure and died.

Necropsy

The principal abnormalities involved the cardiovascular system. They included pericardial effusion, chronic rheumatic valvulitis with mitral stenosis, mycotic vegetative endocarditis of the

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Supported by Grant GM 168-06, Research Training Grants Branch, the National Institutes of Health, U. S. Public Health Service.

Circulation, Volume XXXII, October 1965 589
mitral valve, an interatrial septal defect, and microscopic granulomata of both adrenal glands. The last were probably caused by emboli from the valvular vegetations.

All valves, except the mitral, were normal (fig. 1). The atrial and ventricular surfaces of both leaflets were surmounted by large, friable, gravish-tan vegetations. There was patchy calcification of the mitral anulus and both leaflets. The circumference of the mitral valve was 7.5 cm. The free margins of the leaflets formed a typical fish-mouth appearance, as viewed from above; the valve orifice would not permit passage of a little finger. The leaflets and chordae tendineae were thickened, inelastic, and lusterless; the chordae were fused.

The average thickness of the right and left ventricular myocardium was 1.2 and 0.6 cm., respectively. The left atrium was only moderately dilated and contained no thrombi, but the right atrium and right ventricle were tremendously dilated. The heart weighed 435 Gm.

In the fossa ovalis there was a nearly circular septal defect which averaged 2.0 cm. in diameter (fig. 1). Its margins were normal. The valve of the foramen ovale was taut and somewhat retracted postero-inferiorly.

The coronary arteries showed extensive atherosclerosis, with considerable diminution of the lumina.

Both lungs and the spleen, which was approximately three times larger than normal, were the seat of recent infarction, and there were healing infarcts of both kidneys. Bilateral pleural effusion (500 ml./100 ml.), ascites (1,100 ml.), and severe, generalized visceral stasis were regarded, in part, as manifestations of congestive heart failure, as were patchy centrolobular hepatic necrosis and hepatic fibrosis.

There were recent pulmonary emboli, which were confined to peripheral radicles of the pulmonary arteries. Much of the lung parenchyma was increased in consistency. There was a moderate degree of pulmonary vascular sclerosis.

In sections stained with hematoxylin and eosin the vegetations failed to show organisms. Special stains (Grocott, periodic acid-Schiff, Gridley fungus method) revealed large numbers of fungi (fig. 2A and B). The organisms were located principally near the margins. Most were yeast

Figure 1

Lateral view of left ventricle, mitral valve, and left atrium. Mitral leaflets are covered by vegetations. Arrows indicate valvular-incompetent foramen ovale.
forms, but hyphae were also present. Both forms were often atypical in size and configuration; the yeast forms were nearly circular, except for a few which were budding, and the largest yeast form measured nearly 16 μ in greatest dimension. These organisms were regarded as atypical forms of Histoplasma capsulatum.

The adrenal glands contained microscopic granulomata in which only yeast forms of Histoplasma capsulatum were found.

Sections of the lymph nodes, bone marrow and of the pulmonary, splenic, and renal infarcts showed no organisms.

Cultures of the heart blood and spleen were sterile. Cultures of the mitral valve vegetations showed only a few contaminants.

Death was caused by congestive heart failure.

Discussion

Unfortunately, neither ante-mortem nor post-mortem cultures for fungi were made. However, the morphologic characteristics of the organism were definitely regarded as those of Histoplasma capsulatum. The atypical forms of Histoplasma capsulatum in this case were similar to those described by Binford, Moore, and Emmons et al. Dr. Chester W. Emmons, Head, Medical Mycology Section, National Institute of Allergy and Infectious Diseases, Department of Health, Education, and Welfare, Bethesda, Maryland, was kind enough to examine sections in this case; it was his opinion that the organisms in the vegetations were indeed typical and atypical forms of Histoplasma capsulatum.

The patient lived in a region in which histoplasmosis is endemic. The portal of entry in this case is unknown.

The need to obtain cultures for fungi from patients who are thought to have subacute bacterial endocarditis and from whom cultures are repeatedly sterile has been emphasized by Palmer et al. and Fawell and his associates. That this is not entirely academic is exemplified by the report of Derby and his group, in which treatment for endocarditis caused by Histoplasma capsulatum was apparently successful.

Recently, Akbarian et al. produced histoplasmonic endocarditis in dogs whose aortic valves had been surgically made incompetent. It is interesting that, apparently, in none of the valvular vegetations in which there were organisms were there atypical hyphae or yeast forms.

The severe coronary atherosclerosis was not directly related to the cause of death, but was significant in view of the family history.

The most common type of interatrial septal defect is caused by valvar incompetence of the foramen ovale. Marshall and Warden, however, did not regard patency of the foramen ovale as a true atrial septal defect. Although cardiac catheterization was not done in this case, the fact that the valvar incompetence of the foramen ovale was sufficient to produce a significant left-right shunt is supported by three observations made at necropsy: (1) there was less dilatation of the left atrium than would have been expected with mitral stenosis alone; (2) the dilatation and hypertrophy of the right atrium and right ventricle exceeded that usually observed in mitral stenosis alone; and (3) dilatation of the pulmonic valvular ring was greater than would be expected. These abnormalities are similar to those described by McGinn and White in cases with the Lutembacher syndrome. The hemodynamic alterations in the Lutembacher syndrome have been reviewed in an admirable paper by Sambhi and Zimmerman.

Summary

A case of Lutembacher syndrome in which there was vegetative endocarditis lenta of the mitral valve, caused by Histoplasma capsulatum, is presented.

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Circulation. 1965;32:589-592
doi: 10.1161/01.CIR.32.4.589

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