Mycotic Endocarditis of the Tricuspid Valve
Due to Aspergillus Flavus

Report of a Case

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A recent autopsy disclosed a large vegetation of the tricuspid valve which was composed predominantly of mycelial elements. These were identified as Aspergillus flavus by culture. This paper records the clinical and morphologic details of the case and discusses some of the mechanisms by which fungi, ordinarily nonpathogenic for man, may cause fatal infections.

Report of Case

Clinical History.—The patient, a 50-year-old white man, was admitted to Charity Hospital of Louisiana at New Orleans on Dec. 29, 1954, complaining of weakness and intermittent fever. During the previous two years he had been treated elsewhere for severe anemia and had received iron compounds, intermittent corticotropin, and 26 blood transfusions. A tentative diagnosis of chronic lymphocytic leukemia had been considered on the basis of several bone marrow aspirations that showed hypoplastic marrow containing many mature lymphocytes.

On admission a soft liver was palpable 5 cm. below the right costal margin. The spleen extended 6 cm. below the left costal margin. Moderately enlarged lymph nodes were present in the axillary, supraclavicular, and inguinal regions.

Laboratory findings on admission were as follows: hemoglobin, 6.8 gm. per 100 cc.; hematocrit, 19 vol. per 100 cc.; red blood count, 1,770,000 per cubic millimeter; white blood count, 850 per cubic millimeter; differential blood count, 40% lymphocytes, 30% neutrophiles, 12% band forms, 16% myelocytes, 1% eosinophiles, and 1% basophiles; platelets, 119,000 per cubic millimeter; bleeding time, 4.5 minutes; coagulation time (Lee and White), 6 minutes; erythrocyte sedimentation rate, 76; urinalysis, negative.

Bone-marrow aspiration was attempted, but no marrow was obtained. On Jan. 11, 1955, a surgical biopsy of the sternal marrow was performed, and this revealed the presence of many normoblasts and a heavy infiltration of the marrow with small mature lymphocytes. The findings suggested chronic lymphatic leukemia with a secondary hemolytic anemia, possibly associated with hypersplenism. A needle biopsy of the liver revealed diffuse deposits of hemosiderin pigment but no extramedullary hematopoiesis.

It was felt that splenectomy was indicated, but a staphylococcic infection at the site of the sternal biopsy developed and the operation was delayed. The patient was treated with 1 gm. of oxytetracycline, 250 mg. of tetracycline, and 30 units of corticotropin per day. After 45 days of this regimen and 19 blood transfusions, a splenectomy was performed on March 25, 1955.

The immediate postoperative course was satisfactory. Thirteen days after surgery, however, the patient became dyspneic and much weaker. X-ray of the chest revealed a pneumonic infiltrate of the right upper lobe and a small amount of fluid in the right pleural cavity. He was given increased doses of penicillin, streptomycin, and tetracycline, in addition to 20 units of corticotropin daily. Three days later, on the 16th day after splenectomy, the patient developed sudden peripheral vascular collapse and died the following day.

Histologic examination of the spleen revealed numerous deposits of hemosiderin but no extramedullary hematopoiesis. There were many small areas of granulomatous inflammation, in which no organisms could be identified.

Autopsy Findings.—The major findings were limited to the heart, lungs, mediastinal lymph nodes, and bone marrow.
The heart weighed 350 gm. Upon opening the right ventricle and pulmonary artery, a large, firm, reddish-brown polypoid mass was encountered, which measured 7x4x3 cm. The mass was firmly attached to the interior surfaces of all three leaflets of the tricuspid valve, which was virtually destroyed (Fig. 1). On section, the mass was seen to consist of dry, grayish-pink strands of friable material. The region of attachment to the tricuspid valve and the adjacent ventricular myocardium was yellow and necrotic. Fibrinopurulent material exuded from this region of the myocardium.

The lungs weighed 1400 gm. together. Both lower lobes were firm, dark red, and covered on their pleural surfaces by rough fibrinous exudate.

The mediastinal and tracheobronchial lymph nodes were enlarged and matted together. Most of them were caseous on section.

Bone marrow, taken from multiple sites, was red and appeared to be hyperplastic.

Other significant gross findings included thrombosis of the portal vein at its bifurcation into right and left branches and of the splenic artery and hemorrhage into the tail of the pancreas.

Microscopic study showed that the vegetation consisted almost entirely of branching hyphae and spores of a fungus (Fig. 2). In many areas the hyphae had penetrated deeply into the myocardium, and here the muscle was necrotic and infiltrated by neutrophilic leucocytes (Fig. 3). In several regions adjacent to the tricuspid ring, fungi had penetrated completely through the myocardium and were accompanied by an inflammatory reaction extending to the epicardial surface.

The visceral pleura of the lower lobe of both lungs was thickened. This thickening was composed of fibrin and collagen deposits, among which were aggregates of septate hyphae surrounded by lymphocytes, macrophages, and polymorphonuclear leucocytes. Throughout the lung substance there were small and large granulomas, consisting of epithelioid cells, giant cells, lymphocytes, and areas of necrosis. In only one granuloma were fungi identified. However, many of the veins and arteries contained masses of hyphae occluding their lumens and extending into their walls (Fig. 4).
The fungi stained poorly by the periodic acid-Schiff method but were brought out clearly with the Gridley and Bauer stains. The hyphae were large, septate, and in chains. Many round, thick-walled chlamydomospores were present. These histologic findings suggested that the fungus was probably a member of the genus Aspergillus. Cultures of the endocardial vegetation and of caseous lymph nodes yielded yellow-green colonies on Sabouraud’s agar. The conidiophores on microscopic examination revealed pitted walls. According to Gilman, these findings lead to the identification of A. flavus.

No fungi were identified in sections of the caseous mediastinal and tracheobronchial lymph nodes.

The sections and smears of the bone marrow revealed hyperplasia of all elements with areas of mature lymphocytes. No abnormal forms were identified, and no granulomas were found. In spite of the clinical and hematological findings that suggested the diagnosis of chronic lymphocytic leukemia, no unequivocal evidence at autopsy substantiated this diagnosis. In spite of the nests of mature lymphocytes in the marrow, it seemed unlikely that leukemia was present.

The portal vein contained a partially organized thrombus.

Comment

Three cases of endocarditis caused by Aspergillus have previously been reported. Zimmerman’s two cases were diagnosed histologically without cultures. Welsh and Buchness reported one case confirmed by culture. In two of these cases the vegetations were large, and each measured up to 2.5 cm. in diameter. In one case the aortic valve and in the second case both aortic and tricuspid valves were involved. In the third case there was a velvety yellow plaque, 2 cm. in diameter, on the endocardium of the right ventricle. In our case a 7×4×3 cm. polypoid vegetation attached to the tricuspid valve had propagated and partially obstructed the outflow tract of the right ventricle.

Zimmerman recently reviewed the literature and stressed the increasing frequency of fungus infections as serious complications of other diseases. He attributed the invasion, localization, and dissemination of these organisms to a combination of three factors. First, there appears to be an increased susceptibility to fungus infections in patients with any debilitating disorder. Secondly, the presence of a local lesion of the skin or mucous membranes may serve as a portal of entry. Thirdly, an ecologic disturbance between fungi and bacteria may result from various therapeutic combinations of antibiotics and hormones. The suppression of bacterial growth by broad-spectrum antibiotic treatment combined with the suppression of the inflammatory response by corticotropin and cortisone may produce an environment favorable to the growth of normally nonpathogenic fungi. Our patient was a debilitated man with severe pancytopenia who was treated by multiple broad-spectrum antibiotics and corticotropin. The portal of entry for the fungus may have been the sternal wound, but more probably was the respiratory tract. It is of interest that in both our
case and the one reported by Welsh and Buchness \(^3\) splenectomy was performed because of leucopenia. Both patients were treated with numerous broad-spectrum antibiotics and corticotropin. The two patients reported by Zimmerman \(^2\) had also received large doses of antibiotics. The anti-inflammatory properties of cortisone and corticotropin are well documented,\(^6\) as is the development of certain fungus infections during broad-spectrum antibiotic treatment.\(^6\) In our case and in those of Zimmerman and of Welsh and Buchness one or both of these factors were contributory. These findings suggest that the administration of anti-inflammatory hormones and broad-spectrum antibiotics may lead to conditions favorable to fatal dissemination and growth of fungi which are not ordinarily pathogenic for man.

**Summary**

A case of endocarditis of the tricuspid valve caused by Aspergillus flavus is reported. The history of this case and of three others from the literature suggests that ordinarily nonpathogenic fungi may produce fatal infections in debilitated patients who have been given massive doses of broad-spectrum antibiotics. The possibility that anti-inflammatory hormones, such as cortisone, play a role in the pathogenesis of such infections is considered.

Species identification was performed by Dr. John D. Schneider Jr., of the Department of Microbiology, Tulane University of Louisiana School of Medicine.

**REFERENCES**


**A Carotic Subclavian**

**Richard A. MacDoll**

The purpose of this paper is to present a case of a carotid branching high on the left side of a human male. From a morphologic standpoint it would appear to represent a branch arising from an aortic body tumor. It is unusual for at least aortic body tumors to be found as far above the aortic arch as in this case. It is possible that this tumor was found as a result of atherosclerosis. It is of interest that this tumor was found in a location that had previously been described as arising from an aortic body tumor. The normal carotid and aortic body tumors have been considered to represent a chemoreceptor system similar to the carotid sinus. The carotid and aortic bodies have been studied extensively in the past several hundred years.

**Review of Literature**

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