Sclerosing Mediastinitis and Terminal Valvular Endocarditis Caused by Fungus Suggestive of Aspergillus Species

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ABSTRACT

Cohen, Donald M., and Goggans, Eliza A.: Sclerosing mediastinitis and terminal valvular endocarditis caused by fungus suggestive of Aspergillus species. Amer. J. Clin. Path. 56: 91-96, 1971. The case of a 60-year-old woman with the unique combination of fungal sclerosing mediastinitis of at least 12 years' duration with late onset of aortic valvular endocarditis caused by similar hyphae suggestive of Aspergillus is presented. The patient was maintained in good health by repeated bronchoscopies to relieve bronchial mucoid impactions until her rapid demise after the onset of aortic valvular insufficiency. A brief discussion concerning the relationship of this case to other reported cases is presented.

Sclerosing mediastinitis with a demonstrable etiologic agent and fungal endocarditis are both uncommon. Described in this communication is a woman with mediastinal fibrosis of 12 1/2 years' duration who died of aortic insufficiency and heart failure due to destructive vegetations of two aortic valve cusps. Hyphae suggestive of Aspergillus species were demonstrated by special stains of mediastinal mass biopsy specimens obtained in 1954 and in both the mediastinal mass and aortic valve lesions found at autopsy in 1966. Ante- and postmortem cultures unfortunately were negative for fungi.

Report of a Case

A 60-year-old woman, a farmer's wife, was admitted to Harris Hospital on January 3, 1966, because of marked shortness of breath, chest pain, and increased cough with mucoid sputum. Marked pulsations of the right subclavian artery were observed. Both diastolic and systolic aortic murmurs which had not previously been observed were noted. The patient was considered to have developed severe aortic insufficiency.

The patient had first been seen by a physician in 1948 with a history of chronic cough, expectoration, and repeated attacks of pneumonitis. Bronchograms at that time demonstrated bronchiectasis involving the middle lobe of the right lung and the lower lobe of the left lung.

The patient had first been admitted to the hospital in 1953 with a 7-month history of cough, difficulty in raising sputum, fever, and shortness of breath. Roentgenograms revealed a mass extending outward from the right hilum and infiltrates in both lung bases. Bronchoscopy demonstrated a large amount of thick, tenacious, gelatinous ma-
FiG. 1. Roentgenogram taken in 1965, showing right mediastinal mass, associated tracheal deviation, and atelectasis of the upper lobe of the right lung.

ter extensive right pulmonary hilum, phrenic nerve, and esophagus were fixed in the mass. Surgical removal was considered impossible and biopsy was done. Microscopy of the specimen showed prominent desmoplasia with diffuse chronic inflammation and scattered foreign body giant cells. Histologic diagnosis at that time was “chronic granulomatous inflammation of undetermined etiology.”

The patient was readmitted to the hospital 11 more times because of recurring atelectasis and obstructive pneumonia involving one or more lobes of the right lung (Fig. 1). Bronchoscopy with removal of obstructing thick mucoid or cheesy material was necessary on 10 of the 11 admissions. Additional antibiotics used were Achromycin and Chloromycetin. Examination of peripheral blood smears disclosed eosinophilia on five admissions: 17% in 1965, 8% in 1957, 15% and 24% in 1964, and 27% in 1965. None of the cultures of bronchial secretions were positive for fungi, acid-fast organisms, or other consistent bacterial agents. The various organisms identified from multiple bronchial specimens and sputums included Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus. No evidence of heart disease was observed during early admissions, and blood pressures before the last hospitalization varied from 110/70 mm. Hg to a single high recording of 210/110 mm. Hg. VDRL serologic tests for syphilis were consistently negative.

Past history revealed no definite allergy or asthma. The patient lived in a small town in eastern Texas and helped her husband with farm work.

During the final hospitalization the patient manifested severe cardiac decompensation, with wide pulse pressures of 160/0 to 140/60 mm. Hg, pulmonary edema, and sinus tachycardia of 100 to 180 beats per minute. Roentgenograms demonstrated collapse of the middle lobe of the right lung.
and patchy areas of increased density, with marked increases of vascular markings radiating from the hilus of both lungs. Blood cultures were negative. Three days prior to death the patient became semicomatose and lost the use of her right arm and hand. Temperatures were subnormal (96 to 97 F.) during most of this last hospitalization, but terminally rose to 104 F. The patient died January 12, 1966.

Autopsy Findings

Autopsy was performed on the unembalmed body 3 hr. after death. Significant findings were limited to the chest.

Pleural Cavities. The right pleural cavity was almost completely obliterated by filmy fibrous adhesions. The left chest cavity contained 425 ml. of serosanguinous fluid.

Mediastinum. In the upper mediastinum, extending around the hilum of the right lung and superior vena cava, and between the atria of the heart, was a firm, rubbery, gray-white mass with indefinite borders. No extension to the arch of the aorta, vertebral column, or left hilum was observed.

Lungs. The right lung weighed 690 Gm. and the left, 460 Gm. The fibrous tissue surrounded the right hilum and major divisions of the right bronchi and constricted lumina only slightly in a few areas. The bronchi distal to the right hilum were markedly dilated and filled with thick, yellow-green material. The parenchyma of the right lung was firmer than normal, except in anterior segments of the lobes. The left bronchi were not prominently dilated and not encased by the fibrous mass.

Heart. The heart weighed 500 Gm. The fibrous mass enveloped the base of the heart as described above. The inner atrial walls were separated by dense gray tissue 2.5 cm. in thickness. A fine nodularity of left and right atrioseptal walls was noted in areas contiguous with the thickened septum. The anterior and medial aortic valve cusps were markedly distorted by two ovoid, yellow-tan to yellow-green, somewhat friable masses. The larger mass, 2.5 cm. in diameter, was attached to the anterior leaflet and projected downward into the left ventricle (Fig. 2). The cusp was thickened and firm. The medial aortic cusp was distorted by a 1.2 by 0.6 cm., similar, but more irregular, mass attached along the cusp margin. The fibrous tissue on the outside of the aorta appeared to extend through the vessel wall and be in continuity with the described vegetations. The mitral, tricuspid, and pulmonary valves were normal. The left ventricle was 1.2 cm. thick and the right ventricle, 0.2 cm. thick.

Fig. 2. Gross photograph of opened left ventricle, showing ball-like vegetation (indicated by arrow) on anterior aortic cusp. Separation of opened ascending aorta from pulmonary artery by thick fibrous mass is also evident, at upper right.
Permission to examine the central nervous system was refused by the family.

**Microscopic Examination**

*Mediastinal Mass.* The mass consisted chiefly of densely hyalinized fibrous tissue encompassing, but not destroying, blood vessels, nerves, and bronchi. Numerous areas throughout the tumor contained granulomatous inflammation, with macrophages, plasma cells, lymphocytes, and multinucleated giant cells (Fig. 3). In a few areas some polymorphonuclear leukocytes were seen. Gomori's methenamine-silver nitrate stain revealed broad, septate, irregular-staining and vacuolate, branching hyphae with no spore forms throughout the fibrotic tumor. Some of the hyphae had a bulbous or club-shaped tip resembling the conidial head of Aspergillus.

*Lungs.* The inflammatory fibrous mass encircling the major bronchi of the right lung extended into the peribronchial tissues engulfing the cartilage, but did not impinge upon the lumen. The basement membrane was thick and prominent, with moderate submucosal inflammatory infiltration by lymphocytes, plasma cells, polymorphonuclear leukocytes, and eosinophils. Obstructing mucoid material containing numerous eosinophils and other inflammatory cells was found in the major and minor bronchi of the right lung. Both lungs contained multiple foci of acute and organizing pneumonitis, areas of edema, and atelectasis.

*Heart.* The fibrous mass extended into the cusps of the aorta. The aortic cusp vegetations were formed by septate branching hyphae (Fig. 4).

*Other Organs.* Examination of the liver showed congestion and areas of centrilobular necrosis. No evidence of generalized granulomatous disease was seen. Embolic episodes were suggested by the multiple small splenic infarcts seen on microscopy. No definite hyphae were evident in the splenic blood vessels.

*Biopsy Specimen 1954.* Microscopic slides of the mediastinal biopsy specimens ob-
Fig. 4 (left). Microscopic section showing outer edge of aortic valve vegetation made up of branching, septate, vacuolated hyphae. Septa are not well shown in this photograph. Hematoxylin and eosin. × 1,000.

Fig. 5 (right). Microscopic section of biopsy specimen obtained from the mediastinum in 1954, showing branching, septate hyphae with club-shaped terminus resembling the conidial head of Aspergillus. Identical structures were present throughout the mediastinal mass and extending through the base of the aorta. Gomori's methenamine-silver nitrate stain. × 1,000.

tained in 1954 were restained with Gomori's silver stain and examination revealed hyphae (Fig. 5) identical to those present in the tissue removed at autopsy.

Discussion

Although the etiology of sclerosing mediastinitis in a particular patient is rarely demonstrated, multiple causes are suggested in the world literature: 2, 4, 8:

I. Infection
   A. Bacterial
      1. Tuberculosis associated with fibrocaseous mediastinal nodes, or involving the spine.

2. Contamination by bacteria secondary to esophageal or tracheal perforation into the mediastinum and other localized suppurative processes.
   B. Mycotic—histoplasmosis
   C. Spirochetal—syphilis

II. Autoimmune disease
   A. Rheumatoid arthritis
   B. Lupus erythematosus
   C. Arteritis

III. Neoplasm
   A. Desmoplasia induced by lymphomas and other malignancies

IV. Organizing hemorrhage secondary to trauma

V. Coniosis

VI. Drug reaction
   A. Possible reaction to methysergide therapy
We were unable to find a previously reported case of sclerosing mediastinitis demonstrating septate hyphae in the fibrotic process. In the majority of previously reported sclerosing mediastinitis cases associated with Mycobacterium and Histoplasma, the organisms were limited to caseous nodes and not seen in the adjacent or encircling desmoplastic process. Slides from the present patient were reviewed by Drs. Ajello and Kaufman of the Mycology Unit at the Communicable Disease Center, Atlanta, Georgia, and by Dr. Jan Schwarz of the Jewish Hospital, Cincinnati, Ohio. These reviewers agreed that the morphology was consistent with Aspergillus, but definitive identification was not possible without positive culture. The presence of broad, septate hyphae and the absence of spores rule out Candida, Histoplasma, Rhizopus, Absidia, and Mucor species.

Finegold and associates, in their review of Aspergillus infections, stated “Primary aspergillosis is encountered in bird fanciers, hair sorters, millers, threshers, and others who inhale dust or grain particles, in farmers and other workers who are constantly exposed to any form of dry or powdered vegetable matter.” Pulmonary aspergillosis is frequently found in patients with underlying bronchiectasis or asthma. The patient presented in this report was a farmer’s wife with a long history of symptomatic bronchiectasis. Plugging of bronchi by thick mucoid material containing eosinophils and resultant atelectasis and associated eosinophilia are features of allergic bronchial aspergillosis.

The patient described herein manifested no symptoms of vena caval obstruction during a 12-year history of confirmed extensive mediastinal fibrosis, although this is the most common finding reported in the world literature.

Fungal endocarditis is very rare, with only six reported cases of vegetative valvular endocardial aspergillosis in adults as of 1967. Candida and Histoplasma are the most commonly reported causative fungi. In the present case, the inflammatory process extended directly through the base of the heart into the aortic cusps.

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References