ASPERGILLUS ENDOCARDITIS, MYOCARDITIS AND LUNG ABSCESSES

REPORT OF A CASE

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The present report concerns the finding at autopsy of two pulmonary abscesses, endocarditis and myocarditis of the right ventricle. Our original premise that the abscesses were embolic from the heart was revised when the cultures revealed a different species of Aspergillus from each site.

REPORT OF CASE

An 18-year-old white man was admitted to this hospital on October 1, 1953, because of a mild fever which had begun in April 1953. Complete laboratory examinations during previous hospitalization had not revealed the cause of the fever. The patient had suffered repeated upper respiratory infections throughout his life. In March 1951 a splenectomy had been performed at another hospital for "primary splenic neutropenia." The neutropenia was corrected for at least a year but gradually returned.

Physical examination. The patient was thin and appeared chronically ill. Aside from a left suprapatellar effusion, the remainder of the findings were normal.

Progress. The patient had an intermittent fever of low grade throughout hospitalization. Numerous laboratory tests were not helpful in establishing a diagnosis; many blood cultures, including those for Brucella, were negative; routine agglutinations were negative. Until early in December there was a leukopenia ranging between 1100 and 3300 per cu. mm. A "collagen disease" was suspected and ACTH therapy was begun on October 21. The patient showed general improvement and was maintained on 17.5 mg. daily, except for a short period when oral administration of cortisone was substituted. The response to cortisone was not as satisfactory. Penicillin therapy for 1 week had no effect. On November 13 a roentgenogram revealed a diffuse fine nodularity throughout both lung fields with some coarse infiltration in the left base. On December 21 a roentgenogram of the chest showed considerable resolution of the infiltrate. His temperature continued to show daily spikes to 100 F. He spent Christmas day at home, and on returning to the hospital developed diarrhea and high fever. Stool cultures contained Salmonella choleraesuis. On January 17 a small subcutaneous abscess was drained from the right side of the neck. This proved culturally to be the same type of Salmonella. Terramycin therapy was begun on January 17. Subsequent blood cultures were negative. The ACTH therapy was discontinued on January 22. His temperature continued to spike wildly. Terminally he showed physical signs of a pneumonia in the right lung. He had further respiratory distress and died on January 31. No electrocardiograms were made terminally; all previous electrocardiograms had been normal.

AUTOPSY FINDINGS

Gross examination. The heart weighed 300 Gm. There was a velvety yellow plaque, 2 cm. in diameter, on the endocardium of the right ventricle at the junction of the interventricular septum with the posterior wall (Fig. 2). Sagittal section through the plaque showed extension of a broad zone of yellowish infiltration into the septum almost to the endocardial surface of the left ventricle (Fig. 1). The right lung weighed 1150 Gm. An abscess (Fig. 3) measuring 3 cm. in diameter with a thin soft wall was found at the base of the right lower lobe. A similar abscess measuring 1 cm. in diameter was present in the right upper lobe. Both were roughly oval in outline and did not show the characteristics of septic infaracts. The remainder of the right lung was firm, noncrepitant and grayish yellow on cut section. The left lung weighed 870 Gm. The upper lobe was firm and grayish yellow on cut section. The left lower lobe was congested and contained a large amount of edema fluid. No abscesses were present on the left side. No emboli could be found in the pulmonary arteries. An accessory spleen weighed 50 grams.

Microscopic examination. The endocardium in the area described above was covered by a fibrous thrombus containing a dense feltwork of large, septate, branching mycelia and numerous neutrophils. These mycelia (Fig. 4) extended deeply into the underlying myocardiurn. The myocardial fibers in this area were necrotic with loss of all nuclei. There was a broad zone of polymorphonuclear leukocytes at the peripheral margin of the penetrating mycelia. The abscesses in the lungs were surrounded by polymorphonuclear leukocytes and lymphocytes. The adjacent inner portion was made up of necrotic debris infiltrated by numerous septate, branching, mycelial elements showing no significant morphologic differences from those seen in the heart. Sections from all lobes of the lungs showed a varying picture. Predominately there was diffuse thickening of alveolar walls with infiltrations of lymphocytes, histiocytes, scattered neutrophils, and fibroblasts. Collagen was increased in the alveolar septa. There was diffuse fetalization of alveolar lining cells. Large patchy areas of fibrous alveolar exudate containing a few neutrophils were present. The picture varied from area to area with irregular fibrillar organization of the alveolar exudate. Many alveoli were packed with foamy macrophages. Other large emphysematous air sacs contained masses of a pink, granular, amorphous material in which large slitlike clefts were present. No viral inclusions could be found. No fungi could be found outside of the abscesses in the lung using the periodic acid-Schiff reagent technic and Gridley fungus stains. The abscesses were both located in areas of severest accumulation of the pink amorphous intraalveolar material described above.

The white pulp of the accessory spleen was diminished. The sinusoids were congested. No other abnormalities could be detected.

Cultural studies. Direct wet preparations from the lung abscesses and the heart revealed numerous mycelial elements. Culture of the myocardial lesion grew Aspergillus flavus but no bacteria. Culture of abscess from right lower lobe resulted in a growth of A. fumigatus. The right upper lobe abscess yielded A. nidulans. No mixed fungus species were found from any one site. Proteus and an alpha streptococcus were isolated from both lung abscesses and from lung tissue separate from the abscesses. No Salmonella organisms were
recovered from any site. A small subcutaneous abscess over the left trochanter contained *Staphylococcus aureus hemolyticus* and was negative for fungi.

**DISCUSSION**

The Aspergillus infection in this case is recent and represents a terminal complication. A combination of factors may have led to the fungus infection: (1) increased susceptibility manifested by the leukopenia, (2) altered pulmonary physiology secondary to the chronic interstitial inflammation and (3) therapy consisting of adrenocorticotropic hormones and wide-spectrum antibiotics. Since the neutropenia was initially relieved by splenectomy, the large accessory spleen probably was involved in the recurrence of neutropenia. The basic pulmonary disease is interpreted as a chronic interstitial pneumonia. The exact etiology is unknown. No known bacterial pathogens were isolated. Virus studies performed by inoculating filtrates intranasally and intraperitoneally into newborn mice were unsuccessful. The picture does not fit the classic description of diffuse interstitial fibrosis described by Hamman and Rich. Zimmerman discusses the prominent role played by antibiotics in disseminated fungus diseases.

The review by the Armed Forces Institute of Pathology of the slides in this case (AFIP Accession No. 659250) was in essential agreement with our findings.

The different species of Aspergillus in this case probably do not represent contamination. Each lesion was cultured on 2 tubes of Sabouraud's dextrose medium, and there were no mixed species in the same tube. Cultures from other areas of the lung were negative for fungi.

With the severe pulmonary disease, antibiotic therapy and ACTH, conditions were ideal for implantation of aerial fungus spores. The sites of abscess formation were in the areas of most severe chronic inflammation.

There is no apparent reason for the localization of infection at such a site in the right ventricle. The source of the fungus may have been from any of numerous intravenous injections.

Zimmerman reported a case of endocarditis caused by a fungus morphologically consistent with an Aspergillus species, but no cultures were made. The finding of 3 different species of Aspergillus in this case makes it imperative that all future cases be cultured from every lesion. To our knowledge, systemic aspergillosis caused by more than one species of Aspergillus has not been previously reported.

**SUMMARY**

A case of aspergillosis caused by 3 different species of Aspergillus is reported as a terminal complication of a severe chronic interstitial pneumonia of unknown etiology.

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*Fig. 1 (left upper).* Sagittal section of interventricular septum and right ventricle showing depth of penetration by fungus and myocardial necrosis.

*Fig. 2 (right upper).* Arrow points to velvety endocardial plaque.

*Fig. 3 (left lower).* Abscess of right lower lobe of lung.

*Fig. 4 (right lower).* Necrotic myocardial fibers, showing mycelia and inflammatory reaction. X 500.
Acknowledgment. Species identification was kindly performed by Dr. Chester W. Emmons at the National Institutes of Health, Bethesda, Maryland.

REFERENCES

CARCINOMA OF BREAST WITHOUT A VISIBLE OR PALPABLE LESION

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Paget’s disease of the nipple has usually been associated with some visible alteration of the skin of the breast such as an eczematoid lesion, erosion, erythema or thickening of the skin. In the present case no lesion of the nipple was visible and no lump was palpable within the breast. Although the patient reported a slight watery discharge from the nipple, the physician was unable to confirm this finding on examination. The patient had a fear of cancer and was referred to the hospital pathologist for his examination and recommendations.

REPORT OF CASE

A 57-year-old married woman complained of a watery discharge from the left nipple of 8 months’ duration. She was fearful because her mother had had a similar watery discharge from the nipple prior to development of cancer of the breast.

Examination of the breast revealed no palpable masses. No fluid could be expressed from the nipple. The patient was given glass slides and was instructed in making and fixing of smears from the discharge. These were stained by the method of Papanicolaou.

Examination of secretions from the nipple revealed some clumps of blurred, partially disintegrated epithelial cells with pyknotic nuclei and a mitotic figure. Other clumps of epithelial cells had large hyperchromatic nuclei with coarse chromatin networks and large nucleoli (Figs. 1 and 2). Some masses of hyperchromatic nuclear material were observed and some cells were undergoing karyorrhexis. Carcinoma of the ductal system of the breast was suspected and exploration of the breast was advised.

One week later the breast was explored surgically. Since no gross lesion could be found, a simple mammectomy was done.

PATHOLOGIC EXAMINATION

Gross examination. The nipple and the skin of breast appeared normal. No gross lesions were identified in the duct system. The ampulla was slightly dilated and a small ridge was seen in the main duct near the nipple.

Microscopic examination. The skin of the nipple and epithelium lining the ducts appeared normal in structure. Sections from the main duct contained clumps of cells similar to those described in the smear of the secretion from the nipple (Fig. 3). These cells were piled up within the duct and lacked orientation. These epithelial cells varied in size and shape and in intensity of staining. Nuclei were irregular in size and hyperchromatic; some cells had large nucleoli. There was no evidence of invasion of the underlying connective tissue. In additional sections of nipple the epidermis had the characteristic picture of Paget’s disease.

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