Some Aspects of Pulmonary Aspergilloma in Portugal*

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The tumor-like forms of pulmonary aspergilliosis (pulmonary "aspergilloma"), are presently by far the most frequent fungus diseases of the lungs to be found in Portugal. Since 1957, over 200 cases have been diagnosed, mostly by pathologists aware of the condition.

The fact that so many cases are not clinically diagnosed is partly due to it being impossible to recognize clinically, with any degree of certainty, certain phases of the disease process.

The pathologic study of pulmonary "aspergilloma" by one of us (J.C.P.) leads us to consider five different morphologic aspects, presumably corresponding to different stages of the disease. In an initial stage, which culminates in the "fully developed aspergilloma," one can distinguish an early phase in which the fungus is mostly alive, and a second phase during which a progressively larger portion of the fungus dies. Finally, a residual stage can be seen in which the cavitary contents are reduced to small fragments of degenerating mycelium. These may calcify and present as broncholiths or cavernoliths. The whole fungus ball may calcify giving the so-called "calcified aspergilloma." In certain cases we have found what appear to be residual aspects of pulmonary "aspergilloma," apparently not preceded by the "fully developed aspergilloma" stage. This pathologic aspect, which has no clinical translation and so cannot be diagnosed except by the pathologist, seems to correspond to a frustrated attempt at proliferation on the part of the fungus "forme fruste."

The early phases of the initial stage, before the "aspergilloma" is fully developed, are rarely found and we have only seen four cases. Probably this low incidence is due to the fact that at this stage there are no clinical or radiologic signs and to the short time it takes the fungus to attain the fully developed stage. Diagnosis at this phase is purely anatomic and is based on the finding of small fungus masses, generally no bigger than an olive, within "clean" bronchopulmonary cavities.

The "calcified aspergilloma" is also a rare form, probably because the dead fungus, as a rule, rapidly liquefies and is eliminated with the sputum so that total calcification of the fungus mass becomes an impossibility. The correct diagnosis of this form of "aspergilloma" can only be made by the identification of hyphae in the previously decalcified intracavitary concretions. This is best done using the methamine-silver staining methods, which can also be used to show up the fungus in necrotic tissue of lung abscesses.

To study the calcification process of the mycelium better, we x-rayed the surgical specimens, not only of known "aspergillomas," but of all conditions usually associated with this condition. In this way we found that in "fully developed aspergillomas" containing mostly live fungus, it is already possible to find, sometimes quite plentiful, calcified foci. On the other hand, the x-ray films of surgical specimens of bronchiectasis or "healed" tuberculous cavities, have shown up tiny broncholiths, generally widely dispersed throughout the bronchial tree of the resected lobe. These small concretions, when studied after decalcification, are seen to contain hyphae of aspergilli.

These facts lead us to believe that the endobronchial proliferation of aspergillus is very frequent, although true "aspergil-
lomas” develop only when they find the right environmental conditions.

In the cases we have examined, the distribution among the sexes is fairly even. “Aspergillomas” have been found in all ages from 10 to 63 years, the highest incidence being between the ages of 30 and 40 years (40 per cent).

In all but three cases there had been previous lung pathology. Pulmonary tuberculosis was by far the most frequent condition found (50 per cent), followed by the various types of pulmonary suppuration (25 per cent), in which bronchiectasis prevailed. Echinococcus disease of the lung was the previous pathology in 8 per cent of the cases. In most of these cases, residual pathology after operative treatment was involved, but in one patient, the fungus ball and the hydatid membrane were found within the same cavity. Staphylococcus cysts, bronchogenic cyst, silicosis, sarcoidosis and irradiation pneumonitis were the background for the “aspergillomas” in isolated cases.

Sixty per cent of the “aspergillomas” studied were found in the right lung, the great majority (80 per cent) in the upper lobes. On the right side there was a definite preference for the anterior segment of the upper lobe (24 per cent), followed by the apical segment (17 per cent), while on the left the apico-posterior segment was more often invaded (25 per cent). In the lower lobes there was a marked preference for the apical segment (75 per cent). The middle lobe was only involved in 5 per cent of the patients. Only in one case were bilateral “aspergillomas” found, and in three, the fungus developed within the pleural cavity.

Although one of the striking features of the clinical picture of pulmonary “aspergiloma” is the lack of general physical deterioration, in 8 per cent of the cases studied, poor general condition was found.

Hemoptysis was by far the most frequent symptom, having been reported by 85 per cent of the patients. In 58 per cent it was the only symptom. Signs of pulmonary suppuration were present in 32 per cent and was the only symptom in 5 per cent of the cases.

Hemoptysis was associated with pulmonary suppuration in 28 per cent of the patients.

While general symptoms, such as fever, weakness and loss of appetite were part of the clinical picture in 28 per cent, they appeared alone in only 12.5 per cent of the cases.

Only rarely did physical examination give any clue as to the nature of the disease. In one patient we heard a sudden suspension of expiration, giving the sensation of a stop valve caused by a mobile mass within the cavity.

Examination of the sputum of these patients rarely shows any particular characteristics, but in approximately 1 per cent of the cases, hard particles were noted by the patient when expectorating, and dense yellowish-brown flecks could sometimes be seen in the sputum.

Sputum cultures were positive for one of the aspergilli, generally Aspergillus fumigatus, in 35 per cent of the cases in which they were done. This depended largely on the condition and viability of the fungus at the time.

On standard x-ray film, the most frequent aspect is that of an “inhabited” cavity, giving the classic “bell-like” image. This was found in 50 per cent of the patients. The cavity was generally thin walled and cyst-like (55 per cent), but sometimes its wall was thick and irregular. The contents of the cavity were generally a rounded, homogenous, low density mass, but in some cases this was speckled with calcium and in others it was more completely calcified giving a coral-like appearance. What may be a forerunner of this latter phase is the mass of dead fungus, full of air bubbles, found in one case. In other cases, where the fungus mass has become infected and liquefied, the radiologic aspect is that of a cavity with a fluid level and, in these cases,
the diagnosis of pulmonary "aspergilloma" is impossible.

In one case, the radiologic picture was that of a retained echinococcus membrane and, on removing this, the surgeon found a fungus ball within the cavity.

Another less recognized but quite frequent aspect (35 per cent), is that of pulmonary condensations, generally segmental, but sometimes involving one or more lobes. As the anterior segment of the right upper lobe and the apical segments of the lower lobes are so often involved, the densities are often rounded (64 per cent) and have poorly defined edges. In these cases tomography will either show a mass within a cavity or a thin transparent halo that brings up the diagnosis. In these cases it is very important to take tomograms from different angles and with the patients in different positions as not only will this help to bring out the details mentioned, but will also prove the mobility of the intracavitary mass which we consider of the greatest importance in the diagnosis of pulmonary "aspergilloma."

Among other exceptional radiologic aspects of "aspergilloma" we saw what looked like the scar of what had been a tuberculous cavity but which tomogram showed not to be completely closed, a cystic disease of the lung and three cases in which the fungus mass was within the pleural space.

Bronchography was inconclusive in 37 per cent of the cases in which it was done. It showed bronchiectasis around the fungus lesion in 12 per cent and amputation of the lesion's drainage bronchus in 19 per cent. However, in 38 per cent, the contrast medium penetrated the invaded cavity, displaced the mass and gave us the diagnosis.

Although a set of rules can be set up for the differential diagnosis of "bell-like" images in the lung, we have seen so many exceptions to these rules that we felt the need for further laboratory help to make early and correct diagnoses of pulmonary "aspergillomas."

For this reason, one of us (R.A.) undertook the immunologic study of aspergillosis.

The sera of 110 patients were investigated for precipitating antibodies against Aspergillus fumigatus antigens, kindly supplied by Dr. Pepys and the Pasteur Institute of Paris. Hartmann and Toilliez's micromethod of double diffusion, and later immunoelectrophoresis according to Scheidegger were the methods employed.

The patients were divided into three groups: 1) Ten with clinical and x-ray signs highly suggestive of pulmonary "aspergilloma;" 2) 96 with chronic pulmonary conditions with which pulmonary "aspergilloma" is frequently associated; 3) four in whom a pulmonary "aspergilloma" had been surgically removed from 11 to 24 months before testing.

In the first group, precipitins were demonstrated in two cases, one proved at surgery to have an "aspergilloma" and the other refused surgery. In the eight negative cases, no "aspergillomas" were found in the surgical specimens.

In the second group, three cases showed precipitation on double diffusion, but two of these failed to give any precipitation lines on immunoelectrophoresis. On the other hand, the immunoelectrophoretic analysis of the 96 sera showed precipitation lines in two cases, only one of which was positive on double diffusion. Both these cases were proved at surgery to be "aspergillomas," one pleural, the other pulmonary.

In the third group, no precipitating antibodies were demonstrated by either method.

From these results we feel that the investigation of precipitating antibodies against Aspergillus fumigatus antigens in the sera can be of great help in the differential diagnosis of pulmonary "aspergilloma." It should become a routine test in all cases of chronic pulmonary disease, especially when there is hemoptysis, as perhaps the early diagnosis of pulmonary "as-
pergilloma" would permit medical treatment of this condition to be effective.

**SUMMARY**

The tumor-like form of aspergillosis ("aspergilloma") is at the present time, the most frequent mycotic infection of the lungs to be found in Portugal.

The various stages of pulmonary "aspergilloma," from the initial phases to the "calcified aspergilloma," and some less known forms, are described.

From the clinical point of view, hemoptysis is by far the most frequent symptom, but the diagnosis remains radiologic. Besides the classic "bell-like" image, other aspects are presented such as different types of lobar and segmental densities, calcifications within cavities, etc.

Based on a series of 110 determinations in patients suspected of having "aspergilloma" or with chronic pulmonary disease, the importance of the precipitin test in the diagnosis of this condition is stressed.

**RESUMEN**

La forma tumoral de la aspergilosis (aspergilloma) es actualmente el tipo mas frecuente de micosis pulmonar observada en Portugal.

Se describen las varias etapas de la aspergilosis pulmonar, desde la fase inicial hasta el "aspergilloma calcificado," así como formas menores conocidas. Desde el punto de vista clínico, la hemoptisis es con mucho el síntoma mas frecuente pero el diagnóstico sigue siendo radiológico. Además de la clásica sombra "en campana" otros aspectos son observados como distintas variedades de densificaciones lobares y segmentarias, calcificaciones intracavitarias, etc.

Basados en una serie de 110 determinaciones en pacientes sospechosos de aspergilloma, o con otras enfermedades pulmonares crónicas, reafirmamos la importancia de la prueba de precipitina en el diagnóstico de esta afección.

**ZUSAMMENFASSUNG**

Die tumorartige Form der Aspergillose (Aspergillom) stellt zum gegenwärtigen Zeitpunkt die häufigste Pilzinfection dar, die in Portugal angetroffen wird.

Die verschiedenen Stadien der Pulmonalen Aspergillose, von den Anfangsständen bis zu ihrer verkalkten Form und darüber hinaus einige weniger bekannte Formen werden beschrieben.

Vom klinischen Standpunkt gesehen, ist die Haemoptyse das sein weitest häufigste Symptom, jedoch basiert die Diagnose auf dem Röntgenbefund, abgesehen von der klassischen "glockenartigen" Bild, lassen sich andere Erscheinungsformen ermitteln, wie z.B. verschiedene Typen von lobären oder segmentalen Verdichtungen, Kalkeinlagerungen in Kavernen usw.

Aufgrund einer Reihe von 110 Untersuchungen bei Patienten mit Verdacht auf Aspergillom oder mit chronischer Lungenerkrankung wird die Bedeutung des Precipitin-Testes für die Diagnose dieses Krankheitsbildes besonders hervorgehoben.

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**POSTOPERATIVE TRANSIENT HYPOALBUMINEMIA**

After a surgical operation accompanied by considerable bleeding, transient hypoalbuminemia is unavoidable even with adequate blood transfusion. The cause of postoperative transient hypoalbuminemia is due to the use of homologous blood. Most of the homologous serum albumin thus given is inadequate in quality for the host. The inadequate part of homologous serum albumin is in the subfraction Fr. II obtained by hydroxyl-apatite column chromatography.


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**UREMIC PERICARDITIS AND CARDIAC TAMPOONADE**

The authors report 27 cases of chronic renal failure with uremic pericarditis diagnosed during life. All patients were treated by hemodialysis and some survived for periods up to 28 months. Cardiac tamponade occurred in 15 patients, ten of whom survived four months or more. Percardietectomy is frequently needed, but partial pericardiectomy may be indicated in some patients. The use of regional heparinization is recommended when dialyzing patients with uremic pericarditis. Cardiac tamponade needs early recognition and treatment.


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