Mucoid Impaction of the Bronchi Associated with Aspergillus*
Report of a Case

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In 1952, Hinson, Moon and Plummer described three patients with an "allergic" form of pulmonary aspergillosis. Subsequently, other physicians from England have confirmed their findings. Except for the presence of aspergillus in sputum and evidence of hypersensitivity to aspergillus by skin tests, bronchial tests and precipitins, these patients very closely resemble cases described as having idiopathic mucoid impaction of the bronchi (mucous plugs in the bronchi associated with recurrent pulmonary infiltrates which cleared after the plugs were coughed up).

Although aspergillus is worldwide in distribution, the association of hypersensitivity to this fungus with the mucoid impaction syndrome has not been reported by American observers. It is not clear whether aspergillus is a rare cause of mucoid impaction of the bronchi in this country or whether this association exists, but has not been reported. This case illustrates this association in an American patient.

Case Report:
This 26-year-old white sergeant was admitted to Fitzsimons General Hospital in January, 1966 with the diagnosis of suspected pulmonary tuberculosis. He had had pneumonias at ages 12, 19 and 24, all of which responded promptly to antibiotic therapy. In May, 1964, he was assigned to Korea as an intelligence specialist. His duties were largely clerical and no unusual exposure to birds or dusts was recalled. In November, 1964, he developed cough productive of thick white sputum. A chest x-ray film at that time was normal. No therapy was prescribed. The patient noted an unusual tendency for protracted "colds" during the winter of 1964-65. During this time, his cough would become severe and productive.

In April, 1965, he coughed up a small amount of bloody sputum. Chest x-ray film revealed an infiltrative process in the left upper lobe. (Fig. 1). A sputum smear contained spores which led the admitting physician to suspect a fungus infection of the lung. However, he was placed on a tuberculosis ward with patients with active tu-

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Figure 1: Initial admission in April, 1965 showing infiltrative process in left upper lobe.

Figure 2: Second admission with typical "V"-shaped mucoid impaction of bronchi in left upper lobe and shadow at right hilus with elevation and pleural reaction of the minor fissure.
MUCOID IMPACTION OF THE BRONCHI

FIGURE 3: Collapse of right upper lobe and partial clearing of infiltration in left upper lobe.

Mucoid impaction of the bronchi. Since his tuberculin skin tests were negative and the chest x-ray film showed rapid clearing without therapy, he was returned to duty after two weeks.

In July, 1965, a follow-up chest x-ray film disclosed persistence of the infiltrate in the left upper lobe, interpreted as old scarring of the lung. In late October, 1965, he developed afternoon feverishness, night sweats, loss of appetite and the recurrence of productive cough. In November, he noted right-sided pleuritic chest pain and a weight loss of 15 pounds. Chest x-ray film showed a "V"-shaped shadow with the apex at the left hilum, a density adjacent to the right hilum and elevation of the minor fissure (Fig. 2). His temperature rose to 101.6°F daily for a few days after admission, but thereafter remained normal without therapy. White blood cell count was 5,1000 per mm³ with 8 per cent eosinophiles.

In December, 1965, a chest x-ray film revealed fluid in the right costophrenic angle and the major fissure. Intermediate purified protein derivate skin test was now positive with 10 mm of induration. Only 5 ml of amber-colored fluid which subsequently proved sterile could be obtained by thoracentesis. Needle biopsy of the pleura showed only pleural thickening without granulomas or inflammatory cells. Pneumothorax following the pleural biopsy rapidly resolved as did the pleural effusion. Multiple cultures of the sputum and gastric aspirates were negative for tuberculosis. He was medically evacuated to the United States for evaluation of possible pulmonary tuberculosis because of the tuberculin skin test conversion, previous exposure to tuberculosis and abnormal chest x-ray findings.

On admission to this hospital in January, 1966, he was afebrile and his only symptom was productive cough aggravated by physical exertion. Physical examination was normal except for bronchovesicular breath sounds over the right upper and left lower lobes. He denied any past or family history of asthma. Urticaria had been noted after eating berries. He considered himself allergic to cats since he had developed puffiness of the eyes and itching with running of the eyes and nose after exposure.

Intermediate purified protein derivate skin test caused 13 mm of induration. He was started on INH and PAS after six sputum cultures for tuberculosis were obtained. These were subsequently negative.

In February, he started coughing up green, sour-tasting sputum in which there were "chunks of mucus." At this time, two sputum cultures

FIGURE 4: Two precipitin bands are apparent on the agar gel between the Aspergillus extract (Asp) and the patient's serum (Pat). Control serum (con) is negative.
showed abundant growth of Aspergillus. Chest x-ray film revealed collapse of the right upper lobe (Fig. 3). Bronchoscopy on March 2 disclosed inflammatory changes around the right middle lobe bronchus and complete obstruction of the right upper lobe bronchus by a white plug which could not be dislodged despite vigorous washing and suctioning. Bronchograms a week later confirmed complete occlusion of the right upper lobe bronchus. On March 15, the plug in the right upper lobe bronchus was again visualized and biopsy of it obtained. It consisted of mucus in which there were hyphae identified in culture as Aspergillus. Multiple differential white blood cell counts had revealed eosinophilia ranging from 5 to 20 per cent. Skin test with aspergillus antigen was positive. The skin test was unusual in that the site became indurated a few hours after the immediate wheal and flare had subsided. Agar gel diffusion with the patient’s serum against an extract of his aspergillus culture revealed two definite precipitin lines (performed by Dr. J. T. Poulos), (Fig. 4). Intermittent positive pressure treatments with N-acetylcysteine over the next six weeks failed to result in re-expansion of the right upper lobe. For the last two weeks, IPPB therapy was used two hours with positive and negative pressure and helium and oxygen as a carrier gas.

On April 18, prednisone in a dosage of 80 mg/day was begun. On April 24 and April 28 the patient coughed up large mucous plugs with relief of the constant tightness he had had in his right chest. The right upper lobe re-expanded. The ten-day course of prednisone therapy was discontinued and over the next few days sputum production rapidly decreased. Repeated cultures of the sputum have remained negative for aspergillus. The clearing of the infiltrations in both lungs was maintained over the next six weeks (Fig. 5), and the patient was discharged from the hospital. Repeat bronchogram revealed residual bronchiectasis in the re-expanded right upper lobe (Fig. 6). INH and PAS therapy were continued because of the tuberculin skin test conversion.

**Discussion**

This patient had blood eosinophilia, recurrent pulmonary infiltrates, productive cough, mucous plugs in the sputum, hemoptysis, fever and weight loss. These findings are commonly associated with mucoid impaction of the bronchi with or without sensitivity to aspergillus. In both conditions, a history of asthma is usual, but not invariably present. In this case, there was a definite atopic background although wheezing was denied.

The appearance of the chest x-ray films in mucoid impaction of the bronchi recently have been reviewed by Carlson et al. Changes are characteristic enough to permit a radiologic diagnosis. The filling of the second order bronchi with thick mucus often causes a characteristic “V”-shaped shadow with the apex pointed to the hilus or an elliptic shadow resembling a “cluster of grapes.” Beyond the point of obstruction, the bronchi may be dilated or the lung

**FIGURE 5:** After prednisone therapy, the right upper lobe has re-expanded. There is residual bronchiectasis in the right upper lobe.

**FIGURE 6:** Bronchogram after re-expansion of the right upper lobe showing typical bronchiectatic changes in the proximal bronchi. The distal bronchi appear normal.
may be atelectatic. A unique feature of the residual bronchiectasis is the involvement of only the proximal bronchial segments, the distal bronchi continuing to taper and branch normally (Fig. 6). In the 85 cases observed by Urschel, Paulson and Shaw,\textsuperscript{5} the upper lobes were involved twice as often as the lower lobes. Most commonly, a single lobe was involved. A main stem or first order bronchus was not involved. However, in our patient there was a mucous plug obstructing the first order bronchus to the right upper lobe. In the aspergillosis cases reported by Pepys \textit{et al.},\textsuperscript{9} second order bronchi were characteristically involved. Ellis,\textsuperscript{6} however, has recently reported two cases of aspergillosis with mucoid impaction in whom there was total collapse of a lung. More observations are required to determine whether involvement of the major bronchi is a differential point in distinguishing mucoid impaction with aspergillus sensitivity from those cases not associated with aspergillus.

Although pleural effusion as seen in our case was not described with the "allergic" form of pulmonary aspergillosis,\textsuperscript{14} pleuritic chest pain suggestive of pleural involvement as a suppurrative complication of bronchial obstruction was common in the series of Urschel, Paulson and Shaw.\textsuperscript{4}

The abundant growth from repeated sputum specimens and identification of \textit{Aspergillus fumigatus} from a biopsy of the mucous plug in the right upper lobe bronchus clearly indicate that this fungus was not an incidental contaminant in this case. Furthermore, the patient had positive intradermal and precipitin tests. However, patients without the mucoid impaction syndrome may have positive skin tests\textsuperscript{16} or positive precipitins\textsuperscript{17} in their blood. Pepys\textsuperscript{5} has postulated that both reagin and precipitin are required to produce "pulmonary eosinophilia" in association with aspergillus. He has noted a peculiar skin test reaction to aspergillus in these cases. The wheal from the positive skin test disappeared in one and one-half to two hours to be followed by an erythematous nodule and edema appearing in six hours and lasting 18-24 hours. A similar delayed induration at the skin test site was observed in our patient. Pepys\textsuperscript{5} stated that corticosteroids abolished this second phase of the skin test and also caused the pulmonary infiltrates to disappear. Severe local reactions precluded desensitization in these patients.

Campbell and Clayton,\textsuperscript{11} in reviewing 273 patients with various forms of aspergillosis, concluded that the skin test most closely correlated with "allergic aspergillosis," whereas the precipitin test was associated with infection. They pointed out that aspergillus might be present in the lung, yet the sputum culture may still be negative. This may be due to small numbers of fungi expectorated or to the tendency of the hyphae to be engulfed by macrophages.\textsuperscript{12} When sputum is negative for aspergillus in patients with mucoid impaction of bronchi, a positive skin test might suggest an association with the fungus.

Although amphotericin B is the drug of choice in the treatment of systemic aspergillosis,\textsuperscript{13} toxicity does not justify its use in the treatment of this hypersensitivity state. No reports of its use in this condition have appeared.

Shaw, Paulson and Kee\textsuperscript{1} noted that medical therapy was of little benefit, whereas resectional surgery greatly improved patients with mucoid impaction of the bronchi. Recently, it has been reported that N-acetylcysteine had been highly successful in relieving the bronchial obstruction.\textsuperscript{1} In our patient, six weeks of N-acetylcysteine therapy helped to clear the infiltrates in the left lung, but failed to lyse the mucous plug in the right upper lobe bronchus. A ten-day course of prednisone was dramatically effective in relieving the right upper lobe obstruction. It is suggested that these patients be treated by nebulization with N-acetylcysteine. If this fails, corticosteroids should be tried in an attempt to decrease the possible allergic reaction to aspergillus in the bronchus. In view of the tendency for recurrence of mucoid impaction, sur-
surgery should be employed only as a last resort.

References

Laboratory and Clinical Studies of Cephalexinidone
The new semi-synthetic antibiotic, cephalexolinidone, was effective in the treatment of 22 of 24 pulmonary and soft tissue bacterial infections due to staphylo-
coccii, pneumococcii and streptococcii. Although 18 of 18 patients with pneumonia responded well to therapy, those treated with a higher initial dose of cephalexolinidone seemed to improve and become afebrile more rapidly. Anemia developed during therapy in two patients and was the most significant adverse effect observed.

In vitro sensitivity studies of 138 Gram-positive organisms indicated that with the exception of enterococcii, the single high-concentration disc method compared favorably with the tube-diffusion method and was reliable in determining the antimicrobial sensitivity of strains of staphyloocci, pneumococcii and streptococcii to cephalexolinidone.

Bronchial Asthma and Urticaria
The authors report three cases of bronchial asthma and urticaria that presented angioneurotic edema caused by vegetable (chick-peas, French beans and kidney beans) sensitization. The food sensitization already suspected in the clinical history was demonstrated by cutaneous tests, passive transfer of the sensitization and test of provocation and suppression of the responsible allergen. Besides investigating the existence of cutaneous reagins, the existence of precipitant antibodies was studied by means of the microprecipitins technique and the Ouchterlony tests.