Treatment of Pulmonary Aspergillosis

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Treatment of most of the pulmonary mycoses has been unsatisfactory until the advent of a new antifungical drug, Amphotericin B. This has so far shown promise of being a useful addition to the meager stock of therapeutic weapons we now have available.

Aspergillosis, and particularly pulmonary aspergillosis, has not been much of a problem in the past because of its rarity. This, however, is not much help to the one patient who happens to be unfortunate enough to develop it. The increase of fungal infections seems to be general throughout this country in the past few years and may make this more or less unknown disease more frequent and increase the need for an effective remedy.

Since the lack of clinical cases, which makes this a special problem, also acts to hinder research, it is important to report results—good or bad—from any new method of treatment. This follows even though there may be no statistical value to the report.

Amphotericin B has been and is being used in the treatment of fungal infections of many types. In some cases it has proved of more value than in others. So far there is no report on its use in the treatment of aspergillosis. It has now been used successfully in one case of pulmonary aspergillosis, which is the basis of this report.

Mrs. S. Z., a 61 year old, white woman of Russian descent, gave a past history of pulmonary tuberculosis since 1937. This was treated with right-sided pneumothorax, and she was clinically well until July of 1964. Then she developed recurrence of the disease on the right side with positive sputum. She was admitted to a sanatorium and treated with streptomycin and sodium para-aminosalicylate for almost two months, at which time streptomycin was discontinued and isoniazid was substituted. The antibiotics converted her sputum and her condition improved clinically so she left the sanatorium and returned home still on antituberculous drugs.

In May of 1966, she was about to discontinue the drugs when she fell and broke a hip. This was pinned and because of the trauma from the surgery and the fracture, it was decided safer to continue chemotherapy. This was therefore continued until December 1966 when she was discharged with the diagnosis of pulmonary tuberculosis, far advanced, inactive.

Some months later she developed a cough with slight loss of weight. The cough did not respond to non-tuberculous antibiotic therapy, nor did it respond to a retrial of antituberculous drugs, including seromycin.

X-ray films and sputum examinations were negative for any change during this time.

On May 28, 1967, fluoroscopy showed the presence of air and fluid in the right pleural space, confirmed by x-ray film. She was admitted to the hospital and the fluid was aspirated. This revealed a pure culture of Aspergillus fumigatus. The diagnosis of the particular species of fungus was made at the Communicable Disease Center of the Public Health Service at Chamblee, Georgia.

Injection of dye into the pleural space at the time of aspiration and subsequent expectoration of the dye revealed the presence of a broncho-pleural fistula as had been suspected. Penicillin and streptomycin were injected into the pleural space with no particular benefit, and she ran a rather high fever during this period. When the diagnosis was confirmed, and due to the absence of other methods of treatment, and in spite of the possibility of reactivating her tuberculosis, she was started on potassium iodide, 5 grains 3 times per day. This was increased until it reached the dose of 50 grains 3 times per day. She seemed to get some benefit from this massive iodide therapy but still had fever and was quite sick.

In the beginning of July a supply of Amphotericin B was obtained through the courtesy of Doctor Hildick-Smith, Associate Medical Director of the Squibb Institute for Medical Research. Nothing was known about the dosage of this drug in the treatment of Aspergillosis, but from experience and treatment of other mycoses, we started with a dose of 10 mg. dissolved in 500cc of 5 per cent glucose and given intravenously over a period of not less than six hours. This was given daily and slowly increased, with the
exception of one day of rest. This was ordered because of a slight increase in the nitrogenous constituents of the blood and the feeling that the drug might be doing some damage to the kidneys. However, the one day of rest was sufficient to return the blood picture to normal and the medication was continued, finally reaching a dosage of 35 mg. per day by the 21st of July. On three occasions 5 mg. of a concentrated solution of the drug were injected intra-pleurally.

Her temperature, which had been running between 101 and 102°F, came down to normal a short time after the use of the Amphotericin B. Her cough markedly diminished and injection of dye intra-pleurally did not lead to presence of the dye in the sputum and therefore it was apparent that the broncho-pleural fistula had closed. She had received a total of 390 mg. of Amphotericin B over a period of 17 days. Since it was not known how long to continue and since our supply of Amphotericin B was temporarily exhausted, she was sent home.

It is of note that a fasting blood sugar was 106 mg. per cent since many cases of mycoses appear in diabetics.

We later learned that the Amphotericin B this patient had received was probably not sufficient in amount to cure the condition and unfortunately several weeks following discharge the broncho-pleural fistula re-opened and she began to run a fever. A further supply of Amphotericin B was obtained and she was re-admitted to the hospital for its administration. However, at this time examination of the pleural fluid and the sputum were both positive for tubercle bacilli and she was transferred to a tuberculosis sanatorium.

COMMENT

It is probable that the fungus was able to become pathogenic in this patient because of the lowered resistance following the fracture of the hip, the surgery necessary to repair it, and the long convalescence. Blood studies done in the hospital revealed a considerable degree of anemia upon admission which undoubtedly contributed to the lack of resistance. The anemia improved during her hospital stay with proper treatment.

At the time of development of the broncho-pleural fistula, tubercle bacilli were not found in the pleural fluid or in the sputum. The question of whether the large doses of potassium iodide used in the treatment of her mycosis before the Amphotericin B was received was sufficient to soften up the pulmonary fibrosis enough to allow a reactivation of tuberculosis cannot be answered. The re-opening of the broncho-pleural fistula with the presence of tubercle bacilli in the fluid make it possible that this second episode was actually not connected with Aspergillosis and that this actually had been healed. No fungi were found at the time of her second admission to the hospital.

Defervescence of the fever and the closing of the broncho-pleural fistula would seem to testify to the effectiveness of Amphotericin B for the treatment of Aspergillosis, whether the Aspergillus fumagatus was a primary or secondary invader.