Treatment of Broncho-Pulmonary Moniliasis by Dye Inhalation

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Often the picture of pulmonary mycosis is clinically indistinguishable from the clinical and roentgenologic manifestations produced by tuberculosis and certain primary neoplasms. If the sputum is negative for tubercle bacilli and no tumor can be demonstrated by biopsy or cytologic examination, the sputum should be examined for fungi. The following case clearly demonstrates some of the principles involved.

R.B., a 58 year old white female, entered the Jewish Consumptive Relief Society Sanatorium April 30, 1949. There was a 30 year history of pulmonary tuberculosis, during which time there had been numerous hospitalizations. On admission, her chief symptoms were incessant and distressing cough, weight loss, night sweats, and anorexia. Roentgenograms of the chest revealed a bilateral fibroid involvement extending, on the right, from the second anterior rib to the apex and, on the left, from the first anterior intercostal space to the apex (Figure 1). Twenty-eight consecutive sputum concentrates and cultures were negative when examined for tubercle bacilli. It was noted, however, that smears of her sputum contained a number of ovoid cells. In October 1949, a pure culture of Candida albicans was isolated from sputum cultured on Sabouraud's medium. The following clinical studies were made to rule out systemic moniliasis.

Renal: Urine specimens cultured for tubercle bacilli, pyogenic organisms, and fungi were negative. The phenolsulfonphthalein excretion test showed 25 per cent excretion in 30 minutes and 50 per cent in two hours. Intravenous urograms demonstrated poor excretory function in the left kidney. Cystoscopic examination showed moderate scalloping of the bladder neck with moderate trigonitis and urethritis. Ureteral catheters were passed to the renal pelvis without difficulty.

Hepatic: Thymol turbidity—10.5 Maclagen units. Cephalin flocculation, negative in both 24 and 48 hours. Serum bilirubin, 0.8 milligrams per hundred cubic centimeters. There was 10 per cent bromsulfalein retention in 30 minutes when a dose of 5 milligrams per kilogram body weight was administered. Repeated attempts at cholecystography failed to visualize the gall bladder.

Cardiovascular: Electrocardiogram within normal limits.

Skeletal: Roentgenograms of ribs and the entire spine were negative.

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FIGURE 1

Gastrointestinal: Roentgenograms revealed an essentially normal digestive tract.

Miscellaneous: Skin tests with coccidioidin and histoplasmin were positive in 72 hours.

On October 28, 1949, a course of autogenous vaccine therapy was begun. The initial dose of 0.01 cc. given subcutaneously caused no reaction, and the dose was gradually increased until she was receiving 1 cc. twice weekly. On December 15, 1949, therapy with Lugol's solution was started, beginning with five drops three times a day and increasing by one drop per day. On January 5, 1950, symptoms of iodism developed and iodide therapy was discontinued. The in vitro sensitivity of the organism to several different antibiotics was then determined (Table I).

Treatment

The patient was given five courses of brilliant green aerosol inhalation therapy, each course 10 days long. At first 2 cc. of a 0.1 per cent solution were administered five times a day. In subsequent courses, the concentration was increased until a 0.3 per cent solution was used. No toxic effects were noted. There was a marked reduction in cough and sputum volume following the second course. The symptoms did not recur even though the therapy was interrupted. At the time of her discharge, November 15, 1950, she was still free of symptoms (Table II).

Discussion

Monilia is usually present as a saprophyte without producing any reaction in the host. Of the members of the genus Candida only one species, C. Albicans, is potentially pathogenic, producing lesions in the mouth, vagina, skin, nails, bronchi or lungs, and occasionally causing septicemia, endocarditis or meningitis. Cas-
### TABLE I

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Organism grows in a concentration of 30 units per cc.</td>
</tr>
<tr>
<td>PAS</td>
<td>Organism grows in concentration of 10 micrograms per cc. of PAS.</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Organism grows in concentration of 100 micrograms per cc.</td>
</tr>
<tr>
<td>Potassium Iodide</td>
<td>Organism grows in 100 micrograms per cc. of potassium iodide.</td>
</tr>
<tr>
<td>Polymyxin Sulfate B</td>
<td>Partial inhibition in a concentration of 6.25 micrograms per cc.; complete inhibition at 12.5 micrograms per cc.</td>
</tr>
<tr>
<td>Brilliant Green**</td>
<td>Complete inhibition in 0.2 micrograms per cc. or 1-5,000,000 concentration.</td>
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*Furnished by Burroughs, Wellcome and Company, Incorporated. **Suggested by Dr. Henry Welch, Director, Division of Antibiotics, Food and Drug Administration.

### TABLE II

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/17/50 0.1 per cent Brilliant Green</td>
<td>Direct smear of sputum showed many epithelial cells and many streptococci with fusiform organisms, but no fungi seen. Culture positive for C. albicans.</td>
</tr>
<tr>
<td>4/7/50 0.1 per cent Brilliant Green (with 0.2 gram streptomycin added to each inhalation)</td>
<td>Direct smear revealed mostly epithelial cells with moderate number of streptococci although much less than previous examination. Culture positive for C. albicans. Marked improvement clinically. Decrease in cough and sputum.</td>
</tr>
<tr>
<td>4/25/50 0.2 per cent Brilliant Green (with 250 mg. chloromycetin q.i.d. orally)</td>
<td>Direct smear showed no fungi. Occasional staphylococcus and streptococcus. Culture was positive for C. albicans.</td>
</tr>
<tr>
<td>5/24/50 0.3 per cent Brilliant Green</td>
<td>Direct smear showed moderate number streptococci, but no fungus. Culture showed no growth in 24 hours; some growth in 48 hours.</td>
</tr>
<tr>
<td>6/16/50 0.3 per cent Brilliant Green (with 250 mg. chloromycetin, q.i.d. orally)</td>
<td>There were no direct smear many pleomorphic fungi which grew into yeast cell form in broth. The organism was found to grow in 25 micrograms of Brilliant Green inhibited in 50 micrograms per cc. Organism now 200 times more resistant. Clinical improvement maintained.</td>
</tr>
<tr>
<td>7/10/50 0.1 per cent Methylene Blue 11/15/50</td>
<td>Complete cessation of expectoration. Discharged; cough and expectoration still completely absent.</td>
</tr>
</tbody>
</table>
tellani's early description of pulmonary moniliasis was that of a disease closely simulating tuberculosis in its clinical picture. Fever, weight loss, night sweats, fatigue, chest pains, cough, hemoptysis, dyspnea and anemia are usually present.

Primary infection in man is generally attributed to direct contact or inhalation. In debilitated individuals, systemic infection may result from the extension of oral or cutaneous lesions. In each instance, it must be determined whether C. albicans is the primary cause of the disease or a secondary invader of some pre-existing infection. A case report of systemic mycosis (moniliasis) in a drug addict illustrates the necessity of considering the possibility of this syndrome whenever the clinical picture of subacute bacterial endocarditis cannot be confirmed by the demonstration of streptococcus viridans. Sutphin et al. investigated the relationship, in five cases, (three siblings) between idiopathic hypoparathyroidism and moniliasis. No definite conclusions were drawn, but it was noted that the moniliasis preceded the hypoparathyroidism.

In the present case, the data suggest borderline hepatic involvement. The serum bilirubin and thymol turbidity are elevated; there is an increase in bromsulfalene retention. This, however, does not appear to be on the basis of systemic moniliasis. The failure of the gall bladder to visualize indicates that chronic cholecystopathy may be causing secondary hepatic dysfunction.

One should not use brilliant green in the treatment of fungus infection unless sure that the organism is sensitive to the dye in vitro. Studies in the presence of 25 per cent serum indicate a disparity between in vitro and in vivo sensitivity. Welch found that "an organism classified as C. albicans was sensitive to brilliant green in a concentration of 1-6,000,000 for a 24 hour period. When tested over a period of 48 hours the effective concentration was 1-2,000,000. In the presence of 25 per cent serum, brilliant green was active against the organism in a concentration of 1-5,000 after 24 hours and 1-2,500 after 48 hours." He surmised that we would need a concentration of 1-100,000 in our case, but the in vivo concentration required was actually much greater.

It is possible that a more pronounced fungicidal effect could have been obtained if a greater concentration of dye had been used. The dye concentration, however, was limited by the fact that solutions of brilliant green with a concentration greater than 0.3 per cent had a tendency to clog the nebulizer. Achieving a higher systemic brilliant green level would thus involve either "dust inhalation" or intravenous administration. Stoval and Greeley have recommended intravenous gentian violet in the treatment of pulmonary moniliasis. Our patient showed satisfactory response
to methylene blue inhalation after the fungus had become resistant to brilliant green. In some cases, inhalation of gentian violet or malachite green would probably prove effective.

Streptomycin and chloromycetin were used as adjuvant therapy because a penicillin-resistant streptococcus was found in the sputum. Polymyxin B sulfate was not used because the necessary blood concentration of 6.25 to 12.5 micrograms would be inordinately high in view of the nephrotoxic properties of polymyxin.

SUMMARY

Pulmonary moniliasis, like tuberculosis, manifests itself in many ways, and does not necessarily respond to any one type of therapy. This case is presented because the gratifying clinical response to treatment suggests that brilliant green or compounds of similar structure can be of clinical value if properly used.

RESUMEN

La moniliasis pulmonar como la tuberculosis se manifiesta de varios modos y no responde obligadamente a tipo alguno de tratamiento. Se presenta este caso porque la satisfactoria respuesta clínica al tratamiento sugiere que el verde brillante o los compuestos de estructura similar pueden ser de valor si son usados adecuadamente.

RESUME

La moniliasis pulmonaire, comme la tuberculose, a des manifestations variables, et ne répond pas nécessairement à un traitement univoque. Les auteurs rapportent cette observation parce que les résultats cliniques favorables qu’ils ont obtenus grâce au traitement suggèrent que le vert brillant ou des composés de structure analogue peuvent avoir une valeur clinique, si l’on en use convenablement.

REFERENCES

1 Welch, H.: Personal communication.