BRONCHOMONILIASIS IN PORTO RICO

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Since the discovery by Castellani in 1905 that various types of hemoptysis and chronic bronchitis may be due to infection with a genus of microorganisms of the class "fungi imperfecti", known as monilia, many reports have been published of cases of bronchomoniliasis arising in tropical, subtropical and even temperate climates. It has seemed of interest, therefore, to publish in this Review a summary of our studies on a case originating in Porto Rico, together with a brief discussion of the etiology, symptomatology, diagnosis and treatment of this relatively uncommon infection.

ETIOLOGY

Castellani and Chalmers state that in Ceylon, South India and the Malay States bronchomoniliasis is generally due to Monilia *tropicalis*. They believe that the fungus is the real cause of the disease, since no other etiological agent, such as the tubercle bacillus, is found. Moreover, when the patient gets better, the fungus becomes very scanty or disappears completely. Castellani also described other non-pathogenic species of monilia in chronic bronchitis. Among these species are *M. paratropicalis, M. pinoy, M. krusei*. The present writers have found *Monilia psilosis* (ashfordi) in a case developing in Porto Rico.

In recent years there has been a widespread interest in the study of monilia in relation to chronic affections of the respiratory tract. Many types of yeast-like organisms have been isolated from the sputum of cases of chronic bronchitis and asthma by various investigators, particularly Kotkis, Wachowiak and Fleischer of St. Louis, and Steinfield of Philadelphia. Relief of symptoms was obtained in many of these patients by treatment with autogenous monilia vaccines. The St. Louis investigators assume that "the monilia are secondary or concomitant factors, although possibly they may be the chief ones in maintaining the chronicity of the symptoms. It is quite possible that some irritant agent, bacterial, toxic or mechanical, may initiate in the mucosa of the bronchus, certain

changes as a result of which the monilia are now able to grow and maintain their existence here." There is, however, at present no agreement among writers as to what constitutes the genus monilia and as to whether they have a primary or merely secondary role in the etiology of non-tuberculous chronic bronchitis.

SYMPTOMATOLOGY

Mild, intermediary and severe types of the disease are described by Castellani. The symptoms in general are: Dyspnea, cough, expectoration, with or without blood, and fever. The disease is characterized by frequent remissions and exacerbations. During the periods of remission the fungus grows less or may entirely disappear from the sputum.

DIAGNOSIS

The diagnosis of bronchomoniliasis is based upon the constant finding of a pathogenic species of monilia in the expectoration of the patient. It is difficult to rule out the significance of various bacteria such as the pneumococcus, streptococcus and staphylococcus which are commonly present in the sputum. By the method of Bull and Tao it may be shown that monilia will grow better in the blood of the patient than in normal controls (Weiss and Landrón).

The sputum should be collected after thorough rinsing of the mouth with an alkaline antiseptic solution and placed in a sterile Petri dish. Occasionally the monilia may be seen by direct microscopic examination, but usually it is best to streak the sputum (after washing it with sterile saline) over the surface of a Sabouraud agar plate pH 6.0, and to incubate at 35°C. for one to four days. One should look for rather large, creamy white, opaque colonies. By means of the low-power objective (1/6) the colonies of *Monilia psilosis* may be seen as coarsely granular in appearance. resembling a mosaic of tiny glass marbles.

A pure colony should be transplanted to various carbohydrate media in fermentation tubes and into gelatin and litmus milk. Most of the monilia do not ferment lactose, mannite, dulcite, dextrin, the various vegetable starches, or glycerin. The characteristics of *Monilia psilosis* (ashfordi) are given below.

Rabbits should be injected intravenously and into the lung to see if the strain of monilia is pathogenic and capable of producing pulmonary lesions. Many saprophytic monilia may be encountered. Other species of monilia may kill rabbits upon intravenous injection

but fail to produce pulmonary lesions, hence are considered by Castellani to be merely secondary invaders. The species of monilia is considered by Castellani to be the real causative agent when it produces in rabbits (upon injection into the lung) a number of small pulmonary nodules showing endothelial proliferation, giant cells and monilia.

DIFFERENTIAL DIAGNOSIS

Primary bronchomoniliasis should be differentiated from the secondary type not infrequently met with in cachectic diseases such as cancer, tuberculosis, diabetes, etc. In these cases the mucous membrane of the mouth, pharynx, larynx and bronchi is covered with the fungus, whereas in genuine bronchomoniliasis the mouth and pharynx are not affected. It should be differentiated from tuberculosis by the absence in the expectoration of the tubercle bacillus and the negative animal inoculations; from broncho-spirochetosis and endemic hemoptysis by the absence of spirochetes and ova of *Paragonimus westermanni.*

Prognosis is favorable in the mild cases; the intermediary types are chronic and difficult to cure, and the severe types, as a rule, end fatally.

Potassium iodide is considered to be a specific in this affection and mild cases often recover with its use. Doses of 0.50–1.50 gm. well diluted in water or milk, are given three times daily. In severe cases the drug is useless.

In addition to medication with potasium iodide, creosote and tonics, especially phosphoric and arsenical compounds, nourishing food and residence in suitable climates should never be neglected. Vaccine therapy may be tried. Farah obtained excellent results from the use of intramuscular injections of 2 cc. of lipiodol into the gluteal region on alteranate days. As many as forty injections were given without any signs of iodism. The mild and intermediary types of cases were greatly benefited. This treatment appears to be useful in early cases before any serious damage has occurred to the lungs.

REPORT OF A CASE IN PORTO RICO

G. A. S., adult white American male, age 34. Occupation, clerk in a stationery store, married. Has lived in Porto Rico twelve years.

Present illness: The patient was admitted to the Presbyterian Hospital on April 23, 1926, for diagnosis of his pulmonary condition, complaining of pain in the chest, night sweats, persistent morning

cough with occasional blood tinged sputum, frequent headaches, occasional attacks of diarrhea alternating with constipation, and daily fever. He gave the following history: During the war he had been in the military service in Porto Rico and suffered from a severe attack of influenza. He was discharged in 1918 in poor physical condition and complaining of cough, pain in the chest, shortness of breath, afternoon fever and night sweats. His condition was diagnosed as tuberculosis and he went to a local sanitarium where he spent six months, most of the time in a recumbent position. He made very little improvement in his general condition during this treatment and showed a daily rise of temperature. During the interval between 1918 and 1926 numerous examinations of the sputum were made for tubercle bacilli, but all were negative. The diagnosis of tuberculosis was made in this sanitarium on the basis of physical findings and X-ray examinations.

Previous Medical History: Measles, whooping cough and chicken pox during childhood. Typhoid fever at the age of twelve, and malaria some time later. Influenza in 1917. He states that he had no venereal infections.

Physical examination: Good state of nutrition. Chest examination reveals rough breathing below the angle of the right scapula. Some roughness of the breath sounds at the end of inspiration in the left intra-clavicular area close to the sternum. The percussion note is impaired over the right upper and middle lobes and slightly impaired over the left apex. Just below the right clavicle moist bubbling rales are heard which disappear after coughing, but return promptly. Broncho-vesicular breathing is heard below this area. The heart is somewhat enlarged, the apex being in the sixth interspace in the anterior axillary line. Rhythm and tone are regular; there are no murmurs.

During the two weeks of observation in the hospital, the patient's temperature was usually about 99° F. but on a few occasions it rose as high at 100.4°F. The pulse fluctuated from sixty to ninety and the respirations were usually about twenty per minute.

The patient's weight on admission was 141.5 pounds. It was the same when he left the hospital.

Since his discharge from the Presbyterian Hospital in 1926, the patient has been under observation in our clinic. He has continued his work and has refused to take any medical treatment. About two months ago (January 27, 1928) he had an attack of hemotypsis. Our laboratory and X-ray examinations (see below) still failed to

reveal any evidence of tuberculosis. Monilia were present in abundance in his sputum.

LABORATORY EXAMINATIONS AND STUDIES

A Von Pirquet tuberculin test was made in 1926 and repeated on April 1928 and found to be negative.

Urine:

Reaction, acid; Sp. gr. 1027. No albumem or sugar; no casts; no abnormal findings in the sediment.

May 27, 1927. Monilia psilosis not found in cultures.

Feces:

April 23, 1926. Tricuris trichuria eggs present.

June 7, 1927. *Monilia psilosis* isolated on Sabouraud glucose-agar plates.

Blood:

April 23, 1926. R. B. C., 4,400,000. W. B. C., 8,100. Hgb., 80 per cent. Polys, 70 per cent. Monos, 30 per cent.

April 29, 1926. W. B. C., 9,700. Polys, 64 per cent. Eosin, 9 per cent, Monos, 24 per cent. Trans., 2 per cent.

January 26, 1928. R. B. C., 3,300,000. W. B. C., 7,800. Hgb., 70 per cent (Dare). Polys, 66 per cent. Small Lymphos, 30 per cent. L. Lymphos, 2 per cent. Trans., 2 per cent. 100 W. B. C. counted.

Blood Chemistry:

May 27, 1927. Sugar, 125 mg. per 100 cc. Urea, 7.0 mg. per 100 cc. Uric Acid, 4.2 mg. per 100 cc. Creatinin, 1.5 mg. per 100 cc.

Sputum:

(Bacteriological and Cytological examinations)

May 7, 1926 to June 5, 1926. Specimens of sputum taken at daily intervals for one month were negative for tubercle bacilli.

June 10, 1927. Several specimens were again examined by the direct and antiformin methods and found negative for tubercle bacilli. Cultures of the sputum on Lubenau's medium were also negative. Pneumococci, streptococci and staphylococci were isolated. Dark field examination revealed no spirochetes.

Cytology of the sputum: Large round cells were seen and also much mucus and bronchial epithelium, a few R. B. C. and W. B. C.

Mycologic Examination: Cultures on Sabouraud agar gave on numerous occasions several colonies of *Monilia psilosis.*

June 20, 1927. Two guinea-pigs were inoculated with the patient's sputum treated with antiformin. They showed no signs of tuberculosis for four months.

June 24, 1927. A rabbit was injected intravenously with 2 cc. of a saline emulsion made from a three-day culture of *Monilia psilosis* isolated from patient's sputum. The animal died on the sixth day.

Post-mortem examination revealed congestion of the lungs and large white kidneys. The monilia were isolated from these organs.

Microscopic examination of the tissues of the animal were made by Dr. R. A. Lambert, Professor of Pathology in the School of Tropical Medicine of the University of Porto Rico. He reported as follows:

"Acute destructive inflammatory foci are found in the lung, kidneys and tongue. The lung shows a widespread oedema, and small poorly defined foci with necrosis and polynuclear infiltrations in the center surrounded by a zone in which there is mononuclear infiltration and epithelial and connective tissue proliferation. The kidney shows more marked inflammatory changes, though qualitatively like those in the lung. The section of the tongue includes a small area of ulceration covered by a membranous exudate."

Diagnosis:

Acute focal inflammatory lesions of tongue, lung and kidney. (Experimental moniliasis.)

January 20, 1928. Patient coughed into Petri dish containing Sabouraud medium. A few colonies of monilia were found.

January 26, 1928.—Patient expectorated a thick viscid sputum with much visible blood. Microscopically, a mass of leucocytes and red blood cells were seen embedded in mucus. Tubercle bacilli could not be demonstrated by either direct smear or the antiform methods. Guinea-pig inoculation was negative for tubercle bacilli. (The animal was observed for three months)

CULTURAL STUDIES

The monilia which we isolated conformed in every way to the description given by Dr. Ashford. The latter himself corroborated our mycological findings in this case. The colonies on Sabouraud glucose-agar are thick and cream colored. If cultivated for several weeks in the surface of a Sabouraud slant, the culture assumes the appearance of a cameole with delicate arborizations extending into the substance of the medium.

Yeast-like oval forms are readily found in young as well as in

old cultures. These have a definite capsule containing a hyaline plasma with a vacuole containing one or more actively motile bodies. Mycelial threads are obtained by digging into the agar with the platinum loop. These present subdivisions by means of septa and often motile bodies. Budding cells are often seen.

The following is a summary of the behavior on various media:

Sabouraud glucose-agar: (pH 6.3): Typical creamy elevated colonies.

Gelatin: No liquefaction inverted pine tree present.

Litmus milk: No coagulation; the medium became progressively more alkaline. Acid and gas are formed in glucose maltose, d-mannose and levulose broth. No acid or gas in lactose mannite, dulcite, rhamnose or raffenose broth. Delayed acid production in saccharose and galactose; acid in xylose broth.

Loffler's coagulated beef serum: no liquefaction.

Russell's double sugar: butt, slightly acid, slant alkaline.

Lead acetate agar: butt negative, slant shows brown discoloration. The organism grows well in a J. Howard Brown anerobic jar and produces active fermentation of maltose under a vaseline seal.

X-RAY EXAMINATIONS

November 27, 1922. (Dr. Roses Artau)

Right pulmonary shadow excessively accentuated. Glands enlarged; nuclear condensation. Possibly apical pleurisy, right side.

March 31, 1923.

Both apices slightly less transparent. Increased hilum shadows with diffuse infiltration of both lungs.

September 19, 1923.

Slight infiltration of both apices; increased hilum shadows. Peribronchial nodes calcified.

June 23, 1925.

Bases and apices normal. Hilum shadows increased; slight fibrosis with discrete mottling.

December 28, 1925.

Slight mottling of median right lobe.

January 27, 1928.

Patient was examined during a period of exacerbation of symptoms while he was in poor general health and suffering with daily afternoon temperature and expectorating a thick sputum containing

much free blood and many cells and monilia. The following was the report of findings:

Extensive peri-bronchial infiltration with apparent calcification of glands near the hila. The parenchyma is mottled throughout; both bases with several small abscesses in the right middle lobe. There is a marked thickening of the pleura on the left side. The left apex is clear; the right is slightly cloudy. The heart shadow is slightly increased.

SUMMARY

A case of pulmonary moniliasis is reported occurring in a continental American white, male, adult who has been living in Porto Rico for twelve years. The symptoms simulate chronic pulmonary tuberculosis but repeated examination of the sputum over a period of ten years by the direct microscopic and antiformin methods as well as by animal inoculation have failed to show the presence of tubercle bacilli. On the other hand there is present at all times in the sputum a yeast-like organism of the genus *Monilia psilosis* (ashfordi) which is pathogenic for guinea pigs and rabbits, producing focal necrosis of the lung upon intra-pulmonary injection into rabbits. These animals usually die within six days and show a general moniliasis with inflammatory lesions of the tongue, lungs and kidneys.

These laboratory findings together with the results of the X-ray examinations and the clinical history of the case lead us to regard this as a case of broncho-moniliasis. That the monilia are the primary cause of the disease and not secondary invading organisms which contribute to the chronicity of the disease and its toxic symptoms has not been absolutely proven.

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