Coexistence of Pulmonary Tuberculosis with Pulmonary and Meningeal Cryptococcosis

Report of a Case

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CRYPTOCOCCOSIS IS INFECTION CAUSED by Cryptococcus neoformans which may involve the lungs, skin or other parts of the body, but has a marked predilection for the brain and meninges.

Cryptococcus neoformans was described as saprophytic yeast when first isolated from fruit juices by Sanfelice.1 A few years later, a similar organism was isolated from milk. Both of these isolates were proved to be pathogenic for laboratory animals. More recently Cryptococcus neoforms was isolated from milk, soil, skin, feces.

Cryptococcosis is not transmitted from man to man and there is no evidence that man has ever contracted the disease from an infected animal. It is thought that the fungus enters the body, as a rule, through the respiratory tract. However, the organism may enter the body through the skin, nasopharyngeal mucosa, and occasionally through the intestinal tract. The pulmonary lesion is often not diagnosed until meningitis appears and the organisms are found in the cerebrospinal fluid. Meningitis usually does not develop without a preceding pulmonary lesion.

Cryptococcosis has been found in association with Hodgkins' disease, leukemias, histoplasmosis and sarcoidosis.9 This writer, in reviewing literature, was unable to find a case in which the coexistence of pulmonary and pleural tuberculosis with pulmonary and meningeal cryptococcosis was described. This is a report of such an instance.

CASE REPORT
A general practitioner of medicine, age 61, was admitted to Catawba Sanatorium on October 24, 1964. He appeared to be in good general condition. Roentgenographic chest examination showed soft infiltration in the left middle lung field and homogenous density in the left base suggesting hydrothorax. Two sputum tests, by concentrate method and cultures, were reported positive for acid-fast bacteria. Cultures from aspirated fluid from the left hydrothorax were also reported positive for acid-fast bacteria. Cultures for fungi were reported negative. He was treated with streptomycin, gram one semi-weekly, isoniazid, 150 mg. three times daily and corticosteroids. Corticosteroids were administered, in decreasing doses, for 74 days and he responded well to this treatment. In February, 1965, roentgenographic chest re-examination showed no evidence of pleural effusion and the previously described density in the left middle lung field underwent marked retraction and fibrosis.

On February 25, 1965, he was discharged from the sanatorium with the recommendation that he continue streptomycin and isoniazid. He continued this treatment at home. He felt well and in April, 1965 went to Florida for a short vacation. After his return, he re-opened his office and began to see patients for a few hours daily.

Present illness: On May 14, 1965, he developed chills and generalized aching. On the following day, he began to complain of frontal headache and, at times, pain in the back of his neck. He also complained of dizziness and occasional nausea, but there was no disturbance in vision.

On May 19, 1965, he was admitted to a local hospital where, on the basis of his previous history of tuberculosis, a provisional diagnosis of tuberculous meningitis was made.

He was admitted to Catawba Sanatorium on May 21, 1965. At the time of his admission, he appeared to be disoriented, confused, irritable, restless and unable to give logical answers. He was nauseated and vomited frequently.

Physical examination: His blood pressure was 150/85, pulse 85 per minute, temperature was 100.4°F, and respiration 20 per minute. Skin was well hydrated, reddish and moist. Eyes were examined by two ophthalmologists; there was no nystagmus, ptosis and fundi were clear. Neck muscles were somewhat tender, but no definite stiffness was noted. Kernig and Brudzinski signs were not definite. The chest expanded well and the lungs were clear.

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Laboratory data: His white blood cell count was 7,200 cells per mm.\(^3\) with normal differential count and his hemoglobin was 15 gram per 100 ml. Urinalysis showed a trace of albumin and four plus cells and one red blood cell per high power field. The following were normal: serum protein, serum calcium, blood urea, serum potassium and electrocardiogram. Sputum tests for acid-fast bacteria, by concentrate method and cultures, were negative. Cultures of sputum for secondary micro-organism and fungi were overgrown by *Pseudomonas aeruginosa*.

Clear cerebrospinal fluid was obtained through the spinal tap. The opening pressure of spinal fluid was 140 mm. of water and the closing pressure of 60 mm. of water. Queckenstedt's test was normal. Spinal fluid studies presented 130 white blood cells per cubic millimeter with 90 per cent lymphocytes. No red cells were seen. Sugar was 40 mg. per cent, chlorides 390 mg. per cent (100 mEq/L.) proteins 300 mg. per cent (Esbach).

Culture of the spinal fluid for acid-fast bacteria and secondary micro-organisms was reported negative. *Cryptococcus neoformans* was identified from the culture for fungi. This was also confirmed by the Communicable Disease Center, Kansas City Field Station, Kansas City, Kansas.

Roentgenographic examination of the chest on May 21, 1965, showed no appreciable change in the left lung, as compared with his x-ray film of February, 1965. In the right lung behind the first anterior rib, a dense, irregular nodule about 3 x 2 cm. in diameter was seen. This nodule later was interpreted as the primary focus of cryptococcosis. After careful re-examination of the roentgenograms of February, 1965, a very small nodule, hidden behind the first rib on the right, was noted.

Hospital course: During the first days of his hospital stay, his body temperature was recorded between 99° F., the lowest, and 102° F., the highest. He was perspiring profusely. Intermittent frontal headache became severe and radiated to the right maxilla and the neck. Occasionally he held his head with both hands. He appeared to be drowsy and sleepy most of the time and when questioned, his answers were illogical. On the third day after admission he became convulsive for a few minutes and also lost urinary control during this period. Nausea and vomiting were frequent and later associated with hiccoughs.

After admission, streptomycin and isoniazid with pyridoxine were continued.

On June 1, 1965, after diagnosis of cryptococcosis was established, treatment with amphotericin B (Fungizone) was initiated. Ten days later he appeared to feel better and was more alert. Nausea and vomiting decreased in frequency and his temperature became normal. After six weeks of treatment with amphotericin B the previously described symptoms almost completely disappeared and he complained only of generalized weakness. He received a total of 2,160 mg. of amphotericin B. It was discontinued because a drop in hemoglobin (from 15 gm. to 12 gm.), increase in blood urea (from 16.8 mg. per cent to 48.8 mg. per cent) and sclerotic changes in the veins used for amphotericin B infusions.

During this treatment, frequent blood analysis, urinalysis, and liver function tests were done. The spinal tap was repeated on June 21, 1965, 20 days after the treatment with amphotericin B was established. On examination, the spinal fluid showed 70 white blood cells per cubic millimeter with 90 per cent lymphocytes; proteins were 50 mg. per cent; sugar and chlorides were normal. India ink smear and culture failed to demonstrate *Cryptococcus neoformans*. A spinal fluid examination was done again on July 19, 1965. It was free of blood cells and sugar, chlorides and protein contents were normal. Culture for *Cryptococcus neoformans* again was reported as negative.

Repeated roentgenographic examinations of the chest showed definite decrease in size of the nodular density in the right lung. There was no change in the left lung.

He was discharged on September 9, 1965 and is being seen every month in the Regional Chest Clinic. As of this writing, he is free of meningeval symptoms with the exception of slight personality changes. The tuberculosis in his left lung is stable. Nodular density in his right upper lung (which was interpreted as the primary focus of cryptococcosis) underwent further retraction.

**DISCUSSION**

It is unusual to have documentation of two granulomatous diseases, tuberculosis and cryptococcosis, in the same person. The question has come up whether the administration of corticosteroids might have enhanced occult pulmonary cryptococcosis. It is generally agreed that steroids decrease cellular exudation, decrease phagocytic mobilization, suppress capillary dilatation\(^5\) and cause depression of the synthesis of specific gamma globulin in some lower animals.

It was documented that rats and guinea pigs infected via the respiratory route with *Cryptococcus neoformans* and subsequently treated with high doses of cortisone acetate died at a substantially higher rate than un-
treated control animals. Latent cryptococcosis was capable of being stimulated in both species by sustained treatment with high doses of cortisone acetate.

Corticosteroids are potent, effective drugs for chronic and acute pulmonary diseases. They should be used with discretion, when indicated, under close supervision.

Another question has arisen: Should the lesion in the right upper lung, which was apparently the primary site of cryptococcosis, have been resected? Katz, Birnbaum and Eckmann have reported a case in which pulmonary resection was done following clinical recovery from cryptococcal meningitis treated with amphotericin. In the first place, the patient was somewhat reluctant to have any surgery. It was also felt that the cryptococcus infection was under control by the use of drug therapy. Although it is possible he may have a central nervous system relapse, it is questionable that removal of the pulmonary primary lesion would obviate this.

REFERENCES

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TRANSPOSITION OF AORTA AND PULMONARY TRUNK

One hundred three cases of great vessel transposition have been analyzed with respect to family background, maternal history and the congenital defects and postnatal complications associated with the condition. The early development of the heart has been reviewed with particular emphasis on the truncocoronal segment. As a result of these studies and the examination of more than 40 necropsy specimens, a hypothesis has been formed. Incomplete clockwise or counter-clockwise rotation of the forming great vessels, alone or in combination with incomplete ventricular rotation, is held responsible for a major share of heart defects.


CARDIAC PAIN SYNDROME IN CORONARY ATHEROSCLEROSIS

The author undertook studies of the role played by inflammation of the sympathetic truncus of infectious etiology in the pathogenesis of coronary pain in 50 patients with atherosclerotic atherosclerosis. Angina pectoris and ganglionic (sympathalgia) pain was distinguished in the cardiac pain syndrome of the patients examined. In 24 patients, the concurrence of inflammation of the truncus resulted in more frequent paroxysms of angina pectoris. In 18 patients, inflammation of the truncus transformed the painless form of coronary sclerosis into a painful one. In the period of sympathalgia, there was a change in the electrocardiogram and ballistocardiogram indicating changes in the heart in this syndrome. 

Ganglionic-blocking and coronary dilating agents were successfully employed in the treatment of such patients. Benzathine penicillin G (Bicillin) was used or tonsillectomy recommended for the purpose of prophylaxis of exacerbations of inflammation of the truncus in the presence of chronic focal of infection.