Case Reports

PULMONARY HISTOPLASMOSIS ACCOMPANIED BY ERYTHEMA NODOSUM

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HISTOPLASMOSIS was first described by Darling in 1906[1] as a generalized and usually fatal disease, and it continued to be considered an extreme rarity until attention was called to a total of 141 cases in the literature in 1950 by Rodger, Terry and Binford.[2]

In the last nine years, work in the United States has shown histoplasmosis to be endemic in the Mississippi, Missouri and Ohio River basins, areas in which the rate of symptomless pulmonary calcification is unexpectedly high and where such cases show a greater incidence of positive reactions with histoplasmin than with tuberculin.

In 1945, Palmer[3] reported on a study of roentgenograms and intradermal histoplasmin and tuberculin tests in 3,105 nurses in the U.S.A. This study suggested that infection with *Histoplasma capsulatum* is common in widespread localities in the U.S.A. and that it is probably the principal non-tuberculous cause of pulmonary calcification in the areas from which these nurses came. Geographically, the area showing the highest incidence of both histoplasmin sensitivity and of pulmonary calcification centres on the Missouri, Mississippi and Ohio River basins. Among nurses who had lived in Minnesota almost all their lives, less than 5% showed sensitivity to histoplasmin, while more than 50% of those from Missouri showed sensitivity. Palmer states that it might be assumed from these investigations that mild subclinical infection with *Histoplasma capsulatum* or an immunologically related organism is widely prevalent in certain States of the U.S.A. and relatively infrequent in others, that in general those States showing a high level of histoplasmin sensitivity are those in which pulmonary calcification is relatively high, and that a high proportion of calcifications seen in chest roentgenograms of tuberculin-insensitive persons are due to histoplasmosis and not to tuberculosis.

In 1947, Zwerling and Palmer[4] commented on this and other papers, stating that it is probable that a disease other than tuberculosis or coccidioidomycosis accounts for a considerable number of instances of pulmonary calcification in the U.S.A. and that this disease or group of diseases produces sensitivity to histoplasmin. Christie[5] has reviewed the problem of pulmonary calcification in tuberculin-insensitive persons in the light of research at Vanderbilt University and presents the case for histoplasmosis being responsible for a proportion of the cases.

This evidence tends to show that Histoplasma infection is common in certain areas of the U.S.A., and that the usual course is benign, leaving a symptomless pulmonary calcification and a positive skin reaction.

In 1950 a case of benign pulmonary histoplasmosis was reported in the U.S.A. which was accompanied by erythema nodosum and arthralgia.[6] Erythema nodosum accompanies some cases of primary coccidioidomycosis,[7] which is endemic in the south-west dry belt of the U.S.A. This, however, was the first occasion on which it had been reported accompanying histoplasmosis. A second and similar case, this time originating in Canada, is here reported.

S.M., a 13-year-old schoolgirl, was first seen on August 16, 1954, complaining of headache for three months, pains in the right hip region on and off for a month, lassitude, anorexia, pallor and insomnia for the two weeks previously, and a rash on the lower legs for three days.

Her bowels and bladder were acting normally and she was a well-adjusted child. Her energy and appetite had recently been defective but had previously been normal.

She gave a strong family history of diabetes; her father, paternal aunt, paternal great-aunt and great-uncle suffered from this disease. Her maternal uncle had had rheumatic fever, her mother hay fever, and her brother urticaria.

She had suffered from rheumatic fever at the age of 5 but had made a rapid recovery and her heart had been repeatedly reported normal since then. On examination, she had a temperature of 101° F., a pulse rate of 92 and a respiration rate of 20. She had a mild granular pharyngitis and moderate dental caries, her spleen was freely palpable on deep inspiration only, and there was a typical erythema nodosum rash on the extensor surfaces of both lower legs. She was tall, thin and pale, and her ankles showed slight valgus deformity. General examination showed no signs of abnormality.

Her sedimentation rate was 15 mm. in one hour and the radiographic report of her chest was: "Shadowing is present in the left upper zone. It is due to a post-primary tuberculous complex, affecting the anterolateral segment of the left upper lobe."

She was admitted to the Royal Inland Hospital, Kamloops, for investigation. With penicillin therapy, her temperature fell in 24 hours, her pulse rate also returned to normal, and both remained within normal limits during her stay in hospital. Her rash faded in three weeks. She complained of no further pain in her joints, and her spleen returned to normal size within 10 days. On admission, hæmoglobin value was 90%, white cell count 4,630, red cell count 4,320,000; differential count

showed polymorphonuclears 37%, band cells 7%, lymphocytes 43%, monocytes 6%. Her sedimentation rate was 15 mm. in the hour, falling within a week to 6 mm. Tuberculin patch test and Mantoux, 1:1,000 and 1:100, were all negative, and serial radiographs of her chest showed a rapid and continuous diminution of the lesion, it being barely visible nine weeks later. Culture of gastric washings grew no *Mycobacterium tuberculosis*. While in hospital she gained 7 lb. in four weeks. Before discharge her case was reviewed by Dr. Garner, Director of Tranquille Sanatorium, who expressed the opinion that the case was probably not tuberculous. Seen a month later, in the 8th week of her illness, she was apparently in good health with a gain of a further 3 lb. in weight, and her sedimentation rate was 4 mm. in the hour. Her spleen remained impalpable. In the 9th week of her illness 0.1 c.c. of histoplasmin 1:1,000 (Lilly) was injected intradermally into the forearm; this was followed in 24 hours by the appearance of a raised white wheal ¼ inch (0.6 cm.) in diameter, with slight surrounding erythema, which all faded 24 hours later.

SUMMARY

The literature on histoplasmosis is reviewed, particularly with reference to the modern concept of histoplasmosis as a benign common infection in contradistinction to the old view that it was a generalized and highly fatal disease. A case is described in a child who had lived all her life in British Columbia; arthralgia and erythema nodosum were also present.

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TULARÆMIA AMONG FARMER-TRAPPERS IN NORTHWESTERN SASKATCHEWAN

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IN SPRING 1955, an outbreak of tularæmia occurred among muskrats in the Loon Lake district of N.W. Saskatchewan. Farmers in the area trapping these animals contracted the disease and developed symptoms of tularæmia. The disease caused the animals to lose subcutaneous fat, vigour and sight, and many muskrats were found dead in the sloughs and in their houses. Beneath the hides were pockets of yellow pus.

Seven human cases are presented.

CASE 1

A 24-year-old white farmer started trapping muskrats in November 1954. He noticed that many muskrats in his area were sick and dying and had subcutaneous abscesses. One week later he developed pustules on the backs of his hands, headache and fever. The pustules lasted about one month and cleared spontaneously, leaving tiny scars. About this time he noticed a hard painful lump in the right axilla, and soon afterwards a granulating ulcer developed on the right palm which refused to heal. On January 31, 1955, he sought medical aid. Temperature at this time was 99.0° F. He was admitted to the outpost hospital in Loon Lake. The axillary lump was now an abscess, which was incised and drained of yellow-green pus. The granulating mass on the palm was excised, and the government pathologist in Regina reported "chronic granulomatous inflammation" which contained occasional multinucleated giant cells. No acid-fast bacilli were found in specially stained sections. Blood sent for agglutination testing for tularæmia was hæmolysed on arrival at the government laboratory in Regina.

The patient was treated with penicillin and streptomycin. His temperature spiked to 99° F. for two days before becoming normal. He was discharged on February 3, 1955, with the ulcer resulting from the abscess still unhealed. He was readmitted to hospital on February 16, 1955, for treatment of the ulcer with penicillin, streptomycin, potassium permanganate soaks, heat lamp treatments, and Tyroderm dressings. By March 4, 1955, when the ulcer was about ¼ inch (0.6 cm.) in diameter and dry, he was discharged. In agglutination tests done in May 1955, his blood was positive at 1 in 400 for tularæmia.

CASE 2

A white farmer, age 37, started trapping muskrats in March 1955. At the time he had many small scratches on his hands. He noticed sick muskrats in his area. On April 14, 1955, he developed chills, fever, headache, generalized aches and pains, and abdominal pain; many small ulcers appeared on his hands and refused to heal. At the same time the left epitrochlear and axillary lymph nodes became enlarged and tender. On April 21, 1955, he was admitted to hospital, with a temperature of 101.8° F. He was treated with penicillin and streptomycin and heat to the painful lymph nodes. He was discharged on April 25, after the temperature had been normal two days. An agglutination test for tularæmia on April 27 was negative, but a second on June 21 was positive at 1 in 800.

CASE 3

Since November 1954 a farmer's wife, age 57, white, had been handling the skins of muskrats trapped by her husband. On April 17, 1955, she developed chills, fever, painful reddened eyes and a painful right axillary lump. The right thumb had had a splinter sore for some time before the onset of illness, and an ulcer now developed at this point and resisted all her efforts to heal it. She was admitted to hospital on April 23 with a normal temperature, and treated with penicillin, streptomycin, and heat to the axilla. The temperature rose to 99.4° F. on April 26 but came down to normal two days later. An agglutination test for tularæmia on April 29 was negative, but a second one on May 29 was positive at 1 in 400. A sample of the husband's blood was tested at this time and was negative. He had no symptoms of tularæmia though he had skinned the muskrats from whose hides his wife had contracted the disease.

CASE 4

A white farmer, age 46, had been trapping muskrats all winter. In early April 1955, he developed fever, headache, and left axillary lymphadenitis. Many small, dry fissured lesions which refused to heal appeared on