

MEDICAL GRAND ROUNDS
PARKLAND MEMORIAL HOSPITAL
September 17, 1957

Case #1

[Histoplasmosis]

The patient, a 32 year old white [redacted] from [redacted], Texas, was admitted to [redacted] on [redacted], 1957 with complaints of a "cold" for six days, followed by chills, fever, cough and chest pain. The present illness began on [redacted] with symptoms of nasal stuffiness, sore throat and a non-productive cough. On [redacted], the patient noted chills, fever, generalized myalgia. The cough increased in severity becoming productive of purulent blood streaked sputum (not foul). The cough was associated with pain at the costal margin, not true pleuritic pain. The following day she was seen at [redacted], diagnosed as early pneumonia and treated as an out-patient with penicillin.

There was no past history of chronic cough, loss of consciousness or alcohol ingestion. She had had a hysterectomy performed for "cancer" in [redacted] 1955.

On the admission physical examination her temperature was 101°F, pulse 98 and respiratory rate 22. The significant features included: poor oral hygiene and signs of pneumonitis in the left upper lobe.

Laboratory data of significance included: hemoglobin 11.2 gms.%, leucocyte count varying from 4850 to 9160/mm³, differential 62% PMN, 32% lymphocytes, 5% monocytes, 1% eosinophile, urinalysis unremarkable. No agglutinins for S. typhosa, Brucella, P. tularensis, Proteus OX-19 or cold agglutinins were found. On admission ([redacted]/57) her skin tests with O.T. 1:1000 and 1:100, Coccidioidin and Histoplasmin were negative. On [redacted]/57 (19 days after the onset of symptoms) skin tests to coccidioidin were negative; however, a 2+ reaction was observed with histoplasmin. Sputum culture demonstrated normal flora plus candida albicans on admission. Acid-fast bacteria were not seen.

During her first week in the hospital, she was treated with intravenous penicillin (10 million units daily) and tetracycline (1.0 gram daily). She began afebrile on the third hospital day.

Case #2

The 14 year old [redacted] of the first patient was admitted to [redacted] on [redacted] 1957 complaining of malaise, headache, chest pain and cough. Her illness began on [redacted], when she awakened and noted malaise, yet no localizable complaints. Later that day she developed a headache (bitemporal) and dull aching chest pain. The following day she developed a cough, sensation of fever, and anorexia.

Physical examination performed on admission showed her temperature to be 102°F, pulse rate 82, respiratory rate 20. The remainder of the examination showed only signs of pneumonitis in the area of the right upper lobe.

Laboratory data included: hemoglobin 12.4 gms.%, leucocyte counts 6400 to 9600/mm³, differential smear 73% PMN, 24% lymphocytes, 2% monocytes, 1% eosinophiles, urinalysis unremarkable. As in her mother, agglutinations were negative. On [redacted]/57 her skin tests to O.T. 1:1000, coccidioidin and histoplasmin were negative. Repeated on [redacted]/57 (13 days after the onset of her symptoms), her histoplasmin skin test was 1+, the others remained negative.

She received no antibiotic therapy and became afebrile on her third hospital day.

Epidemiologic History: The family of seven moved into this house in [redacted] four months previously. A history was obtained from neighbors that the previous tenants had moved to Ohio because their three year old daughter had developed "tuberculosis". The father of this child had chronic lung disease. The house is located near the center of [redacted]. Behind the house is a shed-garage to the side of which is attached a small shed. This is presently used as a dog house for three dogs, which appear healthy. There is no history of fowl being kept in the shed.

Family History:

Initials	████████	██████	██████	████████	██████	██████	████████
Age	41	32	14	11	10	7	5
Symptoms	none				none		
malaise		+	+++	0		0	+
fever		+++	++	0		0	+
cough		+++	+++	+		+	0
Physical	neg.	+	+	neg.	neg.	neg.	neg.
X-ray	neg.	LLL	RUL	neg.	+	neg.	neg.
Skin Test*							
Histoplasmin	+++	0 to ++	0 to +	0	0	0	0
Coccidioidin	±	0	0	0	0	0	0
O.T. 1:1000	0	0	0	0	0	0	0

* Done on ████████ 57 on members except patients

**Seen on ████████ 57 at ████████ temperature 101⁴, malaise, fever, pharyngitis.
Afebrile within two days.

References

Review Articles:

1. Schwartz, B. Histoplasmosis of the Lungs, Arch. Int. Med., 94:970, 1954. A good general review, except for his recommendations regarding the use of adrenal steroids
2. Silverman, F.N., Schwarz, J., Lahey, M.E. and Carson, R.P.: Histoplasmosis, Am. J. Med., 19:410, 1955. The most comprehensive of the recent reviews.
3. Leban, P. H. and Furcolow, M. L.: Epidemic Histoplasmosis, J. Chronic Dis., 5:489, 1957. A summary of 41 reported "epidemics" (two or more cases from a point source). None previously reported in Texas.

Historical:

4. Darling, S.T.: A protozoon general infection producing pseudotubercles in the lungs and focal necrosis in the liver, spleen and lymph nodes, JAMA, 46:1283, 1906. The first reported case of Histoplasmosis.
5. Darling, S.T.: Histoplasmosis: A fatal infectious disease resembling Kala-Azar found among the natives of tropical America, Arch. Int. Med., 2:107, 1908. Reports two more cases, one of the "natives of tropical America" was Chinese.
6. Watson, C.J. and Riley, W.A.: A case Darling's Histoplasmosis originating in Minnesota. Arch. Path., 1:662, 1926. The next reported case. The author is THE C.J. Watson.
7. Dodd, K. and Tompkins, E.H. A case of Histoplasmosis of Darling in an infant, Am. J. Trop. Med., 14:127, 1934. The first case diagnosed ante-mortem (from a blood smear).
8. DeMonbreun, W.A. The cultivation and cultural characteristics of Darling's Histoplasma capsulatum, Am. J. Trop. Med., 14:93, 1934. The first successful isolation of the fungus, from the case reported by Dodd and Tompkins.

Progressive Disseminated Histoplasmosis: (A disease with protean manifestations)

9. Parsons, R.J. and Zarafonetis, C.J.D.: Histoplasmosis in man, Arch. Int. Med., 75:1, 1945. A review of 71 cases. The "dawn" of in this subject is breaking.
10. Montgomery, P.O'B.: Histoplasmosis in Texas, Texas S. J. Med., 48:471, 1952. Two cases from McKinney.
11. Curtis, A.C. and Cawley, E.P.: Genital Histoplasmosis, J. Urol., 57:781, 1947. A cause of chancres.
12. Miller, H.E., Keddie, F.M., Johnstone, H.G. and Bostick, W.L.: Histoplasmosis: cutaneous and mucomembraneous lesions, mycologic and pathologic observations, Arch. Derm. & Syph., 56:715, 1947. 50% of patients have such lesions, ulcerative or granulomatous lesions of the mouth most common.

Epidemiologic Aspects of Pulmonary Calcification and Histoplasmosis: (The background to our present knowledge of the spectrum of histoplasmosis)

13. Gass, R.S., Gauld, R.L., Harrison, E.F., Stewart, H.C. and Williams, W.C.: Tuberculosis Study in Tennessee, Am. Rev. Tuberc., 38:441, 1938. Demonstrated pulmonary calcification in 48.1% of tuberculin negative children in an area of Tennessee. The next ten years were spent determining the etiology.
14. Zarafonitis, C.J.D. and Lindberg, R.B.: Histoplasmosis of Darling, Observations on the antigenic properties of the causative agent, Univ. Hosp. Bull., 7:47, 1941. Demonstrated histoplasmin reaction in animals.
15. Smith, C.E.: Coccidioidomycosis, Med. Clinic. N. A., 27:790, 1943. In a discussion of coccidioidomycosis (a good one) states of the central U.S. "This is the area of pulmonary calcifications in tuberculin negative persons and is also the endemic area of histoplasmosis" (progressive fatal). The first suggestion of relationship between these findings and of a benign form of histoplasmosis.
16. Palmer, C.E.: Non-tuberculous pulmonary calcification and sensitivity to histoplasmin, Pub. Health Rep., 60:513, 1945. Demonstrated high percentage of positive skin tests in nurses from Ohio-Mississippi Valley, especially in those with pulmonary calcification.
17. Mochi, A. and Edwards, P.Q. Geographical distribution of histoplasmosis and histoplasmin sensitivity, Bull. World Health. Org., 5:259, 1952. An excellent review up to 1951 - 370 references. Three-fourths of cases are in North America.
18. Forbes, G.B. and Chang, C.C.: Histoplasmin and tuberculin sensitivity in Texas infants and children, Pub. Health Rep., 68:320, 1953. 7% histoplasmin positive.
19. Emmons, C.W., Olson, B.J., Eldridge, W.W.: Studies of the role of fungi in pulmonary disease. I. Cross reactions of histoplasmin, Pub. Health Rep., 60:1383, 1945. There is a high incidence of cross reactions between histoplasmin and blastomycin in experimental animals and in man. Authors suggest that pulmonary calcification and a positive histoplasmin skin test doesn't necessarily mean a cause and effect relationship. The organism must be isolated from mild disease.
20. Bunnell, I.L. and Furcolow, M.L.: A report on ten proved cases of histoplasmosis, Pub. Health Rep., 63:299, 1948. The first proven non-fatal cases (at least 3).
21. Loosli, C.G., Procknow, J.J., Tanzi, F., Grayston, J.T. and Combs, L.W.: Pulmonary histoplasmosis in a farm family: a three year follow-up. J. Lab. and Clin. Med., 43:669, 1954. An epidemic involving six members of a family. Demonstrated the development of miliary calcification over a period of one to two years.
22. Emmons, C.W.: Isolation of Histoplasma capsulatum from soil, Pub. Health Rep., 64:892, 1949. The first demonstration of the natural habitat for H. capsulatum.
23. Campbell, C.C. and Brinkley, G.E.: Serologic diagnosis with respect to histoplasmosis, coccidioidomycosis and blastomycosis and the problem of cross reactions, J. Lab. and Clin. Med., 42:896, 1953. A good description of the antibody titers in relation to various types of histoplasmosis. Unlike coccidioidomycosis and blastomycosis, with advanced disseminating disease the antibody titer may fall.
24. Prior, J.A. and Saslaw, S.: Effect of repeated histoplasmin skin tests on skin reactivity and collodion agglutination, Am. Rev. Tuberc., 66:588, 1952. Doesn't convert negative reactors to positive.
25. Grayston, J.T. and Furcolow, M.L.: The occurrence of histoplasmosis in epidemics—epidemiologic studies, Am. J. Pub. Health, 43:665, 1953. Report 13 epidemics, many of which were previously reported as "Cave Sickness", "An unusual pulmonary disease" "Angle worm pneumonia", which have been shown quite definitely to have been due to inhalation of H. capsulatum from soil.
26. Sutliff, W.D., Hughes, F., Ulrich, E. and Burkett, L.L.: Active chronic pulmonary histoplasmosis, Arch. Int. Med., 92:571, 1953. Histoplasmosis may cause a "reinfection type" illness with cavitation and be indistinguishable from tuberculosis.

Therapy: (Unsatisfactory! except in self limited cases)

27. Smith, D.T.: Therapy for pulmonary and systemic fungus diseases, Postgrad. Med., 20:18, 1956.

28. Fox, H.: Exfoliative dermatitis complicated by fatal acute disseminated histoplasmosis, Arch. Derm. and Syph., 68:734, 1953. Perhaps, an example of dissemination during steroid therapy.
29. Farrell, R.L., Cole, C.R., Prior, J.A. and Saslaw, S.: Experimental histoplasmosis I. Methods for production of histoplasmosis in dogs, Proc. Soc. Exp. Biol. & Med., 84:51, 1953. Adrenal steroid therapy converted a self limited pulmonary infection into disseminated fatal disease.
30. Packard, J.S., Finkelstein, H. and Turner, W.E.: Acute pulmonary histoplasmosis, treatment with cortisone, Arch. Int. Med., 99:370, 1957. At least was not obviously harmful in two patients.

Miscellaneous:

31. Murray, J.F. and Brandt, F.A.: Histoplasmosis and malignant lymphoma, Am. J. Path., 27:783, 1951. The incidence of "Hodgkin" in patients dying with histoplasmosis is 3.4%. These authors question whether the cytologic reaction is a malignant lymphoma or merely a "lymphoma-like" picture.
32. Heilbrunn, I.B. and Cain, A.R.: Mild histoplasmosis resembling atypical pneumonia and accompanied by erythema nodosum and arthritis, J. Missouri State Med. Assn., 47:503, 1950. Erythema nodosum occurs in 2.5% of cases of coccidioidomycosis. This is the only report in histoplasmosis and is most likely due to a penicillin reaction rather than histoplasmosis.
33. Robinson, V.M., McVickar, D.L. and Peterson, J.C.: Some aspects of the epizootiology of histoplasmosis in two boxer breeding kennels, J. Am. Vet. Med. Assn., 119:195, 1951. An interesting study of epidemic (epizootic) histoplasmosis in the dog. The pattern is identical with that seen in man. Brachycephalic type dogs show an increased susceptibility. (There is also an interesting case report of pulmonary hypertrophic osteoarthropathy associated with a lung tumor in the dog in this volume).