Sarcoidosis or Fungal Disease?*

Harlan J. Sicherman, M.D., Howard A. Andersen, M.D., F.C.C.P., and Richard A. DeRemee, M.D., F.C.C.P.

A review of 650 cases of pulmonary fungal disease observed at the Mayo Clinic during a ten-year period revealed that the thoracic roentgenogram in pulmonary fungal disease was readily distinguishable from that in classic sarcoidosis. Nevertheless, in order to exclude a mycologic cause, appropriate microbiologic and serologic studies should be performed in every case in which sarcoidosis is suspected or even seems to be established.

In sarcoidosis, various fungal infections have been found: cryptococcosis,1-8 nocardiosis,9 coccidioidomycosis,10,11 North American blastomycosis,12 aspergillosis,13-14 sporotrichosis,15-19 candidiasis,20 and histoplasmosis.21,22 Although the pathogenesis of these infections in sarcoidosis is unknown, many theories have been proposed. The answer may not be determined until the cause of sarcoidosis is known.

Kent et al23 have claimed that, from the onset, many patients with a diagnosis of sarcoiditis really have tuberculosis or fungal disease. We thought it might be helpful to approach this problem from another viewpoint. We reviewed the clinical and laboratory data, including thoracic roentgenograms of patients with proved pulmonary fungal disease, to ascertain whether these patients resembled those with classic sarcoidosis.

MATERIALS AND METHODS

Six hundred fifty patients with pulmonary fungal diseases were seen at the Mayo Clinic and its associated hospitals from 1960 through 1970. Most of the patients had active disease. The diagnosis was made with the aid of thoracic roentgenograms, tomograms, skin tests, sputum examinations with special staining techniques and cultures, bronchoscopy with culture of bronchial washings, and biopsy of pulmonary tissue. The diagnosis of fungal disease was made unless the stains or cultures demonstrated the fungal organisms.

The thoracic roentgenograms were examined in order to compare the abnormalities with those found in classic sarcoidosis, such as bilateral hilar adenopathy with or without diffuse bilaterally symmetric parenchymal changes.

RESULTS

A diagnosis of histoplasmosis or coccidioidomycosis was made in approximately 70 percent of the 650 cases. In the remainder, the diagnosis was cryptococcosis, sporotrichosis, aspergillosis, nocardiosis, actinomycosis, North American blastomycosis, or candidiasis.

In all 650 cases, the findings on thoracic roentgenograms were abnormal. Infiltrates, enlarged lymph nodes, cavitation, pulmonary nodules, old calcifications, and interstitial fibrosis were noted. There was not a single case, however, in which these abnormalities were bilaterally symmetric such as is the case with classic sarcoidosis. In the roentgenograms that demonstrated bilateral abnormalities, marked asymmetry usually was present. In the rare instance in which the roentgenographic findings approached symmetry, the patient was too ill in other ways—fever, prostration, or abnormal hematologic findings—to consider seriously the diagnosis of sarcoidosis.

DISCUSSION

Kent et al23 emphasized that the condition of the patient must be evaluated thoroughly before it can be concluded that he has sarcoidosis. Yet, in the past two decades, there has been an increasing number of patients with established sarcoidosis in whom fungal disease later developed. Our present study was prompted by the finding of a patient with classic sarcoidosis in whom pulmonary cryptococcosis developed approximately ten weeks after corticosteroid therapy was started. We wondered whether cryptococci could have been present and overlooked.
at the time of the original diagnosis of sarcoidosis; but results of the present study suggest no such oversight.

The reason for the development of fungal infections in sarcoidosis is not clear. It may be that the fungus causes the sarcoid reaction; mycobacteria, fungi, viruses, protozoa, and helminths\(^{24}\) have been reported to cause sarcoidosis. An altered immunologic mechanism may be present in patients with sarcoidosis, increasing their susceptibility to infection. Erythema nodosum, iritis, Sjögren’s syndrome, arthritis, and thyroiditis—conditions that are considered auto-immune—often have been associated with sarcoidosis. In a study of 350 patients with sarcoidosis, Chusid et al\(^{25}\) showed that 85 percent reacted either weakly or not at all to 100 to 250 tuberculin units of purified protein derivative. This depression of delayed hypersensitivity is also seen in cutaneous tests for mumps,\(^{26}\) pertussis,\(^{26}\) and dinitrochlorobenzene.\(^{27}\) Peripheral lymphocytes of patients with acute sarcoidosis have been cultured in vitro and have shown differences in lymphoblastic transformation when compared with normal cells.\(^{28}\) Corticosteroids used in the treatment of sarcoidosis may mask the clinical presentation of an underlying fungal disease owing to anti-inflammatory action, depression of antibody formation, or stabilization of lysosomal membranes.

Although evidence for an altered immune system seems to be well established in sarcoidosis,\(^{29,30}\) one cannot be certain that this predisposes these patients to fungal infections.

Israel et al\(^{31}\) described ten patients who had chronic cavitary pulmonary sarcoidosis with coexistent aspergillomas. Seven of the ten patients had received corticosteroid therapy prior to the manifestation of aspergilloma.

Some workers believe that cryptococcosis occurs more often in patients with sarcoidosis than in normal persons. Some investigators\(^ {6,18,31}\) have noted the secondary development of cryptococcosis in established cases of sarcoidosis even when no corticosteroid therapy has been used. Others\(^ {4,5,32}\) have reported the coexistence of the two diseases with prior corticosteroid therapy.

In two studies\(^ {16,19}\) of coexistent sporotrichosis and sarcoidosis, no prior treatment with corticosteroids was used, and in three reports.\(^ {15,17,18}\) steroid therapy was begun prior to the development of sporotrichosis in patients with sarcoidosis. Similar difficulties of determining the causative factor in such coexistent diseases as nocardiosis, coccidioidomycosis, North American blastomycosis, actinomycosis, and histoplasmosis have been observed.

We agree strongly with Kent et al\(^ {23}\) that patients suspected of having sarcoidosis should have thorough microbiologic and serologic evaluation for possible tuberculosis and fungal diseases before the diagnosis of sarcoidosis is made. Our study of 650 cases of fungal diseases suggests, however, that the thoracic roentgenogram in pulmonary fungal diseases is usually distinguishable from the roentgenogram in classic sarcoidosis.

REFERENCES


16. Lurie HI: Five unusual cases of sporotrichosis from South Africa showing lesions in muscles, bones, and visera. Br J Surg 50:585-591, 1963


20. Winthrop MM: Infectious mononucleosis. In Harrison’s

CHEST, VOL. 64, NO. 1, JULY, 1973
The Mystic Charm of Oriental Carpets

One of the greatest charms of oriental rugs is that the eye hesitates often before becoming able to understand the design. Each person finds there the image which accords with his own dream or philosophy of the moment. If they are so appreciated in Europe, it is simply because they have aroused this kind of bewilderment which we experience when confronted with anything unknown, whether it is a matter of countries, beings, ideas or forms. To the Oriental, nothing exists by itself nor for itself. His conception of the universal spirit, eternal and infinite, expressed and revealed itself equally in the different manifestations of reality, and was required to show itself through the medium of signs, symbols, and colors—all these being the tangible manifestation of a desire to spiritualize all that which could have some transcendental value in the life of man. But, we must not forget that if the artist in Asia was unquestionably drawn to sublimate his every day reality by all the means at his disposal, he was no less deeply enamored with nature. From this state of mind were born works that were essentially decorative and poetic, with roses, palmettes, and exuberant floral motifs which undoubtedly would never find a place in any botanical encyclopedia, landscapes, purely imaginary animals, geometrical shapes and forms elaborated by the Arab imagination which followed in the footsteps of the Pythagorean culture.

de Calatchi, R: Oriental Carpets, Rutland, Vermont, C E Tuttle, 1967