Parasitic Mycelial Forms of Coccidioides Species in Mexican Patients

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Received 27 June 2003/Returned for modification 31 August 2003/Accepted 8 November 2003

Of 26 cases of coccidioidomycosis reported here, 15 showed hyphae, atypical parasitic structures of Coccidioides spp. in fresh cytologic and/or histologic specimen preparations. The finding of this morphology could have implications which should be considered, especially when the disease affects areas of nonendemicity.

Inhalation of the arthroconidia of Coccidioides immitis and/or C. posadasii produces coccidioidomycosis (2). Coccidioides spp. grow in the northern states of the Mexican Republic and in the south of the United States (1, 3). Laboratory diagnosis is very important, since (clinically and radiologically) coccidioidomycosis may be confused with tuberculosis or other lung diseases. Coccidioides spp. typically form spherules that contain endospores in the host; however, other parasitic structures have been reported, among which are hyphae (6, 7).

The aim of the present study was to show the frequency with which hyphae are observed as parasitic forms of Coccidioides spp. in Mexican patients.

An observational transversal and comparative study was performed based on the review of clinical records and laboratory studies of patients diagnosed with pulmonary coccidioidomycosis at the Instituto Nacional de Enfermedades Respiratorias (INER) who were culture positive for Coccidioides spp. between 1991 and 2000.

The most frequently analyzed biological product was sputum followed by bronchial lavage or brushing. All samples were immediately processed and sent to the laboratory. Serology was performed for the identification of anti-Coccidioides antibodies by precipitation in capillary tubes, gel immunodiffusion, complement fixation reaction, enzyme-linked immunosorbent assays, and intradermoeaction testing to assess the cell immune response. Methods employed to confirm or discard lung tuberculosis included the following: smear staining with Ziehl-Neelsen stain, auramine-rhodamine fluorescence, and/or culture in Löwenstein-Jensen agar.

A total of 26 Mexican patients with coccidioidomycosis were registered. The most frequent signs were cough, hemoptysis, and fever. Radiological studies revealed a high proportion of lung cavities. Table 1 shows data of residence, occupation, time of disease evolution, and underlying diseases of the patients. A total of 19 patients reported symptom initiation at least 3 months before entering the INER, with a mean disease evolution of 2 years. Of these patients, 14 suffered from chronic diabetes mellitus type II. The initial diagnosis of all patients had been tuberculosis alone or associated with another lung ailment.

After laboratory studies, the final diagnosis was as follows: 24 patients with coccidioidomycosis as the sole pathology and 2 patients with coccidioidomycosis associated to tuberculosis. Analysis of these results discloses that (approximately) only 1 out of every 8 coccidioidomycosis patients is clinically diagnosed.

In the mycological analysis, microscopic observations revealed that of the 26 patients, 15 showed some of the following atypical parasitic forms of Coccidioides spp.: septate hyphae of variable length and moniliform or branching septate hyphae (Fig. 1a); widened or barrel-shaped arthroconidia (Fig. 1b); small chains of oval or round cells and immature oval spherules (germinating and apparently budding) (Fig. 1c); endospores grouped in morular forms (Fig. 1d); or all these structures with or without the presence of spherules with endospores.

All cultures developed Coccidioides spp. colonies, 21 of them with the classic morphology. Immunological tests were performed for only 15 patients; the results were positive in at least in one of the tests. Since the mycelial structures of Coccidioides spp. were identified in more than half the cases, we consider that even if the presence of these parasitic forms does not identify the fungus definitively, they should be considered possible coccidioidomycosis indicators.

Age, sex, occupation, and residence data differed and had no discernable influence on the frequency of the appearance of hyphae in patient samples. The probability of finding hyphae in sputum is the same as with other invasive procedures.

Coccidioidomycosis was considered for the clinical diagno-
sis for only three patients when they were admitted to the INER. The subregistry of this mycosis, even in patients who come from zones of endemicity, is due to the high incidence of tuberculosis in Mexico, for which it is frequently mistaken. Besides, diagnosis may become more complicated if there has been immunologic damage or when more than one lung pathology is present in the patient. Thus, a surgical procedure is sometimes required for the diagnosis and treatment of this systemic mycosis (4); it is therefore necessary to take into account that Coccidioides spp. can form hyphae in the patient’s tissue that can be confused with other hyphomycetes, for example, Aspergillus spp.

The presence of cavities was a constant clinical parameter among our patients, which can be explained by the high frequency of chronic processes such as diabetes. Among diverse studies performed on diabetic patients, data show that although the lung is not considered the target organ in diabetes mellitus type II, diabetic patients have a probability four times greater than nondiabetics of presenting infections such as tuberculosis and lung mycoses (5).

In addition to the diagnostic importance, other biological implications of the finding of parasitic hyphal elements of Coccidioides spp. should be considered, namely, (i) the danger this represents for the hospital staff and (ii) the possibility of person-to-person dissemination of the disease. This possibility should be investigated, since this morphology is present in cavities with bronchial connections.

All of this renders evident (considering the new Coccidioides species that are being discovered) (2) the necessity for laboratories to know and identify the diverse parasitic morphological manifestations of Coccidioides spp. to avoid erroneous diagnosis. When spherules with endospores are scarce or absent, investigations determining the presence of mycelial structures (supported by other routine diagnostic techniques such as cultures, immunoserology, assays for the presence of exoantigens, inoculation of laboratory animals, and/or the use of specific genetic probes) can provide the key to a correct diagnosis, since a wrong identification of the etiologic agent can lead to inadequate therapeutic regimes, delaying patient improvement and favoring infection progress.

This is the first work to report data of hyphal forms in pathological specimens of Mexican patients with coccidioid-
omycosis, which is surprising in a country that possesses a widespread area of endemicity for this mycosis.

We wish to thank Arturo Aroch for his assessment of methodology and orientation.

REFERENCES


