Coccidioidomycosis in Immunocompromised Hosts

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In Chapter 5, the apparent centrality of the host immune response in determining the outcome of coccidioidal infection has been detailed—in particular, cell-mediated immunity. This suggests that instances of deficiencies of such responses would lead to severe and progressive disease. In fact, observations made in patients with immunodeficiencies have provided strong evidence for our current understanding of the role of immunity in the normal host–pathogen interaction.

Fungal infections are a significant cause of morbidity and mortality in immunocompromised hosts,¹⁻⁵ and in some series with some malignancies are the most common infections at death. The fungi most commonly implicated in such infections are Candida or Aspergillus species, Cryptococcus neoformans, and infections due to zygomycetes. Such opportunistic invaders are present in normal host flora or are organisms which may be encountered commonly in the environment in a variety of geographic areas, and are prevented from causing infection in most circumstances by the defense mechanisms of the unimpaired host, unless anatomic barriers are breached. However, coccidioidal infection can also be a severe problem in such patients if they have or have had the opportunity of exposure to the organism.

Review of the literature indicates that coccidioidomycosis has been reported in association with a variety of malignancies and with immunosuppression for transplantation and for other conditions. Many cases have been reported in association with corticosteroid or cytotoxic chemotherapy or both. The special case of coccidioidal infection in pregnancy is discussed in detail in Chapter 17. The association of insulin-dependent
diabetes mellitus with chronic and/or progressive pulmonary disease, particularly with cavitation, has been referred to in Chapter 10.

In a referral center adjacent to the endemic zone, a series of patients with immune impairment and coccidioidomycosis was analyzed in reference to the host populations with both conditions. Some features of this association emerge in this analysis. Disseminated disease was noted to be 100 times more common (50%) than expected in the normal population. This was particularly clear if the infection occurred after the immune impairment, although infection which resolved and became quiescent prior to development of an immune-impairing condition sometimes can reactivate and disseminate after impairment. The increased risk of dissemination in males and in dark-skinned races each appeared to be accentuated with the presence of the risk associated with immune impairment. Coccidioidomycosis could be an early or late complication of underlying malignancies, unlike the opportunistic invaders which commonly are seen late in the course of the patient's illness. Recent chemotherapy was a more important correlate of dissemination than was radiotherapy or the specific underlying diagnosis. Lymphocytopenia correlated closely with dissemination. Among the Hodgkin's disease patients, dissemination was associated with advanced stages of disease (III and IV).

Dissemination was highly lethal in these patients, whereas pulmonary coccidioidomycosis which remained localized to the lung appeared not necessarily worse than in normal hosts. (In another series, subclinical relapses were also noted in renal transplant recipients. Urine cultures became positive before frank illness.) An unusual feature of disseminated infection was concomitant rapidly progressive pulmonary involvement, with bilateral infiltrates, with patients dying rapidly from the time of their first abnormal X-ray. Miliary coccidioidal disease has also been noted in other immunocompromised patients, and patients with immune impairment comprise a large segment of series of patients with that form of coccidioidal disease (see Chapter 10). Fungemia may also be seen in such patients.

Although the skin test reaction appears blunted in these patients, the serological response was at least qualitatively intact (positive test although titers are reduced). Whereas others have also noted the latter, this is apparently not always the case, particularly with specimens taken at the start of the illness.

An unfortunate number of these patients were diagnosed as having coccidioidal infection only just antemortem or at postmortem examination. The major problem in diagnosis of these patients was lack of suspicion of the diagnosis of coccidioidomycosis, although difficulties in