CORRESPONDENCE

Cutaneous Miliary Tuberculosis in the AIDS Era

SIR—A recent review of cutaneous miliary tuberculosis in the AIDS era [1] emphasized the importance of having a high index of suspicion for this condition in HIV-positive patients with skin lesions and advanced immunodeficiency. However, the authors were able to identify only five such cases in the literature, in addition to the case they reported. In a prospective study, ongoing since October 1994, we have identified only one case of cutaneous tuberculosis among nearly 400 patients with biopsy-confirmed or culture-confirmed tuberculosis; 47% of these patients were HIV-positive. In view of the rarity of cutaneous tuberculosis and the fact that skin biopsy is not usually necessary to make a diagnosis of disseminated tuberculosis, we believe that skin biopsy should be performed primarily to exclude other causes of skin conditions in patients with advanced HIV disease, as the following case report illustrates.

A 48-year-old HIV-infected heterosexual man who had no history of use of illegal substances but who had received treatment for two previous episodes of tuberculosis presented with chronic pathogen-negative diarrhea, colicky abdominal pain, weight loss, fever, and dark maculopapular lesions on his hands. The CD4 cell count was 3×10^6/L, and a chest roentgenogram showed fibrocystic changes in the right upper lobe and possible mediastinal adenopathy.

An ultrasonogram of the abdomen showed adenopathy in the epigastrium. No sputum was obtained, but a blood culture for mycobacteria with use of the radiometric system (BACTEC; Becton Dickinson, Sparks, MD) was negative. Examination of a duodenal biopsy specimen obtained by endoscopy revealed cryptosporidia. One of the skin lesions was biopsied to exclude Kaposi's sarcoma, and the specimen was sent for a routine mycobacterial culture. A diagnosis of disseminated tuberculosis was made on the basis of the patient's clinical presentation and the presence of adenopathy; he was discharged and received antituberculous therapy as an outpatient. *Mycobacterium tuberculosis* was cultured from the skin biopsy specimen 2 weeks later.

While cutaneous manifestations are common in the HIV-positive population in Cape Town, South Africa, few lesions are biopsied, so we may have missed other cases of cutaneous miliary tuberculosis. However, as was true for our patient, the diagnosis of disseminated tuberculosis is usually evident on clinical grounds; cultures are performed to confirm the diagnosis and to exclude drug resistance. Although the positive culture of the skin biopsy specimen confirmed the diagnosis for our patient, the result was unexpected; if the result had been negative, treatment would have been continued. Similarly, in the case reported by Libraty and Byrd, the patient's risk factors and presentation, apart from the short history of symptoms, were suggestive of disseminated tuberculosis. Further, the positive culture result for the skin biopsy specimen became available after acid-fast bacilli had been seen on examination of bronchoalveolar lavage fluid and bone marrow biopsy specimens.

In conclusion, our own experience and that of other investigators [2] is that an HIV-related diagnosis of extrapulmonary tuberculosis can usually be made without performing a skin biopsy. Notwithstanding the findings in two recent reports [3, 4], in most cases it would be more appropriate to use procedures with documented high diagnostic yield, e.g., lymph node biopsy [5], than to perform a skin biopsy. Isolated instances of positive skin biopsy specimens must be weighed against the large number of negative skin biopsy specimens if the recommendations of Libraty and Byrd are followed.

Christopher P. Hudson, Robin Wood, and Elizabeth A. O'Keefe

Departments of Medicine, University of Cape Town and Somerset Hospital, Green Point, Cape Town, South Africa

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Reprints or correspondence: Dr. Christopher P. Hudson, Department of Medicine, Medical School, Observatory 7925, Cape Town, South Africa.

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Cutaneous Miliary Tuberculosis in a Patient Infected with Human Immunodeficiency Virus

SIR—Libraty and Byrd [1] recently described a case of cutaneous miliary tuberculosis in an HIV-positive patient and reviewed the published cases of cutaneous miliary tuberculosis among patients with AIDS [1]. The authors claimed that only six cases (including their own case) have been reported so far. However, they did not mention two cases of cutaneous miliary tuberculosis due to multidrug-resistant *Mycobacterium tuberculosis* in patients with AIDS, which we described previously [2]. Since the publication of our report in October 1995, we have diagnosed a further case of cutaneous miliary tuberculosis, also known as tuberculosis cutis miliaris disseminata (TCMD).

A 38-year-old man with an 8-year history of intravenous drug abuse who was receiving methadone maintenance therapy presented with a 1-week history of high fever (temperature, 40°C), chills, a nonproductive cough, epigastric pain, and dysphagia. He had been aware of his HIV seropositivity for 3 months. He was not receiving any antiretroviral therapy or prophylaxis for *Pneumocystis carinii* pneumonia.

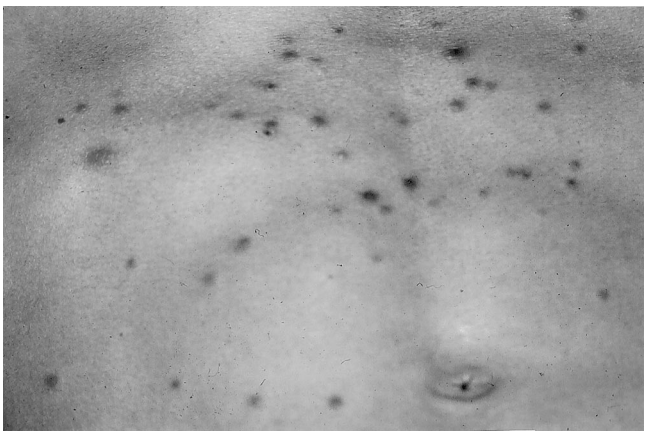

Figure 1. Maculopapular skin eruption in a patient with cutaneous miliary tuberculosis.

Laboratory examinations at the time of admission showed the following values: WBCs, 2,020/mm^3 (72% neutrophils, 24% lymphocytes, and 4% monocytes); hemoglobin, 10 g/dL; RBCs, 5.0×10^{12}/L (mean corpuscular volume, 63 fL); platelets, 46,000/mm^3; CD4 cell count, 2/mm^3; serum urea nitrogen, 112 mg/dL; creatinine, 1.4 mg/dL; aspartate aminotransferase, 777 U/L; alanine aminotransferase, 228 U/L, with a normal bilirubin value; lactate dehydrogenase, 6,520 U/L; and creatine phosphokinase, 1,754 U/L. Findings on a chest radiograph were normal. An ultrasonogram of the abdomen showed hepatomegaly with multiple small hypoechogenic lesions and four solid areas in the right lobe (largest area, 2 cm in diameter) and splenomegaly with multiple pinpoint hyperechogenic lesions. Esophagogastroduodenoscopy revealed a large ulcer (5×6 cm) without protruding edges in the last portion of the esophagus. Multiple blood cultures were performed.

On the second hospital day, the patient developed a diffuse maculopapular skin eruption (figure 1) involving the trunk, abdomen, arms, and legs. He complained of myalgias and severe dysphagia and was confused. A serum cryptococcal antigen test was negative. A skin biopsy was performed, and because of the similarity between the cutaneous lesions and those in the cases of TCMD that we had already seen, we decided to start antituberculous therapy (iv rifampin, isoniazid, and ethambutol at standard doses) plus iv therapy with amikacin (1 g/d). An ophthalmologic evaluation showed yellow choroidal lesions in the right eye that were also compatible with a diagnosis of miliary tuberculosis. Five days later, histological examination of the skin biopsy specimen showed focal areas of necrosis containing multiple acid-fast bacilli. *M. tuberculosis* subsequently grew from cultures of blood and cultures of the skin biopsy specimen. The isolated strain was resistant to isoniazid.

The clinical condition of the patient rapidly improved. His fever disappeared 5 days after the antituberculous therapy was begun, and liver-function test results returned to normal 7 days later. The cutaneous lesions completely disappeared 2 weeks later, and an abdominal ultrasonogram obtained 5 weeks after the first one was obtained showed nearly complete regression of the lesions. The patient was discharged in good health 6 weeks after admission.

Cutaneous miliary tuberculosis is still an uncommon disease, even in the setting of HIV infection, but in recent years the incidence of this form of tuberculosis seems to be increasing. Therefore, when multiple papulovesicular skin lesions are present in a severely ill patient, this condition should be clinically suspected. We agree with Libraty and Byrd that the absence of a miliary pattern on a chest radiograph should not lead to exclusion of the diagnosis of TCMD, since none of our three patients presented with this radiographic picture. The finding of typical choroidal tubercles on ophthalmologic examination could be helpful in supporting the diagnosis of TCMD before the results of histological and microbiological examination of a skin biopsy specimen are available.

Spinello Antinori, Teresa Bini, Laura Galimberti, Luca Meroni, and Roberto Esposito

Department of Infectious Diseases of the University of Milan, L. Sacco Hospital, Milan, Italy

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Reprints or correspondence: Dr. Spinello Antinori, Department of Infectious Diseases of the University of Milan, L. Sacco Hospital, Via G. B. Grassi, 74-20157 Milan, Italy.

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Reply

SIR—Antinori et al. [1] note that they have reported two cases of cutaneous miliary tuberculosis in patients with AIDS that were not included in our review [2]. Furthermore, they present another case that adds to the growing literature on tuberculosis cutis miliaris disseminata in patients with AIDS. We apologize for our oversight and concur with their observations and conclusions.

Hudson et al. point out that they have observed only one case of cutaneous tuberculosis in almost 400 HIV-seropositive patients with tuberculosis. The rarity of cutaneous miliary tuberculosis in HIV-seronegative adults has been well established over the past century. Although cutaneous miliary tuberculosis is obviously not a common entity, its prevalence among HIV-seropositive patients would appear to be higher than among HIV-seronegative patients, as evidenced by the continuing case reports submitted by us [2], Franca et al. [3], Oliva et al. [4], and Antinori et al. [1]. Even a prevalence of 0.5% among HIV-seropositive individuals with tuberculosis would bear out this statement. As mentioned in our article, the occurrence of disseminated cutaneous tuberculosis, like other extrapulmonary manifestations of tuberculosis, simply reflects the stage of HIV disease and consequent cell-mediated immune defects.

We agree that biopsy of cutaneous lesions is not generally the crux of the diagnosis of disseminated tuberculosis in HIV-seropositive patients; when disseminated tuberculosis is suspected, empiri-