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Human Infections Due to *Mycobacterium lentiflavum*

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Three cases of human disease due to *Mycobacterium lentiflavum* are reported. In the first, the mycobacterium was responsible for chronic pulmonary disease in an elderly woman; in the second, it gave rise to cervical lymphadenitis in a child; and in the third, it caused a liver abscess in a young AIDS patient.

CASE REPORTS

Case 1. A 61-year-old woman, bronchiectastic since the age of 30 and with a history of surgical intervention and reiterated cancer chemotherapy because of an ovarian adenocarcinoma, underwent in 1995 a thoracic X ray in the presence of productive cough, weight loss, and slight fever. The radiographic investigation revealed a reticulonodular alteration of the right upper lobe and adenopathy. Following isolation from sputum of numerous colonies of an unidentified scotochromogenic mycobacterium, the patient was hospitalized and treatment with rifampin, isoniazid, and pyrazinamide was undertaken and continued for several months. One year later, the patient was still smear positive and growth from cultures of a mycobacterium subsequently identified as *Mycobacterium lentiflavum* led to replacement of the previous antituberculosis treatment with rifabutin, ethambutol, clarithromycin, and ciprofloxacin. The patient was again microscopically positive for acid-fast bacilli 18 months later when an X ray did not reveal any improvement. Further isolation of *M. lentiflavum* from sputum led to our acknowledging that the treatment was ineffective. At present, the clinical picture remains unchanged and the patient's sputum vacillates between being positive and negative for *M. lentiflavum*.

Case 2. *M. lentiflavum* was isolated from a 4-year-old boy suffering from left cervical lymphadenitis. After excision of the gland, the patient completely recovered and no relapse was observed at follow-up 1 year later.

Case 3. The third case concerns a severely immunocompromised AIDS patient. The subject, a 45-year-old bisexual man, was first hospitalized in 1998 because of fever, weight loss, asthenia, lumbago, and oral candidiasis. On that occasion, he was found to be human immunodeficiency virus type 1 seropositive (viral load, >500,000 copies/ml), with 61 $CD4^+$ lymphocytes/ml. A thoracic X ray revealed a basal opacity in the left lung, while echography and computerized tomography showed a hepatic nodular lesion, 5 cm in diameter and with a hypodense center, most likely due to inflammation. Computerized tomography and scintigraphic studies showed that the fourth dorsal vertebra appeared deformed, most likely as a result of septic inflammation. Treatment with three antiretroviral drugs and with rifabutin and clarithromycin was undertaken. An evident improvement of clinical conditions was soon noted, characterized by disappearance of fever, gain in weight, resolution of the lung opacity, and improvement of the radiographic vertebral picture. There was, however, no change in hepatic status. The microbiological test results of a needle biopsy indicated the presence of *M. lentiflavum*. This finding was assumed to be the link among the pulmonary, bony, and hepatic symptoms. Ethambutol and ciprofloxacin were added to the previous antimycobacterial therapy, but no appreciable results were obtained. In fact, 2 months later, the nodular lesion had enlarged to 6 cm in diameter and continued growing for the subsequent 4 months during which the antimycobacterial treatment was reduced to rifabutin and clarithromycin only. Finally, a lobectomy was performed, and histologic examination led to the diagnosis of non-Hodgkin's lymphoma. At present (1 year later), the patient is in good condition, with a viral load of <400 copies/ml.

Microbiologic analysis. Forty-seven strains of *M. lentiflavum* have been identified in our laboratory within the last 4 years. From this conspicuous cluster, a homogeneous picture of the characteristics of *M. lentiflavum* has emerged. The organism grows slowly at temperatures ranging from 25 to 37°C and is characterized by small, flat, smooth, scotochromogenic colonies. Its biochemical features (3) are similar to those of *Mycobacterium avium*, the majority of tests for both being negative, with only the thermostable catalase test being often positive (Table 1). *M. lentiflavum* is extremely resistant to antimycobacterial drugs; MICs, particularly of isoniazid and rifampin, are very high (5). Lipid analyses have revealed the presence of α-mycolates, α′-mycolates, and keto-mycolates (1). The high-performance liquid chromatographic profile is, as defined in the *M. lentiflavum* sp. nov. description (4), very similar to that of *Mycobacterium simiae*: however, it is distinguished from that of the latter by a closer arrangement of the first and second clusters of peaks (5) (Fig. 1). Genetic investigation of 16S ribosomal DNA has revealed a unique sequence in region A and a short helix 18 in region B, a feature distinc-

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TABLE 1. Biochemical and cultural features of *M. lentiflavum*, as determined by investigation of 47 clinical isolates

Test	Result[a]
Niacin accumulation	−
Nitrate reduction	−
Room temperature catalase	±
68°C catalase	±
Catalase >45 mm of foam	−
Tween 80 hydrolysis	−
Tellurite reduction	−
β-Glucosidase	−
Arylsulfatase	−
Urease	±
Growth rate	Slow
Growth at 25°C	+
Growth at 45°C	−
Pigmentation	
Scotochromogenic	+
Photochromogenic	−
Colony morphology	Smooth
Growth on MacConkey agar	−
Tolerance for:	
NaCl (5%)	−
Thiophene-carboxylic acid hydrazide (1 μg/ml)	+
Thiacetazone (10 μg/ml)	+
p-Nitrobenzoic acid (500 μg/ml)	+
Hydroxylamine hydrochloride (500 μg/ml)	+
Isoniazid (1 μg/ml)	+
Oleate (250 μg/ml)	+

[a] +, positive; ±, variable; −, negative.

tive of rapidly growing mycobacteria but shared also by *M. simiae* and an increasing number of related organisms, (4).

Discussion. *M. lentiflavum* was recognized as a new species in 1996 on the basis of a cluster of 22 isolates (4). Although 11 such isolates were due to a contaminated bronchoscope, all the others were independently isolated in Germany, Switzerland, and the United States. Among them, one isolate was clinically significant, as it had been isolated from a vertebral disk in an elderly patient suffering from spondilodiscitis (4). One year later, a report concerning two cases of cervical lymphadenitis in two very young children was published (2). No other information about the clinical significance of *M. lentiflavum* has been published so far.

The isolation of a nontuberculous mycobacterium always raises doubts about clinical significance, and the touchstone in such cases is represented by the ad hoc diagnostic criteria defined several years ago by the American Thoracic Society (6). The medical relevance of the *M. lentiflavum* isolations reported here appears, on the basis of such diagnostic criteria, unquestionable, because in one case the organism was repeatedly isolated from sputum over a period of 4 years and in the others it was observed in and isolated from biopsy specimens. Some small doubt exists as to the clinical importance of the hepatic isolate, since there was another active disease process (lymphoma) predisposing the patient to opportunistic colonization or infection.

An approximate assessment of the prevalence of cases in which an *M. lentiflavum* isolation may be clinically significant is about 10% in our survey, as of the 29 isolates (out of 47 investigated in our laboratory) for which it was possible to get clinical information, only 3 could be clinically assessed.

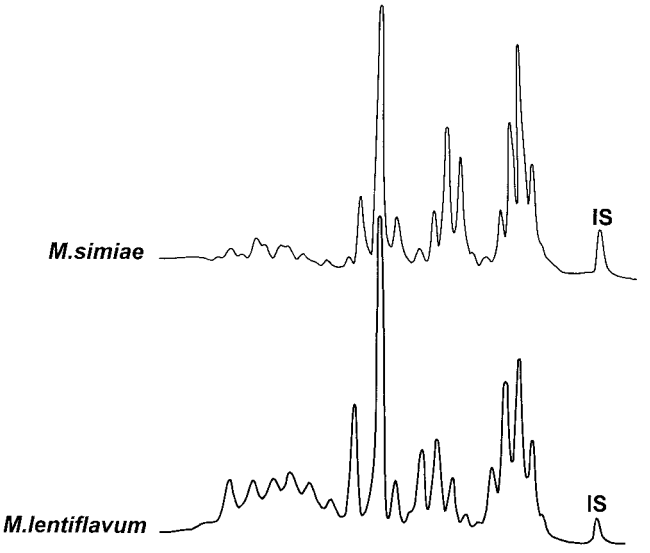

FIG. 1. Comparison of representative high-pressure liquid chromatographic patterns of mycolic acid bromophenacyl esters of *M. lentiflavum* and *M. simiae*. IS, internal standard.

These cases serve to confirm the potential pathogenicity of *M. lentiflavum*, with cervical lymphadenitis in children appearing to be the most common infection, accounting for one half of the pathologies due to *M. lentiflavum* reported so far. On the contrary, the cases described here represent the first report of *M. lentiflavum* pulmonary disease.

Of grave concern is the apparent multidrug resistance of *M. lentiflavum*, first described in in vitro testing (5) and now partially confirmed in vivo by the two cases reported here in which patients remained unresponsive to therapy. If this organism is truly as resistant as our limited data suggest, then it truly may be an emerging opportunistic pathogen.

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