

### The first case of *Mycobacterium sherrisii* disseminated infection in a child with AIDS

*Mycobacterium sherrisii* is a recently described mycobacterium previously included in the *Mycobacterium simiae* group [1]. *M. sherrisii* can be easily confused with *M. simiae* in the laboratory as both are photochromogenic and share the same three-clustered profile when high performance liquid chromatography (HPLC) of cell wall mycolic acids is performed [2].

Only two cases of human disease caused by *M. sherrisii* have been reported [3,4]. Both subjects, a patient with AIDS and an immunocompetent middle-aged man, showed pulmonary involvement.

We report here the first case of a disseminated infection in a child with perinatal HIV infection. The patient, a 7-year-old boy coming from Eritrea was hospitalized in April 2005, at the Department of Paediatrics, University of Florence, because of persistent high fever (up to 39.5°C), chronic diarrhea, abdominal pain and failure to gain weight from 5 months. The child had never been treated with antiretroviral drugs, he had, however, received *Pneumocystis jiroveci* prophylaxis with trimethoprim-sulfamethoxazole. At admission, the HIV-1 RNA plasma load was 1 088 000 copies/ml and the CD4 cell count was 72 cells/ $\mu$ l. The child manifested oral candidiasis and abdominal tenderness. Chest X-ray was negative whereas abdominal tomographic scan as well as ultrasound imaging showed the presence of free peritoneal fluid and mesenteric adenopathy. The child was anemic (hemoglobin 7.1 mg/dl), and presented with 5400 white blood cells/ $\mu$ l, a severe increase of C-reactive protein (more than 10-fold normal values), and slightly increased hepatic enzymes alanine transferase and aspartate transferase (fivefold normal values). Investigations for cytomegalovirus, *Cryptococcus neoformans*, *Amoeba* spp., *Leishmania* spp., malaria, *Cryptosporidium* spp., *Isospora* spp. were all negative. Four days after admission, antiretroviral treatment was started with stavudine (1 mg/kg twice a day), plus lamivudine (4 mg/kg twice a day), plus lopinavir/ritonavir (12 mg/kg twice a day of lopinavir) and empiric antibacterial and antifungal treatments were undertaken, but the general condition worsened. Fever became continuous and severe cramping abdominal pain developed. An intestinal obstruction, probably caused by enlarged lymph nodes, was surgically removed.

In a 3-week period, samples of peritoneal fluid, lymph nodal biopsy, blood, gastric aspirate and urine were investigated for the presence of mycobacteria. Although they were smear-negative for acid-fast bacilli (with the exception of the gastric juice, which was weakly positive) all, but the urine sample, yielded positive mycobacterial cultures after an incubation ranging from 2 to 4 weeks.

All the isolates (which were photochromogenic) were identified using the commercial DNA probe INNO LiPA (Innogenetics, Ghent, Belgium) as *M. simiae*, an identification that was in agreement with the HPLC pattern of cell wall mycolic acids.

Antimycobacterial treatment with ethambutol (20 mg/kg a day), clarithromycin (15 mg/kg twice a day) and ciprofloxacin (30 mg/kg a day) was undertaken.

Susceptibility testing performed by the broth microdilution method, as recommended by the Clinical and Laboratory Standards Institute (previously NCCLS) [5] for non-tuberculous mycobacteria, revealed high minimum inhibitory concentration values with ciprofloxacin, clarithromycin, ethambutol, linezolid, rifampin, streptomycin, and moxifloxacin, with susceptibility only to rifabutin and amikacin (Table 1). Accordingly, amikacin (30 mg/kg a day) was added to the treatment regimen and the patient became afebrile within a few days. Abdominal cramps resolved within one month of treatment but amikacin monotherapy was continued for 6 weeks, because of relapsing fever with interruption of treatment. Currently the child, who is back in Eritrea, is well and his CD4 cell count is 400 cells/ $\mu$ l.

One year later, during a polycentric study of *M. simiae* (in preparation), all of the strains of our laboratory collection identified as belonging to *M. simiae* species were submitted to genetic sequencing of the 16S rRNA gene. Further investigation of the strain reported here revealed 100% identity with the species *M. sherrisii*, and the genetic sequencing of a 440 base pair segment of the gene encoding for the 65KD heat shock protein confirmed this identification.

Our report corroborates the lack of information available concerning *M. sherrisii*. This species may be commonly misidentified as *M. simiae* using HPLC or commercial DNA probes [4] as well as with conventional and biochemical tests [2]. Like *M. simiae*, *M. sherrisii* is highly drug resistant in vitro and, as with many non-tuberculous mycobacteria, may cause disease in HIV-positive patients.

Of the two previously reported cases, the patient with AIDS was successfully treated with a combination regimen of clarithromycin, rifabutin and moxifloxacin [3], whereas the other patient did not benefit from a standard

**Table 1. In-vitro antimicrobial susceptibility of the *M. sherrisii* strain.**

Drug	MIC ( $\mu$ g/ml)	Interpretive category
Amikacin	4	S
Ciprofloxacin	>16	R
Clarithromycin	8	S
Ethambutol	8	R
Linezolid	64	R
Moxifloxacin	2	-
Rifabutin	0.03	S
Rifampin	4	R
Streptomycin	>64	-

I, Intermediate; MIC, minimum inhibitory concentration; R, resistant; S, susceptible. There are no CLSI interpretive criteria for streptomycin or moxifloxacin.

antituberculosis treatment [4]. The source and the number of isolations unquestionably support the clinical significance of the case reported here. The availability of the in-vitro antimicrobial susceptibility, which allowed us to adjust the treatment, played a major role in the excellent response of the patient. Moreover the efficacy of treatment allowed us to contain a disseminated mycobacterial infection while stable immune reconstitution was developing, with the initial worsening of the clinical picture being probably imputable to a precocious immune reconstitution syndrome, often associated with nontuberculous mycobacteria [6].

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