Reviewer's report

Title: Multidrug Resistant M. tuberculosis from Multiple Cutaneous Abscesses in a Patient with Polymyositis: Response to treatment

Version: 4 Date: 23 September 2004

Reviewer: Hendrik Simon S Schaaf

Reviewer's report:

General
Thank you for the opportunity to review the revised manuscript. Although there is a vast improvement from the first manuscript, I still have the following comments:

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Abstract:
The format is much better, but the content does not accurately summarize the case. No mention is made of the initial susceptible TB and treatment leading to the MDR miliary TB and multiple cutaneous abscesses. Also the role of the immunosuppressive treatment and the withdrawal thereof is not mentioned. The final conclusion can probably not be deducted from this case.

2. Background:
Last sentence 3rd paragraph: Delete “The category of” Acquired drug resistance (now called previously treated drug resistance) includes patients in whom M. tuberculosis truly acquired drug resistance during treatment, patients who were primarily infected with drug resistant strains but not diagnosed at that time, and patients reinfected with a drug resistant strain.

3. Case Report:
3.1 Were all abscesses aspirated and to what extent, that is, were they completely drained? This could be an important adjunct to treatment in immunocompromised patients.
3.2 It is most important to describe the findings of the RFLP analyses. This is currently not described in the case report. The authors should very specifically state whether the DNA fingerprint pattern (RFLP result) is identical or different in the two episodes. If the RFLP patterns are different, then the most likely will be a reinfection with a MDR TB strain. If, however, the strains are identical in the two episodes it will be very hard to explain how the strain became resistant to so many drugs in such a short period of time without those drugs even being used.

4. Discussion:
4.1 Second sentence: The case report does not show that the patient has the same M. tuberculosis strain on both occasions (no RFLP results), but only demonstrated that the organism involved was M. tuberculosis on both occasions. There is also no legend to figure 1 to describe what actually was found with the devR test. The case report should clearly state whether RFLP pattern of M. tb was identical or not in the two episodes.

4.2 Van Rie actually showed that in an area of high TB incidence, reinfection with MDR strain is more common than acquiring MDR TB through treatment. Resistant mutations to INH occurs in 1 x 106 organisms and to RMP in 1 x 108 organisms, therefore to develop (acquire) MDR (INH and
RMP) resistance, 1014 organisms should be present – imagine how many organisms should be present to develop 9-drug resistance in only 6 months, and with “compliant” treatment! On the other hand, it is possible for a patient to be infected with more than one strain at the same time. (Warren RM, Victor TC, Streicher EM, Richardson M, Beyers N, van Pittius NC, van Helden PD. Patients with active tuberculosis often have different strains in the same sputum specimen. Am J Respir Crit Care Med. 2004;169(5):610-4.) This needs to be discussed as well.

4.3 “Multidrug resistance is higher in HIV-infected patients” I don’t know whether this statement is applicable in this report, as the patient was HIV-negative. Further, I do not agree with the statement, although it has been documented in a couple of articles and books. This is because of misinterpretation of MDR TB outbreaks, especially in the US and Europe, among mainly institutionalized HIV-infected patients in the early 1990s. Many subsequent reports from countries with high incidences of both TB and HIV has shown that MDR TB is NOT more common in HIV-infected patients compared with HIV-negative patients. The only drug to which increased development of resistance has been documented in HIV-infected patients, most likely due to poor absorption or other factors, is RMP.

4.4 I am confused by the statements about RFLP in the discussion. Did the RFLP analysis show different strains in this patient? Does the sentence following this statement have anything to do with this patient or the context of the case, as no mention was made of any index case with TB?

4.5 I agree with the authors that stopping the immunosuppressive drugs was probably mainly responsible for the cure of this patient. I do think that the inaccuracy of drug susceptibility testing for second line antiTB drugs should also be discussed briefly.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Background:
1.1 “The incidence of sputum smear-positive cases of pulmonary TB and the incidence of extrapulmonary TB cases in India is about 0.9 million and 0.2 million per year, respectively. (Reference) Cutaneous TB is rare (0.1%), with lupus vulgaris the most frequent manifestation of cutaneous TB in a study among dermatology patients in northern India (Ref 2). Similar low incidences…” [I suggest to leave out all other forms of EPTB]
1.2 A reference is needed about increase of cutaneous TB in HIV infected patients. [at the end of the 1st paragraph]
1.3 Last paragraph – reduce to: “We report a rare case of multiple cutaneous TB abscesses and miliary TB caused by multidrug resistant M. tuberculosis in young man treated for polymiositis.”

2. Case Report:
2.1. “He was treated with immunosuppressive drugs including corticosteroids at 1 mg/kg/day for 4 weeks, tapered gradually over 10 weeks to 1 mg/kg on alternative days, and methotrexate at 7.5 mg weekly with gradual increase to 25 mg weekly for a period of one year.”
2.2. “The patient was treated with a 4-drug regimen (isoniazid …), the first 2 months of which was supervised. The M. tuberculosis strain was susceptible to all 4 drugs by drug susceptibility testing in Bactec 460TB system. The patient improved clinically. The patient returned 6 months later with multiple cutaneous abscesses, mainly on his back, left thigh and left arm. The CXR showed miliary mottling. Although treatment was not supervised after the first two months, the patient denied irregular intake of antituberculosis drugs. The patient was readmitted and all immunosuppressive drugs (corticosteroids and methotrexate) were discontinued.

3. Discussion:
First sentence: “…new patients have MDR TB.”
Discretionary Revisions (which the author can choose to ignore)

Background:
The 1st sentence of the 2nd paragraph is correct, but it would add value if the authors could also state what type of skin TB one would expect to find in an immunocompromised patient.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
None