Mediterranean spotted fever: a report of 200 cases in Tunisia

F. B. Romdhane¹, C. Loussaief¹, A. Toumi¹, S. B. Yahia², M. Khaiyrallah², N. Bouzouaïa¹ and M. Chakroun¹

¹Department of Infectious Diseases, Fattouma Bourguiba University Hospital, Monastir, Tunisia and ²Department of Ophthalmology, Fattouma Bourguiba University Hospital, Monastir, Tunisia

INTRODUCTION

Mediterranean spotted fever (MSF) is a tick-borne zoonosis caused by Rickettsia conorii. Its first description was made by Conor and Brush in Tunisia in 1910, where this disease is the most common rickettsiosis.

The characteristic symptoms are fever and rash with the presence of a black eschar ‘tache noire’ in the majority of cases. Early empiric therapy with tetracycline is the standard care for any case considered consistent with a MSF infection while confirmatory laboratory results are pending.

The aim of our study is to assess the effectiveness of a short course of antibiotic treatment in MSF.

MATERIALS AND METHODS

All patients diagnosed with MSF at the Department of Infectious Diseases, University Hospital of Monastir, Tunisia, during the period January 1987 to December 2006, were included in this case series.

Diagnosis was considered confirmed if the patients had an MSF diagnostic score of >25 according to the scoring system described by Raoult et al. [1].

For the analysis of the data, SPSS version 13.0 was used. Contingency data were analysed by use of the $\chi^2$ test; continuous data were analysed by use of the Student’s t-test. Statistical significance was set at $p \leq 0.05$.

RESULTS

A total of 200 patients were diagnosed with MSF during the study period. Most of the cases ($n = 183$) occurred between June and October. The median age was 38.4 years (range, 15–80 years). One hundred and twenty-three (61.5%) of the patients were male. Direct contact with dogs was reported in 153 (76.5%) cases. Patients were admitted to the infectious department after a median of 6.7 days (range 1–15) of fever. Clinically, fever was the most common symptom (100%), followed by rash (98.5%), headache (76.5%), arthromyalgias (64.5%), ‘tache noire’ (63%), conjunctival hyperaemia (23%), local lymphadenopathy (18%), coughing (10.5%) and meningitis (1%).

Among the laboratory studies, leucocytosis (white blood cell count $>10 \, 000/\text{mm}^3$) was found in 133 (66.5%) patients and thrombocytopenia (platelet count $<150 \, 000/\text{mm}^3$) in 132 (66%). AST and/or ALT levels were abnormal ($>50 \, \text{IU/mL}$) in 148 of 177 (83.6%) cases.

Indirect immunofluorescence to R. conorii was performed in 194 (97%) cases. Thirty-six patients had two serum samples with four-fold titre elevation within 2 weeks; 73 had a single serum sample with IgG of $\geq 1:128$ and IgM of $\geq 1:64$; 43 had negative serology both on admission and in convalescence; 42 patients had negative serology on admission and did not have another sample taken after 2 weeks. In all patients the diagnosis has been made on the grounds of the Raoult criteria [1].

Dilated biomicroscopic fundus examination showed retinal involvement in 48 of 88 patients (54.6%). This abnormality was asymptomatic except for four patients who had mild visual loss.

Antibiotic therapy consisted of oral tetracycline (49%), ciprofloxacin (20%), doxycycline (18%), azithromycin (12%) and josamycine (1%). The different group regimens were comparable regarding clinical and laboratory data.

Compared with the standard therapy with tetracycline, disappearance of fever, arthromyalgias and rash were statistically more rapid (respectively, $p = 0.0036$, 0.009 and 0.016) in the group treated with azithromycin (Table 1).

With doxycycline, only fever and rash disappeared much more quickly compared with tetracycline (respectively, $p = 0.039$ and 0.0054).
Thirty-five patients received 3 days of ciprofloxacin. Compared with tetracycline, ciprofloxacin was effective but the differences were not statistically significant.

When compared with each other, there was no statistical difference between the use of a 3-day regimen with ciprofloxacin and 1-day regimen with doxycycline or azithromycin.

The different regimens were equally well-tolerated and no major side-effects were observed. The outcome was favourable in all patients and no relapses were observed during follow-up.

**DISCUSSION**

In our study, we demonstrate that 1-day azithromycin or doxycycline therapy is an effective and safe treatment for MSF in adults. In children, 3-day azithromycin therapy is effective [2]. A shorter duration of this antibiotic in adults had not been tested. It was effective in our study, probably because azithromycin has a long half-life. A single dose of doxycycline (200 mg) has been shown to be sufficient for MSF [3]. Efficacy of 7 days of ciprofloxacin has been reported [4]. In our study, 3 days of this antibiotic was also sufficient to treat MSF.

In atypical forms of MSF, the clinician may hesitate to use a short regimen. In these cases, fundus examination may be helpful in the early diagnosis of this disease [5]. In fact, retinal involvements are frequent in MSF and observed in 54.6% of our cases.

However, for patients with severe forms short regimens should not be considered. Furthermore, there is a need for more well-designed randomized controlled trials to support our findings.

**CONCLUSION**

One-day treatments with azithromycin and doxycycline are effective and may offer an effective alternative treatment to conventional regimens, with potential for better compliance and reduced costs.

**ACKNOWLEDGEMENT**

The authors are greatly indebted to Professor Mahmoud Bchir for his help in improving the language of this article.

**REFERENCES**