

Ofloxacin in miliary tuberculosis

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ABSTRACT: We report one case of severe miliary tuberculosis with liver failure and respiratory insufficiency in a twenty-seven year old patient. We emphasize the presence of hepatic, ocular and vestibular toxicities secondary to the treatment and the usefulness of ofloxacin with cycloserine given for nine months.

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Miliary tuberculosis is one of the most severe clinical forms of mycobacterial infection and an early diagnosis and prompt treatment are essential for a favourable clinical outcome [1, 2]. Occasionally, the prognosis in these patients is darkened by the development of drug toxicity [3] that requires the use of reserve drugs as the case reported here.

Case Report

A 27 yr old man with recurrent renal stones for the previous four months was admitted into our hospital after two weeks of fever, chills, cough, increasing shortness of breath and jaundice. Physical examination showed a febrile patient with tachypnoea, icteric skin and mucosae and a painful 2 cm liver edge. A chest X-ray showed micronodular interstitial bilateral infiltrates and an intravenous pyelogram a left ureteropelvic ectasia. The laboratory results were: ESR 110 mm·h⁻¹, leukocytosis with a left shift, total bilirubin 7.2 mg per 100 ml, direct bilirubin 5.8 mg per 100 ml, serum aspartate aminotransferase 177 IU·l⁻¹, serum glutamic-pyruvic transaminase 168 IU·l⁻¹, alkaline phosphatase 177 IU·l⁻¹, gamma-glutamyltransferase 78 IU·l⁻¹ fibrinogen 0.2 gm per 100 ml, prothrombin time 37%, urea nitrogen 42 mg per 100 ml and microhaematuria. Arterial blood gases on room air breathing were: Pao₂+ 7.9 kPa, Paco₂ 4.6 kPa and the pH 7.34. A Ziehl-Neelsen stain revealed the presence of acid-fast bacilli in the urine and the bronchial washings.

A diagnosis of miliary tuberculosis with severe liver and lung involvement was established and the patient was placed initially on triple therapy with isoniazid (INH) (300 mg per day, orally), rifampicin (RFP) (600 mg per day, orally) and ethambutol (ET) (1,400 mg per day, orally). After eight days because of worsening liver function tests (total bilirubin 14.3 mg·l⁻¹, direct bilirubin 9.8 mg·l⁻¹, serum aspartate aminotransferase 210 IU·l⁻¹, serum glutamic-pyruvic transaminase 189 IU·l⁻¹, alkaline

phosphate 498 IU·l⁻¹, gamma-glutamyltransferase 165 IU·l⁻¹), the treatment was switched to cycloserine (250 mg q 6h, orally) and streptomycin (1g per day IM). After two months on this treatment, the Pao₂ was improved (10.9 kPa) as well as the liver function tests (total bilirubin 1.9 mg·l⁻¹, direct bilirubin 1.5 mg·l⁻¹, serum aspartate aminotransferase 49 IU·l⁻¹, serum glutamic-pyruvic transaminase 44 IU·l⁻¹, alkaline phosphate 210 IU·l⁻¹, gamma-glutamyltransferase 69 IU·l⁻¹) and the pulmonary infiltrates from chest X-ray. However, the patient was still febrile and had acid-fast organisms in the urine. Because of the development of vertigo and changes of his visual acuity, streptomycin and ET were discontinued and replaced by INH and RFP. This was again followed by early abnormalities of the liver function tests (total bilirubin 38 mg·l⁻¹, direct bilirubin 29 mg·l⁻¹, serum aspartate aminotransferase 320 IU·l⁻¹, serum glutamic-pyruvic transaminase 277 IU·l⁻¹, alkaline phosphate 500 IU·l⁻¹, gamma-glutamyltransferase 132 IU·l⁻¹).

A liver biopsy was performed and revealed necrotizing granulomas with acid-fast bacilli and changes consistent with a severe toxic hepatitis. We then decided to add ofloxacin (200 mg q 8h, orally) to cycloserine, and with this combination the patient became afebrile, the sputum and urine cultures became negative, there was normalization of the liver function tests. There were no further complications during the nine months with this treatment. Nine months after having finished the treatment the patient is asymptomatic.

Lowenstein cultures grew *Mycobacterium tuberculosis* sensitive to isoniazid, rifampicin, streptomycin, ethambutol and cycloserine, and resistant to ethionamide.

Discussion

Liver failure, respiratory insufficiency, consumption coagulopathy and drug toxicity are adverse prognostic factors in miliary tuberculosis [3-5]. Our patient had

miliary tuberculosis with severe liver and lung failure, and developed hepatic, ocular and vestibular toxicities secondary to the treatment. Because of these side-effects, INH, RFP, streptomycin and ethambutol had to be discontinued. Due to the persistence of fever and positive cultures, we had to look for new treatment combinations. We based our decision to use ofloxacin in combination with cycloserine, on the works of TSUKAMURA [6, 7] showing the excellent bactericidal activity of this quinolone against *Mycobacterium tuberculosis*. This drug combination achieved a good clinical and bacteriological response.

While waiting for further reports, we feel that the new quinolones may be considered for the treatment of difficult cases of tuberculosis infection such as those with drug intolerance or multiple drug resistance.

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Observation clinique. L'ofloxacine dans la miliaire tuberculeuse. J. Alegre, T. Fernández de Sevilla, V. Falcó, J.M. Martínez Vazquez.

RÉSUMÉ: Il s'agit d'un cas de miliaire tuberculeuse sévère, avec décompensation hépatique et insuffisance respiratoire, chez un sujet de 27 ans. Nous insistons sur la présence de réactions secondaires au traitement, à la fois au niveau hépatique, oculaire et vestibulaire, et sur l'utilité de l'ofloxacine combinée à la cyclosérine pendant neuf mois. *Eur. Respir J.*, 1990, 3, 238-239.