

Multidrug-Resistant Tuberculosis: Review of the Literature from A Case of Choroidal Granuloma Associated with a Pott's Disease Secondary to a Pulmonary Localization



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Abstract

Multidrug-resistant tuberculosis (MDR-TB) is due to resistance of Koch's Bacillus to Rifampicin and / or Isoniazid. Another therapeutic protocol called second line is necessary. It combines in attack phase (6 months) an aminoside, a fluoro quinolone, Ethionamide and Pyrazinamide. The maintenance phase (12 to 18 months) is constituted by a fluoroquinolone, Ethionamide, and Pyrazinamide. Ethambutol may be associated with both phases if the genetic analyzes prove that it is active on the causal strain. New molecules (Bedaquiline, Delamanide) are already in use in so-called ultra-resistant forms when the second classical line is ineffective. All these drugs are not part of the national tuberculosis programs. Their cost is a real brake in Africa. The aim of this work was to examin literature review on MDR-TB from a case with pulmonary, bone and ocular involvement.

Keywords: Multidrug-resistant; Rifampicin; Isoniazid; Pyrazinamide; Ethambutol; Fluoroquinolone; Aminoside; Bedaquiline; Delamanide

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is defined as a form of a Koch's bacillus strain resistant to Rifampicin and / or Isoniazid [1]. These two molecules constitute the major drugs of the first line that they form in association with Pyrazinamide and Ethambutol. This resistance may be primary when the patient has never received an anti-tuberculosis medication or secondary if the patient has already been treated for tuberculosis [2-4]. In case of resistance a second line of drugs is necessary. It combines an aminoside (Kanamycin, Amikacin, Capreomycin), a fluoroquinolone (Ofloxacin, Moxifloxacin), thionamide and Pyrazinamide. The maintenance phase (12 to 18 months) is constituted by a fluoro quinolone, Ethionamide and Pyrazinamide. Ethambutol may be associated if genetic testing proves that it is active on the causal strain. Bedaquiline and Delamanide are used in so-called ultra-resistant forms when the second classical line is in effective [5-7]. This work makes a short

review of the literature on MDR-TB from a clinical form with a multi focal localization.

Case Details



Figure 1: Pneumopathy due to tuberculosis.



Figure 2: Pott's disease due to lysis of dorsal vertebraes.

A patient aged 25 was seen for a decline of right visual acuity evolving for a week. He takes a tuberculosis treatment (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol) since 4 months due to left pneumopathy (Figure 1). This visual decrease was preceded by a paraplegia following a Pott's disease due to lysis of dorsal vertebraes (Figure 2).

His ophthalmological review noted

1. Right eye: no light perception, clear cornea, panuvéïte with an important vitritis making the fundus difficult, ocular tonus 12mm Hg.
2. Left eye: visual acuity at 20/20 without correction, normal ocular structures, ocular tonus 13mm Hg.

Ultrasound showed a choroidal granuloma and total detachment of the retina (Figure 3). PCR revealed the presence of Koch's bacillus DNA in the vitreous. HIV serology was negative. Retinal fluorescein angiography was not performed because of the vitreous blur. The diagnosis of multifocal tuberculosis was retained. A program for the readjustment of anti tuberculosis treatment has been planned. The proposed protocol was formed during the attack phase by Ethionamide, Ofloxacin, Amikacin and Pyrazinamide. This protocol could not be realized because the patient has not returned to the hospital.



Figure 3 : Choroidal granuloma and retinal detachment in tuberculosis.

Discussion

According to the WHO the prevalence of multidrug-resistant tuberculosis (MDR-TB) is just under 1% in rich countries compared to 20% in some areas of black Africa [8,9]. Several factors may explain this, the high prevalence of HIV infection, politico-military conflicts and poverty [10-12]. The first anti-tuberculosis drugs appeared during the Second World War. The arrival of Rifampicin in the 1970's has upset the situation. Combined with Isoniazid it has remarkable efficacy against Koch's bacillus. The four-drug combination of Rifampicin, Isoniazide, Pyrazinamide and Ethambutol is the standard treatment used by most national tuberculosis programs. So much so that it was believed in the 1980 's that tuberculosis would be eradicated before the end of the 20th century [11]. But the situation changed completely in the 1980's with the emergence of the AIDS pandemic. The clinical studies carried out at the time all prove that tuberculosis is one of the main opportunistic diseases of AIDS [13,14]. In the early 1990's the first cases of Koch bacillus strains resistant to classical anti-tuberculosis drugs were described. These strains no longer respond to the combination of the two major antibiotics of the first line, Isoniazid and Rifampicin. A real public health problem around 250000 deaths per year have related to MDR-TB [2,4,8]. The management of these multiresistant forms can be confronted with 3 major obstacles. First of all the diagnosis if one does not suspect the possibility of multi-resistance the affected patients will receive conventional treatments. They will remain contagious and make their bacterial strain even more resistant. Then the duration of the treatment, even with an adapted management the patients take more time to heal. A typical tuberculosis treatment lasts an average of 6 months. Treatment of MDR-TB can last up to 24 months, patients remain contagious for up to 3 months. Molecular biology and genetics have made significant progress in the typing of these resistances. They made it possible to determine in the DNA of the Koch's bacillus the genetic mutations responsible of these resistances. These are the RpoB gene for Rifampicin, and the KatG and InhA genes for Isoniazid. In the highly-resistant forms, resistance to Ethionamide and fluoroquinolones are respectively due to pncA and gyrB genes [15, 16]. We have not found any studies on aminoglycoside resistance. However the systematization of their use is limited by 2 things, their renal and atrial toxicity and to a lesser extent the pain induced by the repeated injections related to their administration. Indeed unlike the other antituberculosis drugs which are presented in the form of tablets aminoglycosides exist only in injection [7,17,18]. Research is advancing but more slowly than hoped. In the last fifty years only two molecules have been placed on the market Bedaquiline and Delamanide less than five years ago. These drugs are active on the highly resistant strains of the Koch's bacillus [19-21]. Outside of South Africa and some Maghreb countries, entire regions of Africa do not have laboratories capable of performing the necessary analyzes in case of suspicion of MRD-TB. Second-line drugs such

as fluoroquinolones and aminoglycosides are available, but the duration of their use significantly increases the cost of treatment by making it unattainable for the majority of patients. MDR-TB should be integrated into the overall strategy of the various national tuberculosis programs.

Conflicts of Interest

There are no conflicts of interest.

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