Case report

Prolonged use of bedaquiline in the treatment for MDR-TB in a child

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ABSTRACT

Bedaquiline (Bdq), a novel TB drug, is referred to the most effective drugs and used for the management of multidrug-resistant tuberculosis (MDR-TB). The drug produces a cardiotoxic effect, and its use is limited to six months. We describe a clinical observation of prolonged bedaquiline use in the treatment for MDR-TB using a restricted number of drugs, to which susceptibility was preserved, in a 12-year-old child. The previous treatment course had failed; the patient remained sputum-positive after eight months of the treatment. We used a personalized approach to chemotherapy correction based on repeat drug susceptibility testing. The treatment regimen only contained those drugs, to which susceptibility was preserved: amikacin, cycloserine, linezolid, bedaquiline (AmCsLzdBdq). Amikacin was withdrawn after three months due to the development of sensorineural hearing loss. The treatment was continued with CsLzdBdq. The total chemotherapy course took 18 months. Sputum conversion was observed after one month, cavity closure – by 18 months of treatment. We did not observe cardiotoxic effects due to prolonged bedaquiline use. The administration of prolonged bedaquiline use was based on life-saving considerations. We achieved favourable treatment outcome and demonstrated safety of prolonged bedaquiline use for a child.

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Introduction

MDR-TB patients is the most challenging group of patients with low treatment effectiveness due to resistance to two major TB drugs – isoniazid and rifampin. The new TB drug, bedaquiline, improves treatment effectiveness in these patients; it has been recommended for the treatment of MDR-TB since 2013 [1]. Bedaquiline produces a cardiotoxic effect, which limits its use to six months. In 2018 WHO revised its classification of TB drugs by priority in the treatment for MDR-TB; Bdq was referred to the most effective drugs [2]. Since 2019 Bdq has been allowed for the use in children aged 6 years or above [3]. WHO has affirmed that the risk–benefit assessment of the use of Bdq in patients aged 6–17 is incomplete due to scarce information; the same situation is with the use of Bdq beyond six months [3]. WHO refers the use of Bdq in adults and children to research priorities related to MDR-TB treatment [3].

The objective of our publication is to share the experience of prolonged bedaquiline use in the treatment for MDR-TB with a restricted number of drugs, to which susceptibility was preserved, in a child.

Case report

A girl aged 12 years was hospitalized after eight months of unsuccessful treatment for disseminated pulmonary rifampin resistant tuberculosis (RR-TB) to determine further treatment tactics. A household contact with the father, who was ill with TB since 2016, was established; drug susceptibility data were absent. The girl was diagnosed with TB in December 2018 at the referral to a health facility with complaints of high temperature (39 °C), expectoration, and weakness. Plain chest X-ray revealed infiltrative changes with cavities in the upper lobe of the left lung with multiple dissemination foci into both lungs. Ziehl-Neelsen sputum smear microscopy result was positive. The Xpert® MTB/RIF assay determined resistance to rifampin. Chemotherapy was administered as follows: AmZELfx – three months; ZELfxEtO – five months. The treatment outcome: a positive sputum smear result by microscopy, lack of positive X-ray dynamics. The BACTEC MGIT-960 detected growth of mycobacteria in culture.

Multidrug resistance (MDR) of M. tuberculosis was established with the following spectrum: isoniazid, rifampin, ethambutol, pyrazinamide, ethionamide, levofloxacin, moxifloxacin, para-
aminosalicylic acid (HREZEtoLfxMfxP AS). Susceptibility to amikacin, capreomycin, cycloserine, linezolid, bedaquiline (AmCmCsLzdBdq) was preserved. Chest computed tomography (CT) showed the presentations of disseminated pulmonary TB (Fig. 1). Considering the prior treatment failure due to drug resistance and severity of the disease, we used a personalized chemotherapy regimen (AmCsLzdBdq) adapted to the specific case. The chemotherapy regimen contained bedaquiline, which was a new drug with age restrictions for that moment: age 18 years or above. We obtained an informed consent for bedaquiline use from the patient’s father. Amikacin was withdrawn after three months due to the toxic reaction (sensorineural hearing loss), and the treatment was continued with CsLzdBdq. We used three courses of bedaquiline due to life-saving considerations. Sputum conversion was observed after one month. Chest CT after 18 months of treatment showed significant resolution of infiltrates and dissemination foci in S 1, 2 of the left lung, cavity closure (Fig. 2). We did not observe cardiotoxic effects of the prolonged use of bedaquiline (the QTc interval did not change during the whole treatment course).

Discussion

Persistent sputum positivity during the management of RR-TB requires extended microbiological testing for the subsequent correction of chemotherapy. The personalized approach to the selection of drugs with the inclusion of bedaquiline and its prolonged administration was preconditioned by the disease severity and the limited choice of TB drugs according to drug susceptibility testing. This observation demonstrates effectiveness and safety of the prolonged administration of bedaquiline for children.

Consent

Consent to publish this case report was obtained from the patient’s family and the copy of the consent is available for the journal on request.

Ethics approval and consent to participate

No ethical approval was obtained for this case report.

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CRediT authorship contribution statement

Marina F. Gubkina: Conceptualization, Analysis and interpretation of data, Writing – original draft preparation. Julia Yu. Khokhlova: Acquisition of data, Patient care, Analysis and interpretation of data. Natalia V. Yukhimenko: Analysis and interpretation of data, Supervision, Writing – review & editing. Irina Yu. Petrakova: Acquisition of data, Patient care, Analysis and interpretation of data, Description of CT images. All the authors participated in the patient management. All the authors read and agreed with the final version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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