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Correspondence

Clozapine for mitochondrial psychosis

Letter to the Editor

With interest we read the article by Demily et al. about a 30 year old male with neuropathy, ataxia, and retinitis pigmentosa (NARP) syndrome due to the mutation m.8993T>C, clinically manifesting as cerebellar ataxia, pyramidal syndrome, and psychosis [1]. Upon antipsychotic medication the patient developed dystonia, akathisia, and extrapyramidal symptoms with falls [1]. Switching to clozapine resolved psychosis but triggered fatigue, myoclonus, and falls. We have the following comments and concerns.

Psychosis is an increasingly recognised phenotypic central nervous system (CNS) manifestation in various mitochondrial disorders (MIDs). Since MIDs are frequently multisystem disorders either already at onset or become multisystemic during the disease course, antipsychotic treatment becomes challenging due to its multiple CNS and extra-CNS side effects. Particularly difficult is the treatment of MID patients who additionally present with movement disorders, cardiac disease, or hematological involvement.

Cardiac side effects of clozapine include dilated cardiomyopathy, myocarditis, long-QT syndrome, atrial fibrillation, and sudden cardiac death [2]. Did the patient develop any cardiac manifestations upon administration of antipsychotic drugs, in particular clozapine?

MIDs may manifest also with hematological abnormalities, in particular anemia, thrombocytopenia, or eosinophilia [3]. Did the described patient develop hematological manifestations either as a manifestation of the genotype or as a side of clozapine, which may induce leucopenia and even agranulocytosis, anemia, and throbocytopenia [4]?

How do the authors explain the extrapyramidal side effects of clozapine in the light of recent findings showing that clozapine metabolites exhibit a neuroprotective effect on dopaminergic neurons through inhibition of microglial NADPH oxidase [5]?

It also should be discussed if the mutation occurred spontaneously or was inherited. Were first-degree relatives investigated for clinical manifestations of MIDs?

Overall, this interesting case could profit from further studies on the interaction of clozapine with wild-type and mutated mitochondria and from cardiac, hematological and CNS monitoring during the further course.

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Josef Finsterer
Krankenanstalt Rudolfstiftung, Vienna, Austria
Corresponding author at: Postfach 20, 1180 Vienna, Austria.
E-mail address: fipaps@yahoo.de.

Sinda Zarrouk-Mahjoub
University of Tunis El Manar, Genomics Platform, Pasteur Institute of Tunis, Tunisia

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