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Letter to Editor

Treating Stroke-Like Episodes with Carbamazepine May Trigger Psychosis

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Abstract: The indication for applying CBZ was obviously the SLE. It was propagated to treat all SLEs with anti-seizure drugs (ASDs) irrespective if the patient presents with seizures or shows epileptiform discharges on electroencephalography (EEG). This management of SLEs has been recently challenged. SLEs may not only be driven by seizures, as mentioned in the introduction, as they occur in the absence of clinical or subclinical seizures and in the absence of epileptiform discharges on EEG.

Keywords: COVID-19, neurological, SARS-CoV-2, brain, nerves.

Letter To The Editor

With interest we read the article by Montano *et al.,* (2020) about a 41 years-old female with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome due to the variant m.3243A>G who presented with a stroke-like episode (SLE) manifesting with confusion, aphasia, seizures, and psychosis (Montano, V. *et al.,* 2020). It was reported that the patient profited from carbamazepine (CBZ), coenzyme-Q, riboflavin, and L-arginine (Montano, V. *et al.,* 2020). For psychosis the patient received delorazepam and haloperidol (Montano, V. *et al.,* 2020). Despite this regiment the patient developed a second SLE, four months after the first one (Montano, V. *et al.,* 2020). We have the following comments and concerns.

The indication for applying CBZ was obviously the SLE. In a recent consensus paper it was propagated to treat all SLEs with anti-seizure drugs (ASDs) irrespective if the patient presents with seizures or shows epileptiform discharges on electroencephalography (EEG) (Ng, Y. S. *et al.,* 2019). This management of SLEs has been recently challenged (Finsterer, J. 2020). SLEs may not only be driven by seizures, as mentioned in the introduction (Montano, V. *et al.,* 2020), as they occur in the absence of clinical or subclinical seizures and in the absence of epileptiform discharges on EEG (Finsterer, J. 2020).

Despite CBZ the patient developed a single, focal motor seizure followed by progressive deterioration of behaviour ending up as psychosis (Montano, V. *et al.,* 2020). We should know how this single focal seizure was treated, particularly if the dosage of CBZ was increased. We also should be informed if an MRI was carried out after the seizure and if another stroke-like lesion (SLL), the morphological equivalent of a SLE on MRI, was documented. We should know the serum levels of CBZ at the time the seizure occurred, particularly if the CBZ level was in the therapeutic range or not. It is unclear for how long the patient received CBZ, particular if she was still under CBZ when she developed the second SLE.

From CBZ, an aromatic AED, it is well known that it can be mitochondrion-toxic (Finsterer, J. 2016). In a murine hepatic microsomal system, CBZ decreased state-3 respiration, decreased ATP synthesis, decreased the mitochondrial membrane potential, increased state-4 respiration, impaired the Ca++-uptake and release, and inhibited Ca++-induced swelling of mitochondria (Santos, N. A. G. *et al.,* 2008). The potential to disrupt mitochondrial functions was lower than that of phenytoin (PHT) or phenobarbital (PB) (Santos, N. A. G. *et al.,* 2008). CBZ exhibited also a hepatotoxic effect, which was mediated by oxidative stress induced by metabolites of these drugs (Santos, N. A. G. *et al.,* 2008). In a study of 5 children with a mitochondrial disorder (MID), CBZ reduced the ATP production (Berger, I. *et al.,* 2010). CBZ may also exhibit beneficial effect to mitochondria (Finsterer, J. 2016). Deterioration of behaviour and development of psychosis could be triggered by several factors. It could be a second SLE, it could be the treatment of the seizure, which was not reported, it could be the natural course, of the first SLE, or it could be a side effect of CBZ. Potentially mitochondrion-toxic ASDs are, in addition to CBZ, valproic acid (VPA), PHT, PB, and topiramate (TPM).

Overall, this interesting case could profit from providing details about the seizure management, from providing serum levels of CBZ and an MRI at the time of the seizure, and from discussing the possibility that CBZ triggered the deterioration to psychosis. We suggest to avoid ASDs for the treatment of SLEs without seizures or epileptiform discharges on EEG and not to use CVZ as a first line treatment of seizures in patients with a MID.

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