CASE REPORT

Choice of anesthesia in molybdenum cofactor deficiency: A case report

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Molybdenum cofactor (MC) deficiency is defined as a progressive neurodegenerative and neurometabolic disease, characterized by convulsions, severe mental and motor retardation resistant to the treatment. Patients with MC deficiency usually need at least sedation for even minor interventions such as dental examination or treatment. Sedation or general anesthesia for these patients may be complicated due to accompanying disorders. However, we were unable to find any reports on anesthetic management of patients with MC deficiency in the literature. In this article, we intend to share our experience of a patient with MC deficiency, who had undergone dental treatment under deep sedation.

Key words: Deep, ketamine, molybdenum cofactor deficiency, sedation

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INTRODUCTION

Molybdenum cofactor (MC) deficiency is a rare, autosomal recessively inherited metabolic disorder. Sulfite oxidase, xanthine dehydrogenase, and aldehyde oxidase enzyme functions are affected by its deficiency, and the enzyme sulfite oxidase is thought to be mainly responsible for the clinical symptoms. The diagnosis is based on the biochemical, the radiological and the genetic findings.[1] Molybdenum cofactor deficiency is characterized by resistant seizures, severe and progressive neurological disorders. The first signs are usually seen immediately after birth, in the form of feeding difficulties, and treatment-resistant seizures. In addition, diffuse brain edema, signs of cortical atrophy, intracranial multiple cystic cavities, axial hypotonia, peripheral hypertonicity, microcephaly, Dandy-Walker malformation, and lens subluxation have been reported in these patients.[1,2]

In the detailed literature search on MC deficiency, we could not find any publications related to anesthesia or sedation practice of these patients. We found that all of the publications were based on the diagnosis and differential diagnosis. However, the presence of intractable seizures and severe neurological disorders make the anesthesia or sedation procedures complicated in these patients. The aim of this paper is to share our experience in a patient with MC deficiency whose dental treatment was performed under deep sedation. The choice of sedation protocol and anesthetic drugs are discussed.

CASE REPORT

A 4-year-old, 15 kg, male patient, admitted to the Gazi University, Faculty of Dentistry, Department of Pedodontics was scheduled for dental treatment and extraction. Since the patient was not cooperative, the procedure was decided to be performed under deep sedation. During the pre-operative assessment, it was found out that the patient was under follow up with diagnosis of MC deficiency, which was established after resistant febrile convulsions at 5.5 months of age. The physical examination revealed mental-motor retardation, bilateral vision loss, and lenticular subluxation. Furthermore, the patient suffered from convulsions, which were under control with levetiracetam suspension. The laboratory findings were normal except for low levels of uric acid in blood and urine. Cerebral MR imaging showed signs of cerebral atrophy.

The patient was placed on the dental treatment unit without any premedication and non-invasive blood pressure, SpO_2 and ECG monitoring were performed. Midazolam 0.05 mg kg^{-1}, and ketamime 0.5 mg kg^{-1} were given intravenously. For maintenance of sedation, N_2O: O_2 (50%:50%) and 2% sevoflurane was administered with nasal mask under spontaneous ventilation.

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In addition, 0.5 mg kg^{-1} IV ketamine was administered for keeping the level of sedation 5 according to Ramsay Sedation Scale during the whole procedure. The patient was examined by the dentist, and after the determination of the teeth to be filled and to be extracted, infiltration anesthesia with articaine was applied where necessary (extraction of a tooth and filling of 3 teeth). The procedure lasted 50 minutes without any complication. The patient was observed for 4 hours after the procedure and discharged after suggesting recommendations. No complications were observed during the 4 hour follow-up after the procedure.

DISCUSSION

MC deficiency was first identified in 1978 by Duran *et al.*,[3] To date, more than 100 cases have been reported in the literature. However, there are no publications on the sedation or anesthesia practices in these patients.

Milder phenotypes with late presentation and survival into the third decade of life are now recognized.[2]

Molybdenum cofactor deficiency has usually a poor prognosis, and patients usually die within the first few days or weeks of life.[1] Milder phenotypes with late presentation and survival into the third decade of life are now recognized.[2] The disease predominantly affects the central nervous system. Although the elevated sulfide levels are thought to be responsible, the exact mechanism of this progressive disease is not fully understood. The neuroradiological findings of MC deficiency are initially cerebral edema followed by subcortical cystic changes. Parenchymal loss, cerebral atrophy and ventricular enlargement are other common findings.[1,2] These findings have been reported to be similar to that of ischemic brain injury.[1,2] Mental-motor retardation, vision loss, bilateral lenticular subluxation, cerebral atrophy and convulsion controlled with levetiracetam suspension detected in our patient are the findings, which are compatible with the findings of MC deficiency.

In these patients, the choice of anesthetic/sedation technique and agent must be done considering the patient's anatomy and systemic pathologies. Since spastic quadriplegia commonly develops in long term MC deficiency, depolarizing muscle relaxants should be avoided. In addition, as in all patients with mental retardation, the risk of frequent lung infections and pulmonary aspiration due to chronic regurgitations and vomiting should be considered and precautions should be taken.[4]

Convulsions which are the major causes of seizures in this age group are commonly seen in the neonatal period. These convulsions are generally resistant to anticonvulsant drugs and they are difficult to control. Therefore, the patients' anticonvulsant medication should not be stopped during the preoperative period and the use of these drugs in the perioperative period should be encouraged.[4] The patient's anticonvulsant medication was not stopped and no premedication was administered.

We decided to implement sedation, since there were no serious anatomic pathologies regarding the airway. The choice of main agent for sedation was ketamine, because in these patients, it is important that the administered drug should not trigger convulsions, and preserve the respiratory and the protective reflexes. Furthermore, in MC deficiency, since the enzyme sulfite oxidase is affected, the accumulation of sulfite metabolites, especially of S-sulfocysteine is held responsible for the encephalopathy. The molecular structure of the S-sulfocysteine is similar to the neuroexitator and neurotoxic amino acids, particularly glutamate. For these reasons, MC deficiency can be also be defined as a neurodegenerative disease characterized by excessive stimulation of N-methyl-D-aspartate (NMDA) receptors. This is the underlying mechanism in patients with convulsions resistant to drugs such as lamotrigine and vigabatrin, who can be treated successfully with drugs such as NMDA antagonists and dextromethorphan, which inhibit voltage-dependent calcium and sodium channels.[5] Ketamine, which is also used successfully in the treatment of refractory status epilepticus,[6] can be preferred due to its NMDA receptor blockade property. In addition, we have used it in combination with midazolam, which is a short-acting benzodiazepine, used successfully in the treatment of status epilepticus. In order to avoid the dose escalation and provide a more effective sedation, we chose for a multimodal approach, in which a combination with sevoflurane was applied.

In conclusion, we believe that ketamine can be used safely together with benzodiazepines in patients with diseases characterized by convulsions, such as in MC deficiency.

AUTHOR'S CONTRIBUTION

MA contributed in the conception of the work, drafting the work revising it critically for important intellectual content, approval of the final version of the manuscript, and agreed for all aspects of the work. GK contributed in the conception of the work, approval of the final version of the manuscript, and agreed for all aspects of the work. SS contributed in the conception of the work, approval of the final version of the manuscript, and agreed for all aspects of the work. DA contributed in the conception of the work, approval of the final version of the manuscript, and agreed for all aspects of the work.

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