



Case Report

Central nervous system toxicity due to mefenamic acid

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ABSTRACT

Mefenamic acid is a fenamate nonsteroidal anti-inflammatory (NSAI) drug, which is used for several years for pain management. However, it has been rarely reported that, mefenamic acid can induce central nervous system toxicity both in toxic doses and therapeutic usage. We report a case of a 27-year-old female who presented to the emergency department (ED) with altered mental status and vomiting. On admission to the ED, she was lethargic and disoriented. Her vital signs were normal and her physical examination was completely normal except dysarthric speech. The etiology of altered mental status was investigated with electrolyte levels, cranial computed tomography, cranial magnetic resonance imaging and EEG, however the results were normal. Her blood gas analysis revealed a deep metabolic acidosis with a pH of 7.14. Neither etiologic agent nor drug use history was provided at the presentation; she had only osteogenesis imperfecta since several years and she had been using various NSAI drugs. However, her relatives later stated that, she took mefenamic acid for her pains since two weeks. After her admission to intensive care unit, her neurologic state was improved gradually after plasmapheresis and she was discharged healthy. Although mefenamic acid has been considered as one of the safe NSAI drugs, its effects due to central nervous system toxicity should be cautiously handled.

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1. Introduction

Mefenamic acid is a non-steroidal antiinflammatory drug (NSAID), which is used for different purposes for several years. As new analgesic medications have become available, the use of mefenamic acid has substantially declined [1]. It is most often used for treating postoperative pain, dysmenorrhea, osteoarthritis, headache and postpartum pain [1–3].

Most reported adverse reactions secondary to mefenamic acid use are epigastric pain, headache, nausea, fatigue, diarrhea and skin rash. The side effects are generally increased with prolonged use and with increased daily doses [1]. Central nervous system toxicity due to mefenamic acid was rarely reported in the literature. In an animal study, its neurotoxicity is specified as depressant effect at lower doses and stimulant effect in higher doses [4]. Specific neurotoxicity secondary to mefenamic acid use is extremely rare; one case with coma and one case with status epilepticus have been reported many years ago [5,6]. We aimed to report a case with neurotoxicity related with mefenamic acid use in therapeutic usage.

2. Case report

A 27-year-old female presented to emergency department (ED) with altered mental status and vomiting. On admission to the ED, she

was lethargic and disoriented. She has osteogenesis imperfecta and uses several analgesic medications for his musculoskeletal pain. Her vital signs were in normal ranges and her physical examination was completely normal except her dysarthric speech. The etiology of altered mental status was investigated with electrolyte levels, cranial computed tomography, cranial magnetic resonance imaging and EEG, however the results were normal. Her blood gas analysis revealed a deep metabolic acidosis with a pH of 7.14. Neither etiologic agent nor recreational drug history were provided at the presentation. However, her relatives later stated that, she took mefenamic acid for her pains since two weeks.

After her admission to intensive care unit, a mild thrombocytopenia (101,700/mcL) developed and fragmented red blood cells (schistocytes) were detected on the peripheral blood smear. After the diagnosis of drug induced thrombotic thrombocytopenic purpura was suspected, plasmapheresis was started immediately. However, ADAMTS13 activity was found 87% and no renal involvement was observed during her stay. After plasmapheresis, her neurologic state was improved gradually and she was discharged healthy.

3. Discussion

Mefenamic acid is an old drug, which lost its popularity with newly marketed drugs with relatively limited side effects. However, it has still a role in chronic pain and some pain syndromes due to its potency. Reported side effects secondary to mefenamic acid are, included but not limited to anaphylaxis, skin reactions, nephrotoxicity, drug-induced acute pancreatitis and enteropathy [7–11].

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In adults and children over 12 years, maximum daily dose of mefenamic acid is 1500 mg per day. It is established that, doses over 40 mg/kg can be toxic in adults and children [12]. Our patient took daily 1000 mg total dose (two times a day) since two weeks and she stopped taking other NSAIDs during this period. She was very careful of taking medications, thus overdose secondary to mefenamic acid is not possible.

Neurotoxicity due to mefenamic acid has been reported in a number of case reports [5,6,13]. All of them were from 1980s and they reported convulsions both in therapeutic and toxic doses. Recently, Kamour et al. conducted a study with telephone enquiries about CNS toxicity in mefenamic acid poisoning [12]. The results of this study revealed that, patients ingesting mefenamic acid are more likely to experience CNS toxicity than those ingesting the other NSAIDs combined. In addition, convulsion and altered mental status are the most frequent conditions in CNS toxicity. Our patient was admitted to the ED with severe metabolic acidosis and altered mental status. The patient's neurotoxicity was not related to TTP, and the patient benefited from plasmapheresis and she was discharged healthy.

There is little documented evidence that mefenamic acid toxicity may cause serious neurotoxicity. However, a small number of case reports provide its effects to CNS. Mefenamic acid provides no proven clinical advantages over other NSAIDs, thus alternative drugs can be prescribed to manage inflammatory conditions. Although mefenamic acid has been considered as one of the safe NSAID drugs, its effects due to central nervous system toxicity should be cautiously handled.

Conflict of interest and source of funding

None declared.

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