Valproate-induced Periorbital Edema

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ABSTRACT

INTRODUCTION: Valproate is an antiepileptic medication that can be used to manage behavioral symptoms associated with Alzheimer's dementia. We present a rare case of valproate-induced periorbital edema.

CASE: A 76-year-old man came to the emergency room with agitation and aggression. He was medically cleared and referred to a psychiatric facility where he was treated with haloperidol. When he developed drug-induced parkinsonism, the haloperidol was stopped, and the patient was started on valproate 250 mg twice daily. The day after valproate administration, the patient developed periorbital edema. After ruling out other causes of periorbital edema, adverse drug reaction was suspected. Valproate was discontinued, and the edema rapidly resolved within five days.

CONCLUSION: Periorbital edema is a rare side effect of valproate. It can occur in patients who are being treated with valproate for behavioral changes in Alzheimer's disease. The edema resolves with discontinuation of the medication.

KEYWORDS: valproate, periorbital edema, dementia, adverse drug reaction

INTRODUCTION

Drug-related peripheral edema is not uncommon; however, valproate-related edema is a rare adverse side effect that has been reported after long-term administration of the medication.[1] Gastrointestinal side effects, hepatitis, pancreatitis, and thrombocytopenia have all been reported with valproate.[2] We present here a rare case of periorbital edema as a side effect of valproate.

CASE REPORT

A 76-year-old man with a history of dementia with behavioral disturbance, who lived at home with his wife, presented to the emergency department due to agitation and aggressive behavior toward his wife. He was medically cleared and transferred to a inpatient psychiatric unit for further management.

In the facility, the patient was aggressive toward staff and other patients. He did not have physical limitations and did not need an assistive device to ambulate. He maintained eye contact, could make his needs known, and was able to engage in a conversation. However, he had delusions and hallucinations, was confused, and was unable to answer questions appropriately.

After several altercations with other patients in the facility, he was deemed a risk to himself and others and started on haloperidol. The haloperidol was stopped when he developed gait changes, rigidity, and cogwheeling. He was transitioned to quetiapine and developed somnolence and decline in his functional status. He was taken off quetiapine, but he developed agitation once again.

He was next started on valproate for symptom management, but the following morning, the patient was noted to have new onset eyelid swelling and bilateral lower extremity edema to the level of the knee. The initial differential diagnosis included facial cellulitis, renal disease, liver disease, heart failure, and medication side effects.

Workup was negative CBC, BNP, BMP, and liver function testing and TSH showed no abnormalities. He was taken off the valproate after a literature search showed edema as a rare side effect of the medication.[3,4] The pedal and periorbital edema rapidly resolved in five days. The patient was diagnosed with valproate-induced facial edema.

DISCUSSION

Valproate can be used in the treatment of agitation with dementia, as well as for generalized or partial seizures, prophylaxis of migraine headache, and bipolar disorder. Gastrointestinal side effects have been seen with valproate along with hepatitis, pancreatitis, and thrombocytopenia.[8] New peripheral edema should prompt a thorough evaluation for underlying conditions such as congestive heart failure, liver cirrhosis, nephrotic syndrome, hypoalbuminemia, and lymphatic or venous obstruction.[3] There have been case reports of valproate causing peripheral edema without other side effects.[4] A few cases reported valproate-induced bilateral lower extremity edema which resolved quickly after the valproate was stopped.[3,4,7]

The mechanism by which valproate causes peripheral edema is not known. Valproate can exhibit its pharmacologic

effects by increasing neuronal concentrations of GABA level in the brain. This can happen by either inhibiting its metabolism or increasing its synthesis.[4,6] Some studies have reported lower extremity edema when using medications that affect the GABA system, such as benzodiazepines. Tiagabine, an anti-epileptic drug thought to generate peripheral edema, is associated with the γ-aminobutyric acid (GABA) system, which is utilized by valproate as well.[3]

GABA receptors have been identified in peripheral tissues with reported effects on modulating peripheral vascular resistance.[4] This might be related to the development of edema as an adverse medication effect.

Some studies report edema in the context of liver injury related to valproate use; however, our patient had no abnormalities in his renal or liver functions and did not develop liver injury.[7] The course of events including development of bilateral lower extremity edema and eyelid edema one day after taking valproate, and resolution of the edema five days after stopping the medication, suggest adverse drug reaction as the cause of our patient's peripheral edema and periorbital edema.

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Acknowledgment

We thank Margo Katz and Richard Besdine, MD, for editing and final manuscript review.

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Disclosures

Conflict of interest: None

Funding: None

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