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Chorea in a Chronic Pain Patient Using Gabapentin

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ABSTRACT

Background: Gabapentin increasingly is being used to treat chronic pain in addition to seizures, anxiety, and bipolar disorder. Chorea has been reported as a potential side effect of gabapentin.

Case Report: We report the case of a patient with chronic low back pain who was treated with a host of modalities, including gabapentin. After she increased her dose of gabapentin, she developed chorea of the upper extremities, neck, and head. With cessation of gabapentin, the bulk of her symptoms resolved within 24 hours, and symptoms completely resolved in the following months.

Conclusions: Chorea is thought to appear when the basal ganglia are deregulated. Gabapentin interferes with gamma-aminobutyric acid, the primary inhibitory neurotransmitter in the motor pathway. Chorea associated with gabapentin has been reported in several case studies, but not at a dose as low as the patient took in this case.

INTRODUCTION

Gabapentin increasingly is being used to manage chronic neuropathic component pain. Gabapentin is also used to treat seizures, anxiety, and bipolar disorder.[1] Chorea has been noted in several case reports as a potential side effect of gabapentin,[2-6] but the dose that produced chorea in our patient was lower than the dose taken by patients in previous reports.

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CASE REPORT

A 70-year-old African American woman with a long history of pain secondary to lumbar spinal stenosis and lumbosacral neuritis was managing her pain with a combination of methods, including the use of gabapentin. She began treatment with gabapentin in August 2011. Ten months later, the patient increased her gabapentin dose from 300 mg once a day to 300 mg twice a day. On day 6 of the increased dose, she experienced a fine tremor. On day 11, shortly after taking her first dose of gabapentin for that day, she began experiencing full chorea involving her head, neck, and arms bilaterally. Additionally, she noticed an involuntary buccal-oral movement consistent with tardive dyskinesia. These symptoms prompted her to discontinue gabapentin. She was seen in the clinic on day 12, by which time the chorea had subsided, but she still exhibited some infrequent buccal-oral movements. In the following months, these remaining symptoms resolved, leaving the patient with no residual movement disorder.

Although the patient received a substantial amount of pain relief from the gabapentin, the decision was made to discontinue it, to switch the patient to pregabalin, and to follow her closely for possible development of dyskinesia.

DISCUSSION

Chorea is thought to arise from deregulations of the basal ganglia. The nigrostriatal pathway within the basal ganglia regulates feedback between the thalamus and the motor cortex through a system of positive and negative regulatory synaptic pathways.[7] The basal ganglia act mainly as a brake for the motor thalamus and the midbrain extrapyramidal area.[8] When the inhibitory mechanism of the basal ganglia is reduced, movement disorders such as chorea arise. Experiments have shown, however, that this phenomenon does not completely explain the appearance of chorea.[8] The possibility remains that the movement associated with chorea originates some-

where else in the motor system that has yet to be elucidated.

Gabapentin appears to increase the synthesis of gamma-aminobutyric acid (GABA), one of the primary inhibitory neurotransmitters in the brain.[1] In rat models, gabapentin was shown to decrease the activity of GABA neurons in the substantia nigra.[1] Because not all patients who take gabapentin develop chorea, some aberrant neurophysiology likely predisposes certain patients to this side effect.

A review of our patient's chart revealed recent magnetic resonance imaging (MRI) showing extensive multivascular ischemia that appeared to be chronic. Two weeks before she escalated her gabapentin dose, the patient had a glomerular filtration rate (GFR) of 23 mL/min. With creatinine clearance >15-29 mL/min and adjusted for age, the recommended calculated dose of gabapentin for this patient would have been up to 700 mg daily. Both the ischemic brain changes and impaired renal function may have predisposed the patient to have a reaction at a dose 100 mg less than the recommended dose. In addition to gabapentin, the patient was taking 13 other medications: tramadol, bisacodyl, megestrol, hydrocodone/acetaminophen, aspirin, pravastatin, metoprolol, furosemide, niacin, doxazosin, clonidine, hydralazine, and amlodipine. Interactions may have occurred between gabapentin and either clonidine or tramadol that could have caused psychomotor impairment. The interaction between gabapentin and clonidine appears to be an additive one,[9] as does the interaction between gabapentin and tramadol.[10] However, the chorea seen in this case appears to go beyond a psychomotor impairment.

Previous case reports have associated chorea with gabapentin doses ranging from 900 mg to 2,100 mg.[2-6] In all of these cases, the chorea resolved once the gabapentin was withdrawn. In one case, the chorea recurred with the reintroduction of gabapentin.[6] Several cases present chorea in patients with no known neurological defect,[2,4,5] whereas 2 cases report chorea in patients with substantial neurological defects.[3,6] All of these cases report the development of chorea at higher doses of gabapentin than in our case.

Although the patient's extensive ischemia seen on MRI may have predisposed her to this reaction, previous case reports have shown chorea in patients both with and without neurological defects. Using the research of Naranjo et al,[11] the probability that our patient's chorea was an adverse drug reaction is "probable" with a score of 6 on a scale of definite >9, probable 5-8, possible 1-4, and doubtful <0, but her 600 mg dose appears to be the lowest reported dose associated with this side effect.

LIMITATIONS

Generalization of this case is limited by certain factors that make this patient unique. The patient had extensive multivascular ischemia as shown by MRI that may have lowered her threshold for the onset of chorea. She also had a significantly decreased GFR, although the adjusted recommended dose for her GFR was still above the dose at which the chorea appeared. The patient was also concurrently taking 13 other medications. Of those, the most likely interactions occurred between gabapentin and tramadol or gabapentin and clonidine, both of which would have had additive effects.[9,10]

CONCLUSION

This case report presents what appears to be a clear adverse reaction to gabapentin in the form of chorea. Not only did the symptoms begin with an increase in dosage, but they also subsided with the cessation of the medication. Chorea is thought to appear when the basal ganglia are deregulated. Gabapentin interferes with GABA, the primary inhibitory neurotransmitter in the motor pathway. Several case studies have reported chorea associated with higher doses of gabapentin, but none at the low dose used in this patient. As gabapentin use increases across multiple fields of medicine, a larger study examining the potential relationship of neurological deficits, chorea, and gabapentin is needed.

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