CASE REPORTS

Ballismus Secondary to Antihistamine Use

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ABSTRACT

Antihistamine usage is commonplace for alleviating allergy symptoms, though they are not without side-effects. We present a case of antihistamine use precipitating upper and lower extremity ballismus in a patient. We also discuss other case reports which outline similar dopaminergic dysregulation secondary to antihistamine usage, as well as our recommendations for prevention of these symptoms.

Key Words: Ballismus, dopamine dysregulation, antihistamine, anticholinergic

1. INTRODUCTION

Ballismus was first described by Russell Meyers, M.D. as a "repetitive, but constantly varying, large amplitude involuntary movements of the proximal parts of the limbs. This activity is almost ceaseless and movements are often complex and combined".[1] Its clinical manifestation often results from brain injury, such as traumatic, ischemic, or hemorrhagic damage.[2] Though these are the most common etiologies, other inciting factors such as adverse medication side effects can result in ballismus. In this case report, we describe a patient presenting with ballismus resulting from antihistamine use.

2. CASE PRESENTATION

A 73-year-old male visited the emergency room in our hospital due to a 6-day history of involuntary, bilateral upper and lower extremity movements. These movements were writhing in nature and only ceasing with distraction, such as while checking pupillary reflexes. Complicating the story was the patient's endorsement of a sore throat and congestion, which had an onset of 2 weeks prior to involuntary movement presentation. The constellation of symptoms contributed to significant dysphagia, which he reported not eating a meal for the past 3 days. The patient had been taking Clarinex(desloratadine) for several weeks prior to onset of ballistic symptoms for congestion alleviation. On further questioning of his onset of presentation, he endorsed a past medical history significant for aortic stenosis status post-percutaneous aortic valve replacement, triple coronary artery bypass, and coronary artery disease which 1 month prior had his atorvastatin dose increased from 40 mg to 80 mg. Patient had no family history significant for Huntington's disease or any other hereditary hyperkinetic movement disorder.

The most apparent finding on physical examination was the presence of bilateral ballistic movement of upper and lower extremities, described as rapid, ceaseless movements large in amplitude. The patient also had tardive dyskinetic facial expressions along with the general appearance. Distractibility of the patient caused the ballistic movement's amplitude to

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decrease, allowing for examination of head, eyes, and throat. Head examination was unremarkable for apparent trauma. Eye examination supported appropriate tracking and lack of any apparent pathology such as Kayser-Fleischer rings. Throat examination revealed tonsillar exudate and multiple small, white lesions in the oropharynx. On questioning, the patient's speech was hoarse, consistent with a 'hot potato voice'.

On admission, a battery of tests was performed to rule out emergent intracranial etiologies. Computerized tomography(CT) of the head without contrast revealed no intracranial hemorrhage or mass effect. Magnetic resonance imaging(MRI) of the brain with and without contrast under anesthesia revealed no ischemic changes, no acute infarct, and no intracranial mass. Cardiologic evaluation via electrocardiography(ECG) revealed normal sinus rhythm, normal axis, presence of possible right bundle branch block and no ischemic changes. Two sequential hs-troponin T evaluations were negative A complete blood count revealed microcytic anemia and leukocytosis of 10.22 K/uL. A complete metabolic panel, serum lab evaluation, and electrolytic labs showed abnormalities with the resultant values as follows: sodium of 132 mmol/L, chloride of 96 mmol/L, blood urea nitrogen of 29 mg/dL, total protein of 6.2 g/d, creatine kinase of 945 U/L and magnesium of 1.5 mg/dL. Glucose was found to be relatively normal with a value of 101 mg/dL. The patient was then admitted overnight and was given Ativan(lorazepam) for rest, however the Ativan(lorazepam) exacerbated the ballistic movements which was counter to the intended goal of administration. Overnight, the patient's ballistic movements concurrently alleviated with his exhaustion. As the patient slept, the movements completely subsided.

On waking up the following morning of admission, the patient's ballistic movements returned, however were greatly reduced in amplitude. The patient endorsed a 'five out of ten' in movement severity throughout the day compared to a 'ten out of ten' the previous day. Continuing to investigate the origin of the involuntary movements, a drawn heavy metal toxicity revealed no toxic levels. A urinalysis was unremarkable for any bacterial infection. Ceruloplasmin and iron studies were also found to be within normal limits. A throat culture was performed to investigate the apparent white lesions, which resulted in Candida albicans growth. The patient was initiated on nystatin 500,000 U/mL administered via oral swish and swallow.

On the 3rd day of admission, the patient's ballistic movements completely resolved. His sore throat and dysphagia, though still present, significantly resolved with antifungal therapy. Complete blood count and complete metabolic panel improved and returned to baseline throughout the hospital course. Patient was restarted on atorvastatin 40 mg from his home dose of 80 mg. The only medication that was held throughout the course was his 2nd-generation antihistamine, Clarinex(desloratadine). This turn of events and clinical improvement begs the question, could the Clarinex(desloratadine) usage have contributed to the patient's ballismus.

3. DISCUSSION

Current pharmacologic literature supports the role of antihistamines in disrupting dopaminergic and cholinergic activity. However the pharmacokinetics and model of understanding still remains controversial.[3] Several case reports have been published revealing possible connections between dopaminergic disruption and antihistamine usage, both in 1st- and 2nd-generation. Jedariforoughi's case report, 'Tardive Dyskinesia with High Dose H1 Antihistamine in a Person Without Comobidities', discusses a patient developing tardive dyskinesia after taking fexofenadine for 11 days.[4] Initially the providers did not realize the possible link between the 2nd-generation antihistamine and the presenting symptoms, having performed a neurologic workup on admission. Similar to our presented case, the patient's electroencephalogram(EEG) and MRI of the brain with contrast were unremarkable. Also correlating to the presented case, the patient's symptoms described in Jedariforoughi's report had alleviated around 24 hours after discontinuing the antihistamine.

Another case report discussing the link between dopaminergic effects and antihistamines can be found in Cho et al.'s report, 'Chorea induced by antihistamine drugs'. This case report discusses a 72-year-old man who developed chorea while taking hydroxyzine HCL 25mg, azelastine HCL 1mg, and emedastine fumerate 1mg for allergic dermatitis. This individual had a 4 week history of taking the medications prior to the onset of chorea. Chorea is commonly seen in the neurodegenerative disorder, Huntington disease, where atrophy of the caudate and putamen causes an increase in dopamine activity in the brain. In this patient, initial neurologic and infectious workup were unremarkable. After 7 days of discontinuing the antihistamine regimen, the chorea movements were minimal and were completely alleviated after 3 weeks. Also a noteworthy comparison between the presented case and Cho et al.'s report is the unexplained alleviation of ballistic movements during sleep.[5]

Based on our research, we have concluded that the irregular motion pathology seen in our patient was likely caused by antihistamine use. Respecting other possible diagnoses such as viral causes like HSV encephalitis to drug toxicities to electrolyte abnormalities, all the performed tests yielded no other

possible explanation. If the patient had not rapidly improved, consideration for a lumbar puncture and cerebrospinal fluid analysis was high on our priority list.

The diagnosis of antihistamine-induced ballismus was made via exclusion due to the spontaneous resolution of the ballistic movements and only medication change throughout the hospital course being the discontinuation of the patient's antihistamine. Again, it is worth restating the negative neurologic workup results of both the internal medicine team and the consulted neurology team.

It is unclear if or to what extent the Candida pharyngitis played in our patient's constellation of symptoms, thus we recommend further investigation in antihistamine use in active infections. Though antihistamines are cornerstone medications for allergy alleviation, providers need to communicate the possible dopaminergic side-effects with continued use to their patients. Especially in elderly patients, who often are poorer metabolizers of medications, dosage and regularity of use needs to be monitored closely when prescribing or suggesting the use of antihistamines. Moreover, we would like to stress the importance of receiving a detailed medical history when examining patients with dopaminergic-base motion abnormalities with an unremarkable neurologic workup.

CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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