Session 3557
Interesting Cases II – Sunday, March 15, 2020

Case Report #5

Author Hoang Pham, MD
Training Program Adult Clinical Immunology and Allergy

Case Title
Recurrent Thunderclap Headache: Think Rhinitis Medicamentosa, Not Birth of Athena

Summary
We present a 52-year-old female presenting with recurrent thunderclap headaches in the setting of increased dosing of intranasal xylometazoline and chronic low dose duloxetine use for back pain. She was found to have a small subarachnoid hemorrhage and multi-vessel stenoses consistent with reversible cerebral vasoconstriction syndrome (RCVS). Although sympathomimetic and serotonergic medications are risk factors for RCVS, RCVS following xylometazoline has not been reported. The patient was treated with verapamil to reverse vasoconstriction, intranasal beclomethasone was initiated and she was weaned off of xylometazoline and duloxetine. Repeat imaging demonstrated interval improvement and the patient was discharged from hospital without neurologic sequelae.
This case highlights an example of a common drug interaction which had serious health effects. In the era of polypharmacy and easy access to over-the-counter drugs, it is important to consider pharmacologic interactions in the differential diagnosis of common and uncommon medical presentations.

Patient Presentation
The patient was a 52-year-old female with a past medical history of long-standing chronic nasal congestion, mild asthma, depression and chronic back pain. Her home medications consisted of duloxetine 30 mg every other day, budesonide- formoterol inhaler, salbutamol, and intranasal xylometazoline once a day. Every few months, she would have a flare up of nasal congestion, prompting her to increase her xylometazoline to 2-3 times a day. Her family history was notable with atopy in her daughters with allergic rhinitis and asthma.
She presented to the Emergency department with 2 episodes of recurrent thunderclap headaches 8 hours apart, both of which occurred while straining in the bathroom. Around the time of presentation, she was using her nasal decongestant 2-3 times a day. For the last 1.5 years, she had been using duloxetine for neuropathic back pain but had been slowly titrating down from 60 mg to 30 mg every other day due to less back pain.
One year prior to the current presentation, she also had a thunderclap headache lasting 8 hours in the context of increased use of nasal decongestants. She had self-titrated off of duloxetine for a few days during that time period.
Upon physical examination, she was initially hypertensive at triage but vitals normalized by the time of neurology evaluation. She had no associated focal neurological deficits or manifestations of seizures or encephalopathy. She had infraorbital darkening and edema. Nasal mucosa was pale with some mild

erythema. There were minimal thin clear secretions, severe nasal turbinate hypertrophy, and a high arched palate.

Diagnosis

Given the presentation of recurrent thunderclap headaches associated with xylometazoline and duloxetine in a middle aged female following straining, it was highly suspicious for RCVS as she had the typical demographics, pharmacologic risk factors, triggering event, and headache phenotype. The combination of xylometazoline and duloxetine likely acted synergistically to cause RCVS; xylometazoline increases adrenergic activity and vasoconstriction through stimulation of alpha-adrenergic receptors, and duloxetine blocks reuptake of both serotonin and norepinephrine thereby effectively increasing the availability of both serotonin and norepinephrine. Serotonin is a well-known potent cerebral vasoconstrictor. This synergy is further supported by the fact that patient self-titrated off of duloxetine independently when she had a thunderclap headache 1 year prior. A head computed tomography (CT) and CT angiogram arch to vertex were performed to confirm the diagnostic impression and rule out aneurysmal subarachnoid hemorrhage.

We also diagnosed rhinitis medicamentosa based on severe chronic nasal congestion and dependence on chronic xylometazoline use. Allergic rhinitis was suspected given her family history of atopy and personal history of mild asthma.

Testing

Initial CT head and angiogram showed small areas of superficial cortical subarachnoid hemorrhage as well as multifocal mild to moderate narrowing in the intracranial arteries of the anterior and posterior circulation, compatible with RCVS.

She was referred to allergy as an outpatient for aeroallergen skin testing to identify a precipitant for her chronic nasal congestion.

Treatment

Given the history of recurrent thunderclap headaches, exposure to 2 medications with vasoconstrictive properties activating both adrenergic and serotonergic pathways to disrupt cerebral vascular autoregulation, and classic imaging findings of small subarachnoid bleeding and widespread symmetric cerebral artery narrowings, we were confident in the diagnosis of RCVS. As such, we weaned off her xylometazoline and duloxetine. Beclomethasone nasal spray was initiated as a more effective and safe long-term therapy for nasal congestion due to suspected allergic rhinitis. The patient was educated on the risk and benefits associated with each type of nasal spray. She was also started on verapamil, a calcium channel blocker, to hasten reversal of the vasoconstriction. She counselled to avoid nasal decongestants, SNRIs, selective serotonin reuptake inhibitors (SSRIs), and other vasoactive drugs such as dihydroergotamine and triptans.

Patient Outcomes

After 2 weeks of therapy, repeat imaging demonstrated interval improvement. The patient had no further episodes of headache. She was discharged without any neurological sequelae and will be followed in both the stroke prevention and allergy clinics. Later, her chronic nasal congestion was attributed to an allergy to the cat she lived with. Cat avoidance was recommended.

Lessons Learned

One case report by Loewen et al. (CMAJ 2004;171(6):593-4) reported a 31 year old female with thunderclap headache associated with chronic use of oxymetazoline, another intranasal decongestant, and sertraline, an SSRI. The patient had clinical and radiologic resolution after stopping oxymetazoline and treatment with nimodipine, a calcium channel blocker.

The learning points of this case are threefold. Firstly, allergic rhinitis is often ignored and managed inadequately, prompting our patients to self-medicate. Next, by affording our patients a proper evaluation for allergic rhinitis, we can identify triggers for avoidance, offer patients highly effective treatments, and educate them on the negative impacts of readily accessible over-the-counter nasal decongestants that can result in rhinitis medicamentosa and serious cerebrovascular complications. Finally, the risk of RCVS with nasal decongestants may be more critical in the setting of polypharmacy as SSRI/SNRI use is widespread. Therefore, this case highlights a serious and potentially widespread drug interaction that we as health care professionals and allergists should be aware of.