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Naratriptan-Associated Spinal Artery Infarction

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To the Editor:

Migraine is a serious public health problem that was shown to affect 8.7 million women and 2.6 million men in the United States yearly.[1] In 2016, the global age standardized prevalence of migraine was 14.4% causing 45.1 million years lived with disability.[2]

Migraine treatment includes analgesics and more specifically triptans among other options.[3] Naratriptan, a serotonin (5HT) receptor agonist, is a commonly used one with a dose ranging between 1 and 2.5 mg that can be repeated in 4 hours if no relief was achieved.[4–6] Paresthesia, nausea, dizziness, drowsiness, and fatigue are among the most common adverse effects of naratriptan.[6]

Migraine is an established stroke risk factor.[7,8] One study showed that migraineurs with aura were 67% more likely to suffer from stroke compared with nonmigraineurs.[9,10] Several pathogenic mechanisms of stroke in migraineurs were proposed including mainly cortical spreading depression and other mechanisms including inflammatory and vascular factors.[7]

Recent literature studying the adverse cardiovascular outcomes of triptans failed to show an increased risk of strokes in patients using triptans.[9,11,12] Nonetheless, the use of triptans in patients with history of stroke is contraindicated.[6]

In this article, we describe a case of spinal infarction in the setting of naratriptan overuse, an adverse event not previously described in the literature.

A woman in her forties with history of chronic migraine without aura was taking naratriptan 2.5 mg as needed for her migraines. She had no vascular risk factors, medical comorbidities. Two weeks before presentation, she has received the flu vaccine and had some flu-like symptoms. On the day of symptom onset, she took twice the amount of her prescribed naratriptan dosage for a severe migraine and after 2 hours with still no relief, she then took another 2.5 mg. Later that day, she developed numbness in her legs followed by severe leg weakness, urinary retention, and thoracic chest pain. Her examination showed flaccid lower extremities and a T4 sensory level with initially absent reflexes, which later became hyperreflexic. MRI scans showed T3 to T6 spinal infarction with restricted diffusion on diffusion-weighted imaging and T2 hyperintensity within the anterior spinal artery distribution (Figure 1). Echocardiogram did not show evidence of Patent Foramen Ovale (PFO). Her spinal fluid analysis was normal and the rest of the neural axis imaging was negative for abnormal lesions. She was given 5 days of IV methylprednisolone 1 g daily for the possibility of transverse myelitis with no response. An extensive inflammatory and vascular evaluation, including computed tomography angiogram of the chest and abdomen, was negative for dissection, vascular abnormalities, or inflammation. She had slow but good recovery and was maintained off triptans and did not have any subsequent neurological attacks over the next 4 years.

Migraine is a major public health issue that affected about 1.04 billion individuals in 2016, with an estimated 45.1 million years lived with disability. Migraine treatment includes a wide range of therapeutic agents that are either nonspecific such as acetaminophen, aspirin, and other nonsteroidal anti-inflammatory drugs, or specific including ergots and triptans.[3] Different classes of triptans have been proven to be effective in treatment of acute migraines of any severity.[3,13] Naratriptan also has a longer half-life of 5.5 hours that is believed to contribute to the lower recurrence of migraines with its use.[4] In addition, naratriptan has been shown to be an effective short-term prophylactic treatment for perimenstrual migraine, with a similar adverse effect severity and incidence compared with placebo.[14] In general, and according to the manufacturer labeling; the most common adverse effects (>2%) were paresthesia, nausea, dizziness, drowsiness, and fatigue.[6]

Migraine is an established stroke risk factor; one systematic review showed that the pooled relative risk for ischemic stroke for any type of migraine was 2.16 (95% confidence interval 1.89–2.48) with a higher risk in patients with aura when compared with those without aura (2.27 vs. 1.83), respectively.[7] Another review showed similar results with higher pooled relative risk of stroke in migraine with aura when compared with those without aura (2.16 vs. 1.23), respectively.[10] Association between PFO and migraines has been in debate since 1995 when Del Sette et al showed a higher PFO incidence in migraineurs when compared with normal controls (41% vs. 16%).[15] However, other studies failed

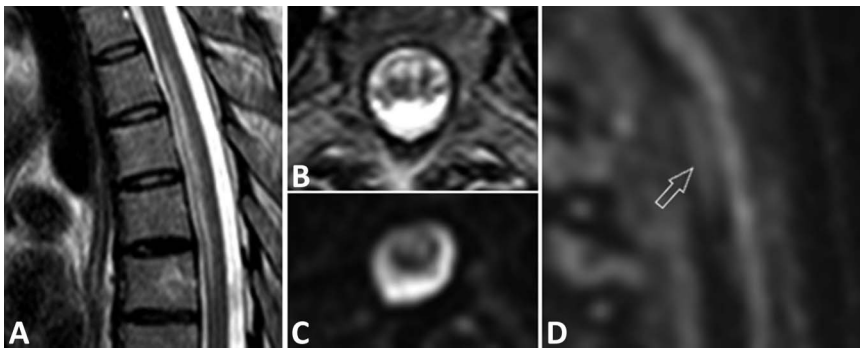

FIGURE 1. (A and B) Sagittal and axial images of the thoracic spine respectively showing increased T2 signal on the ventral aspect of the thoracic spine (T3–T6). (C and D) Axial and sagittal (arrow head) images of the thoracic spine respectively showing diffusion restriction on the ventral aspect of the thoracic spine.

to show similar association.[16] Recent literature studying the adverse cardiovascular outcomes of triptans failed to show an increased risk of strokes in patients using triptans.[9,11,12] Nonetheless, the use of triptans in patients with history of stroke is contraindicated.[6]

This case is the first reported case of naratriptan-induced spinal infarct secondary to high doses of naratriptan. Temporal relation to the excessive use of Naratriptan, typical anatomical anterior spinal artery distribution on MRI with restricted diffusion on diffusion-weighted imaging, and lack of alternative diagnosis strengthen the causal relationship of triptan and spinal infarction.

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The authors have no conflicts of interest to declare.

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