

Sumatriptan Anaphylaxis

A Headache of an Allergy

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Neurology: Clinical Practice June 2021 vol. 11 no. 3 e344-e346 doi:10.1212/CPJ.0000000000000848

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Sumatriptan is an effective and well-tolerated medication used for the acute relief of migraines. It blocks nociceptive neurotransmission by binding onto 5-HT_{1b} and 5-HT_{1d}-like serotonin receptors and vasoconstricting cerebral and dural blood vessels.¹ It contains a sulfonamide chemical group and hence is considered a sulfa drug. We report a rare report of skin test–proven sumatriptan anaphylaxis in an 18-year-old woman.

Case

The patient presented to the hospital after developing blurry vision, presyncope, a tight throat, lip angioedema, thorax rash, and feeling nauseous 15 minutes after taking a 50 mg sumatriptan succinate oral tablet for a mild migraine. This was the second tablet of sumatriptan in a course for a migraine with the first dose taken the day before. She denied taking any other medications, and her last food intake was more than 10 hours before.

She is atopic with a background history of allergic asthma. She is now well-controlled on pro re nata use of inhaled salbutamol, taken mainly on exertion. The patient also has mild intermittent allergic rhinitis, mild eczema, and dysmenorrhea managed with an oral contraceptive pill. She is on no other regular medications and is a nonsmoker.

In the ambulance, her blood pressure was initially 90/70 mmHg with a pulse rate of 94. Her blood pressure rose to 130/90 shortly after 0.5 mg epinephrine administered intramuscularly. No wheeze was noted on examination, and she was saturating 99% on room air. Fluids, antihistamines, and prednisolone were given in the emergency department, and she was discharged after an overnight stay. No tryptase rise was noted (3.7 µg/L 1.5 hours after the event, with a subsequent tryptase of 3.9 µg/L 3 months later).

Five months later, she received skin testing to sumatriptan, rizatriptan, zolmitriptan, and naratriptan showing a positive skin prick test to sumatriptan at 50 mg/mL and an equivocal intradermal skin test result to rizatriptan (no significant increase in wheal, but small flare of about 1–2 mm around the wheal) (table). Maximum nonirritating concentrations, as determined on 5 healthy controls who had an adequate histamine control results, were used for intradermal tests. Medications were diluted in sterile saline and filtered. She successfully underwent an oral 2-step challenge to zolmitriptan. She declined an inpatient challenge to rizatriptan and was subsequently advised to avoid sumatriptan and rizatriptan.

PRACTICAL IMPLICATIONS

Consider the rare side effects of allergy/anaphylaxis when prescribing sumatriptan or any other triptan. Although the full extent of cross-reactivity between triptan drugs is not known, caution should be exercised with other triptans when a patient has had a reaction to a triptan.

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Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at [Neurology.org/cp](https://www.neurology.org/cp).

Table Skin Test Concentrations and Results

	Skin prick test		Intradermal test 1		Intradermal test 2	
Sumatriptan 50 mg/mL	Neat	Positive	Not tested		Not tested	
Zolmitriptan 2.5 mg/mL	Neat	Negative	1:1000	Negative	1:100	Negative
Naratriptan 2.5 mg/mL	Neat	Negative	1:1000	Negative	1:100	Negative
Rizatriptan 10 mg/mL	Neat	Negative	1:1000	Negative	1:100	Equivocal
Histamine 10 mg/mL	Neat	Positive	Not tested		Not tested	
Saline	Neat	Negative	Neat	Negative	Not tested	

Discussion

Sumatriptan is a sulfonamide nonantibiotic medication belonging to the antimigraine group of medications known as triptans. A number of adverse drug reactions may occur with triptans such as coronary artery spasms and even serotonin syndrome,² but sumatriptan allergy has rarely been reported. One case abstract reports a patient who had isolated angioedema 4 hours after taking intranasal sumatriptan.³ The patient subsequently had a positive intradermal test to sumatriptan (1:10—exact concentration not reported) and passed challenges to rizatriptan and zolmitriptan.³ Other case reports exist of skin test–positive delayed urticaria confirmed on rechallenge,⁴ and limb and lip angioedema 5 minutes after subcutaneous administration improved with epinephrine.⁵ These suggest a possible IgE-mediated basis behind these reactions, but cross-reactivity with other triptans was not completely explored. A case also exists of a 36-year-old woman who had an intradermal test–positive large localized wheal and flare to subcutaneous sumatriptan. She was, curiously, subsequently able to tolerate oral sumatriptan, suggesting that perhaps a local concentration of sumatriptan is enough to cause localized mast cell degranulation.⁶

Other sulfonamide-containing triptans are naratriptan and almotriptan, whereas nonsulfonamide-containing triptans include zolmitriptan, rizatriptan, eletriptan, and frovatriptan.⁷ There is no convincing evidence for cross-reactivity between sulfa antibiotics and nonantibiotics,⁸ and consistent with this, our patient received a negative skin test to naratriptan (table). A retrospective investigation also found that in 15 patients who reported sulfa allergy/adverse drug reaction, all could tolerate sumatriptan.⁹ Furthermore, it does not seem that a history of asthma, as noted in our case patient, confers a greater risk of sumatriptan adverse reactions.¹⁰

Whether there is cross-reactivity among the triptans is not known. We and others³ provide some evidence that there is no cross-reactivity; however, we did not subject our patient to all triptan skin testing because of the unavailability of drugs, and furthermore, she did not undergo direct provocation testing to all nonsumatriptan triptans. With uncertainty and an equivocal

result to rizatriptan on intradermal skin testing, we hence advised our patient to precautionarily avoid rizatriptan.

We provide a rare case report of sumatriptan anaphylaxis with oral tolerance to an alternate triptan. Future case experiences of IgE-mediated triptan allergies will help to clarify the degree of cross-reactivity among triptan medications. Internists and neurologists should hence be aware of the rare risk of triptan allergy when prescribing this medication.

Study Funding

No targeted funding reported.

Disclosure

The authors report no disclosures relevant to the manuscript. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Publication History

Received by *Neurology: Clinical Practice* December 1, 2019. Accepted in final form March 2, 2020.

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Name	Location	Contributions
Adrian Y. S. Lee, MBBS	Flinders Medical Centre, Bedford Park, SA, Australia	Clinical care of patient, designed and conceptualized study, and drafted the manuscript
Phillippa A. Pucar, MBBS	Royal Adelaide Hospital, Adelaide, SA, Australia	Conceptualized study and contributed to the manuscript
Anthony J. F. Smith, MBBS, PhD	Flinders Medical Centre, Bedford Park, SA, Australia	Clinical care of patient, designed and conceptualized study, and contributed to the manuscript

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