
Anaphylaxis to celecoxib

Michael B. Levy, MD and Jordan N. Fink, MD

Background: Adverse reactions such as urticaria, angioedema, asthma, and anaphylaxis are known to be associated with nonsteroidal anti-inflammatory agents (NSAIDs). Celecoxib (Pfizer/Searle, Caguas, PR) is a new NSAID that differs in structure and mechanism of action of other similar drugs of this class.

Objective: Evaluation of a case of anaphylaxis to celecoxib (Celebrex).

Methods and Results: This report describes a 55-year-old woman who experienced the acute onset of pruritus, urticaria, respiratory distress, and hypotension minutes after ingesting a celecoxib capsule. She had taken the drug a previous time for tendonitis without difficulty. Treatment with epinephrine, corticosteroids, and intravenous fluids was successful. An IgE mechanism could not be detected. She has avoided the drug and has had no further problems.

Conclusions: This is the first patient report of anaphylaxis attributable to celecoxib, a new NSAID. This suggests that physicians and other health care professionals should be aware of the potential serious side effects of this drug.

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INTRODUCTION

Anaphylactoid reactions to aspirin (ASA) and nonsteroidal anti-inflammatory medications (NSAIDs) are well known and have been described previously.¹ These reactions may result in urticaria, angioedema, bronchospasm, or hypotension and do not seem to be mediated by immunoglobulin E (IgE) mechanisms.² ASA and NSAIDs reduce pain and inflammation by inhibiting the synthesis of the enzymes cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2).

Whereas severe allergic reactions to ASA and the COX-1 inhibitors are well described, selective COX-2 inhibitor-related anaphylactoid events have not been reported in the literature. We report a case of anaphylaxis to celecoxib in a patient with no previous allergic history to ASA, NSAIDs, or sulfonamides.

Patient Report

A 55-year-old physician's wife, with no previous atopic history was treated

with celecoxib (Pfizer/Searle, Caguas, PR) for a right Achilles tendonitis for approximately 1 month in October 1999 with clinical improvement. Because of recurrent symptoms, she continued to use it intermittently. She was on no other medication. Six months later, within 15 minutes of taking a 200-mg celecoxib capsule for the first time in 3 months, she began to note palmar itching with swelling, an erythematous rash over her neck and chest with pruritus, shortness of breath, throat tightness, and nausea. She took 50 mg of diphenhydramine, then felt lightheaded and collapsed. The paramedics were called. Upon arrival, the patient was found to be responsive. Blood pressure was 70/0 mm Hg palpable. An intravenous line was started; however, the patient then became unresponsive. Fluids were administered and she was transported to the hospital. Upon admission to the emergency department, she appeared ill but was conscious. Blood pressure was 93/45 mm Hg, pulse 103 beats/minute, respiratory rate 20 breaths/minute, and pulse oximetry of 90% on room air. Diffuse urticaria over the entire body surface was noted. Auscultation of the chest did not reveal any wheezes. Epinephrine, steroids, and fluids were given

with clinical improvement. Evaluation revealed a normal electrocardiogram, cardiac enzymes, chest x-ray, and head computed tomography. Laboratory was remarkable for hypokalemia of 2.8 mmol/L which corrected with supplementation. The patient was observed for 12 hours, improved clinically, and was discharged.

The patient had no known previous adverse reactions to medications. She had taken ASA as well as NSAIDs in the past without problems. There was no history of sulfonamide allergy. Her only medication was senna (Senokot, Purdue Frederick Company, Norwalk, CT) for constipation which she had not taken before the index episode. She had no previous history of asthma, nasal polyps, sinusitis, or food allergy. She was not taking any vitamins or food supplements.

Laboratory analysis to demonstrate IgE was attempted using an ELISA technique and an extract of a celecoxib capsule, but was unsuccessful.

Skin testing to common inhalant allergens as well as selected foods was negative.

Oral challenge with the drug was not performed because it was felt it was too dangerous.

The patient was advised to avoid ASA and all NSAIDs, including other selective COX-2 inhibitors, and was given an epinephrine auto injector (EpiPen, Dey, Napa, CA).

DISCUSSION

NSAIDs have been known to cause adverse allergic reactions such as urticaria, angioedema, and anaphylaxis. These events seem to be mediated by non-IgE mechanisms and frequently are correlated with coexistent adverse reactions to aspirin.² The cyclooxygenase (COX) theory proposes that adverse reactions to ASA and NSAIDs are the result of a cascade of events related to the specific inhibition of in-

Allergy-Immunology Section, Department of Pediatrics and Medicine, Medical College of Wisconsin, Milwaukee, WI.

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tracellular COX enzymes. The COX enzymes, which exist as COX-1 and COX-2, are coded by distinct genes. COX-1 is synthesized in most mammalian cells and its products, and prostanooids are involved in many physiologic functions. One of these products, PGE₂, is protective of gut mucosa and is a regulator of respiratory tract inflammatory processes. COX-2 is induced during inflammation and augments the synthesis of inflammatory prostanoids. ASA and NSAIDs exert their anti-inflammatory properties by inhibition of COX. Disruption of COX-1 activity, however, leads to such side effects as interference with platelet function and gastrointestinal ulcerations. The recent development of selective COX-2 inhibitors, such as celecoxib, which have potent anti-inflammatory effects, have reduced these adverse reactions, presumably by preserving the activity of COX-1. In theory, these drugs should not cross-react with ASA or COX-1 class NSAIDs.³

The rapid onset of pruritus, swelling, shortness of breath, and syncope occurring in this patient after the ingestion of celecoxib is highly sugges-

tive of anaphylactic sensitivity. Although the package insert does note anaphylactoid reaction as a potential adverse effect,⁴ our review of the literature did not reveal previous reports of anaphylaxis to celecoxib or other available selective COX-2 inhibitors. The celecoxib molecule contains a sulfonamide moiety, and it is therefore recommended that patients with sulfa sensitivity avoid this drug. As noted, our patient did not have a history of sulfa allergy. Our unsuccessful attempts to show an IgE mechanism may be because of the lack of appropriate tests. In contrast, this may be consistent with other studies in ASA or NSAID sensitivity in which IgE has not been demonstrated.²

The reason for the hypokalemia remains unknown, although it is listed as an adverse effect of celecoxib in the product package insert.⁴ The patient had no previous history of nausea, vomiting, or diarrhea.

CONCLUSION

This is the first patient report, to our knowledge, of anaphylaxis to the COX-2 inhibitor, celecoxib. As with medications of the NSAID COX-1

class and ASA, health care professionals should be aware of this potentially life-threatening side effect.

REFERENCES

1. Stevenson DD, Simon RA. Sensitivity to aspirin, and nonsteroidal antiinflammatory drugs. In: Middleton EJ, Reed CE, Ellis EF, et al, eds. *Allergy: Principles and Practice*. 5th ed. Vol 2. St Louis, MO: Mosby, 1998:1225-1234.
2. Stevenson DD. Aspirin and nonsteroidal anti-inflammatory drugs. In: Virant FS, ed. *Immunology and Allergy Clinics of North America*. Vol 15, Number 3. Philadelphia: WB Saunders, 1995: 529-552.
3. Szczeklik A, Stevenson DD. Aspirin-induced asthma: advances in pathogenesis and management. *J Allergy Clin Immunol* 1999;104:5-13.
4. Celebrex package insert.

Requests for reprints should be addressed to:
Michael B. Levy, MD
Allergy-Immunology Section
Medical College of Wisconsin
9000 W. Wisconsin Avenue
P.O. Box 1997
Milwaukee, WI 53201
E-mail: mlevy@chw.org