

## Ventricular Fibrillation and Kounis Syndrome Can Result from a More Severe Delayed-Onset Allergic Reaction

To the Editor,

In the fascinating case report by Honggen Cui et al,<sup>1</sup> a 59-year-old woman, who had been treated with levofloxacin tablets for a urinary tract infection 2 days prior, developed itching on her limbs and chest along with sporadic urticaria. One day later, she started experiencing recurrent burning pain in her chest that radiated to her pharynx. Each episode lasted 2-3 minutes and was relieved on its own. The patient was administered aspirin and clopidogrel bisulfate in addition to other medications upon arrival. Thirty minutes later, the patient experienced severe chest pain and eventually lost consciousness while twitching. Ventricular fibrillation was detected and the patient was shocked with 200 Joules right away and regained consciousness.

According to emergency coronary angiography, there was no visible stenosis or blockage in the left main trunk, left anterior descending artery, left circumflex branch, or right coronary artery, and obstruction, and thrombolysis in myocardial infarction risk score blood flow grade 3.

This case highlights significant problems with the use of aspirin, clopidogrel, and the delayed allergic reactions. Paradoxically, these drugs, which are used to treat Kounis syndrome, thrombosis, and myocardial infarction,<sup>2</sup> may actually cause these conditions:

1. Instead of inducing a true immunoglobulin E-mediated allergy, aspirin causes allergic-type reactions by inhibiting the cyclooxygenase-1 enzyme, which diverts arachidonic acid metabolism to produce more leukotrienes. These extra leukotrienes directly cause symptoms including bronchospasm, urticaria (hives), and nasal obstruction. Although aspirin is good for cardiovascular conditions, it can cause Kounis syndrome. The Samter–Beer trio is a combination of asthma, nasal polyps, and aspirin allergy that causes myocardial infarction and vasospasm syndrome.<sup>2-4</sup> Treatment for this condition focuses on reducing the allergic reaction. Another article describes a case of Kounis syndrome brought on by asthma triggered by aspirin used to treat angina pectoris.<sup>5</sup> A case study of a patient with a history of aspirin allergy who experienced coronary vasospasm after taking aspirin is also presented in another article.<sup>6</sup>
2. There are currently 3 documented cases of Kounis syndrome brought on by clopidogrel. A 61-year-old man was admitted to the hospital in the initial report because of worsening chest discomfort that was accompanied by frequent episodes of severe chest pain during rest and regular activities, as well as excessive smoking. He also had a history of hypertension, atopic eczema, and allergic responses. Type I Kounis syndrome as a result of a clopidogrel allergic response was the ultimate diagnosis.<sup>7</sup> After receiving a loading dose of clopidogrel, a 56-year-old male patient with Kounis Syndrome suffered angioedema, respiratory distress, and vasospasm in the right coronary artery.<sup>8</sup> All of these instances have made desensitization to clopidogrel imperative. Desensitization is safe and highly effective for people who are sensitive

### LETTER TO THE EDITOR

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to clopidogrel and require long-term dual antiplatelet therapy.<sup>9</sup>

3. Delayed allergic reactions can exacerbate subsequent rapid allergic reactions by increasing inflammation, attracting more immune cells, and perhaps causing chronic reactions—especially after repeated exposure. This can occur by causing a second, more severe wave of symptoms hours or even days later. Indeed, in severe delayed reactions or a biphasic reaction, the original anaphylactic symptoms recur without additional exposure to the allergen. Even while the majority of acute reactions are T-cell-mediated and antibody-independent, the immune system may still be primed, and further exposure to the allergen or its breakdown products may trigger a fresh, frequently more severe reaction.

Since it is frequently impossible to differentiate between hypersensitive reactions and the worsening of the basic inflammatory condition, diagnosing allergic reactions is difficult. Therefore, a high index of suspicion is required to determine the causal culprit and discover a safe substitute drug. By concentrating on the IgE pathway and the related inflammatory processes, there may be hope for lowering allergy-associated Kounis syndrome.<sup>10</sup>

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