

# Food-Dependent Exercise-Induced Anaphylaxis Induced by Low Dose Aspirin Therapy

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## ABSTRACT

**Background:** Food-dependent exercise-induced anaphylaxis (FDEIA) is a distinct form of common food allergy characteristically induced by a combination of causative food ingestion and physical exercise. Recent investigations have documented that aspirin consumption, in place of exercise, also induces allergic symptoms.

**Case Summary:** A 63-year-old man began low dose aspirin therapy on September 2005. Since January 2006, he had repeated episodes of generalized urticaria and lost consciousness while he was exercising after eating wheat. He was strongly positive for  $\omega$ -5 gliadin in a cap-system fluorescent enzyme immunoassay. Therefore, a diagnosis of wheat-dependent exercise-induced anaphylaxis was made.

**Discussion:** Patients with aspirin-provoked FDEIA have been reported previously as taking ordinary doses of aspirin for reducing pain, inflammation and fever. However, in our patient, low dose aspirin therapy for reducing cardiovascular risk possibility induced FDEIA. Growing numbers of elderly people take low doses of aspirin for prevention of cerebral or myocardial infarction. Therefore, physicians should remember that aspirin consumption, even at low doses, is a risk factor for FDEIA.

## KEY WORDS

cap-system fluorescent enzyme immunoassay, food-dependent exercise-induced anaphylaxis, low dose aspirin,  $\omega$ -5 gliadin

## INTRODUCTION

Food-dependent exercise-induced anaphylaxis (FDEIA) is a distinct form of food allergy, characteristically induced by a combination of causative food ingestion and physical exercise. In Japan, wheat is the most frequent cause of FDEIA.<sup>1</sup> Recent investigations have documented that aspirin, in place of exercise, also induces allergic symptoms.<sup>2,3</sup> On the other hand, serum gliadin levels increase in accordance with allergic symptoms in patients with wheat-dependent exercise-induced anaphylaxis (WDEIA), strongly indicating that the blood antigen level is a key factor in the induction of symptoms. Therefore, aspirin has been hypothesized to provoke symptoms of FDEIA by facilitating allergen absorption from the gastrointestinal tract. In fact, ingestion of aspirin combined with exercise increased gastrointestinal permeability

in humans,<sup>4</sup> and serum gliadin can be detected in patients with WDEIA and even in healthy subjects who consume aspirin before wheat ingestion.<sup>5</sup>

## CLINICAL SUMMARY

A 63-year-old man diagnosed on September 21, 2005 with vertebrobasilar insufficiency began low dose aspirin therapy (81 mg/day). Two days after eating spaghetti in October, he developed a rash associated with itching which resolved within 2 hours. Then, on January 31, 2006, he developed generalized urticaria and lost consciousness while he was cleaning his house after consuming a breakfast of toast and milk. He recovered consciousness after a short period, but the urticaria required intravenous drip treatment at a nearby hospital. The next day, after consuming the same breakfast of toast and milk, he walked for 15 minutes to the hospital for a regular check-up. While

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waiting for his doctor, he felt ill, experienced low blood pressure (50/25 mmHg) with generalized urticaria, and lost consciousness. A subdural hemorrhage, detected by computed tomography, was surgically treated on February 6; he remained hospitalized until mid-February. After being discharged from the hospital, he resumed the low dose aspirin therapy. While walking on March 15 after eating tomato pasta, he nearly lost consciousness and experienced low blood pressure (80/50 mmHg). He was then referred to our hospital with a suspected diagnosis of FDEIA.

His blood cell counts and liver function tests were normal. Total IgE (2200 IU/ml) was high, even though he had never been diagnosed with any allergy. Radio-allergosorbent testing (RAST) for specific IgE revealed positive reactivity to grains, wheat, rye, and gluten. Because of the low specificity of commercially available RAST for wheat protein and gluten, a cap-system fluorescent enzyme immunoassay (CAP-FEIA) for either  $\omega$ -5 gliadin or high molecular weight (HMW)-glutenin-specific IgE was performed as a substitute for a provocative test.<sup>6</sup> In this system, peptide A contained the IgE-binding epitope sequences of  $\omega$ -5 gliadin, and peptide B contained three epitope peptides of HMW-glutenin. CAP-FEIA has been successfully used to reveal specific IgE to peptide A and/or peptide B in 97% of patients with WDEIA.<sup>6</sup> The patient in our case was strongly positive for  $\omega$ -5 gliadin (peptide A: 35.9 UA/ml, normal: <1). Therefore, a diagnosis of WDEIA was made. We advised the patient to refrain from exercise after eating wheat, and to stop aspirin therapy (after consulting with a neurosurgeon). He did not experience any more episodes of anaphylactic shock since instituting these changes, except on November 3, 2006 when he happened to take common cold medicine which contained salicylamide and acetaminophen.

### **PATHOLOGICAL FINDINGS**

We did not perform any histopathological examination in this patient.

### **DISCUSSION**

Since its introduction as Aspirin in the year 1899, acetylsalicylic acid has widely been used world-wide for the therapy of painful, inflammatory and feverish states. Recently aspirin has also been used for reducing cardiovascular risk. However it is not well known

that aspirin consumption is a risk factor for FDEIA.

It has been previously reported that patients with aspirin-provoked FDEIA took ordinary doses of aspirin (500–1000 mg/day) for reducing pain, inflammation and fever. However, in our present case, the time at which our patient started taking low dose aspirin is consistent with the onset of WDEIA, suggesting that low dose aspirin therapy may possibly induce WDEIA. Growing numbers of elderly people consume low dose aspirin for prevention of cerebral or myocardial infarction. Therefore, physicians should remember once again that aspirin consumption, even at low doses, is a risk factor for FDEIA.

### **ACKNOWLEDGEMENTS**

Hiroko Fujii cared for the patient and wrote the paper. Naotomo Kambe designed the research, analyzed the data, and helped in writing the paper. Akihiro Fujisawa cared for the patient. Kunie Kohno and Eishin Morita performed CAP-FEIA analysis for either  $\omega$ -5 gliadin or high molecular weight-glutenin-specific IgE, and helped in writing the paper. Yoshiaki Miyachi managed and discussed the research.

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