Case Report

Development of non-steroidal anti-inflammatory drug intolerance over a 3 year period

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ABSTRACT
We report the detailed clinical course of a 47-year-old woman with aspirin-induced asthma in which non-steroidal anti-inflammatory drug (NSAID) intolerance developed over a 3 year period. The patient had mild asthma and was admitted with a femoral fracture in August 1996. Although she was given NSAIDs, including rectal diclofenac and oral loxoprofen, there was no worsening of asthma. After discharge, she was followed as having NSAID-tolerant asthma. When she developed perennial rhinitis and anosmia subsequent to an upper respiratory tract infection, asthma control was well maintained. Later, she experienced three episodes of severe asthmatic attacks after intake of aspirin or ketoprofen. Thus, we investigated her NSAID tolerability in September 1999. Sodium tolmetin inhalation challenge demonstrated a positive reaction, leading to the diagnosis of aspirin-induced asthma. Open challenges with loxoprofen and diclofenac also provoked positive reactions. The present case illustrates the potential variability of aspirin-induced asthma. Aspirin or NSAIDs challenge tests should be performed when nasal symptoms, particularly anosmia, develop or worsen.

Key words: aspirin-induced asthma, diclofenac, loxoprofen, non-steroidal anti-inflammatory drug, sodium tolmetin inhalation challenge.

INTRODUCTION
Some patients with aspirin-induced asthma have a past history of taking non-steroidal anti-inflammatory drugs (NSAIDs) safely.1 We report herein on an uncommon variant of the development of aspirin-induced asthma.

CASE REPORT
A 47-year-old woman was admitted to Fujinomiya City General Hospital with left femoral fracture in August 1996. She had a 5 year history of asthma and had been given a prescription for 200 mg theophylline, 20 µg clenbuterol, 1 mg betamethasone, 8 mg chlorpheniramine and inhaled salbutamol on an as-needed basis at a local clinic. She was given NSAIDs, including 50 mg rectal diclofenac and oral loxoprofen three times a day, as analgesics by an orthopedist. However, there was no worsening of asthmatic symptoms since the initial administration. After discharge, the treatment regimen was changed to 400 µg beclomethasone dipropionate, 400 mg theophylline and 450 mg pranlukast. However, ingestion of 60 mg loxoprofen three times a day did not provoke any symptoms and the patient was followed as having NSAID-tolerant asthma. After she developed symptoms of perennial rhinitis over a period of months, she began to experience anosmia subsequent to an upper respiratory infection in August 1997 and the diagnosis of chronic sinusitis was made. However, asthma control was well maintained and there were no NSAIDs taken since February 1998. In September 1998, she experienced a severe asthmatic attack after the ingestion of 330 mg aspirin. In July and September 1999, similar episodes occurred after ingestion of aspirin and the administration of 50 mg ketoprofen intramuscularly,
respectively. Thus, we needed to investigate her NSAID tolerability.

Laboratory data demonstrated a white blood cell count of 4300 /µL, with 13% eosinophils, and a total IgE of 140 IU/mL. Specific IgE analysis was negative for common inhalant allergens. The forced expiratory volume in 1 s (FEV$_1$) was 2.49 L (104.6% of predicted values) and the provocative concentration of methacholine causing a 20% fall in FEV$_1$ was 2.97 mg/mL. Challenge tests with NSAIDs were performed after informed consent was obtained. Sodium tolmetin inhalation challenge demonstrated that the threshold concentration causing a greater than 20% fall in FEV$_1$ was 0.5%, leading to the diagnosis of aspirin-induced asthma. Open oral challenge with 30 mg loxoprofen and rectal challenge with 12.5 mg diclofenac provoked dyspnea, conjunctival injection, facial flushing and a greater than 20% fall in FEV$_1$ 70 and 120 min after administration, respectively. This patient has been instructed not to ingest any form of NSAID since that time.

The minimal concentration of NSAID causing an adverse reaction had decreased to less than one-quarter for diclofenac and half for loxoprofen. Some medications, including corticosteroids and antihistamines, attenuate aspirin-induced reactions, leading to false-negative results on aspirin challenge tests. However, NSAIDs did not provoke any symptoms without an oral corticosteroid or antihistamine in our patient. Furthermore, it was unlikely that desensitization of NSAIDs had occurred by chance because neither medication was administered daily during the course. We speculate that NSAID intolerance developed after the appearance of anosmia subsequent to a viral infection, which is reported to be the typical natural course of aspirin-induced asthma in the literature. However, we rarely encounter the conversion of NSAID-tolerant asthma to NSAID-intolerant asthma over a 3 year period. This case illustrates the potential variability of aspirin-induced asthma. Aspirin or NSAIDs challenge tests should be performed when nasal symptoms, particularly anosmia, develop or worsen.

**REFERENCES**


