

Acetaminophen anaphylaxis with aspirin and sodium salicylate sensitivity: a case report

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Background: Aspirin idiosyncrasy can present with bronchospasm or cutaneous reactions, but combined pulmonary and cutaneous reactions are rare. High-dose acetaminophen has been reported to provoke bronchospasm in aspirin-sensitive asthmatic patients.

Case History: We report an asthmatic adolescent female who had anaphylaxis with 650 mg acetaminophen after tolerating 325-mg doses for years. She subsequently in sequence had urticaria with aspirin and ibuprofen, and anaphylaxis with sodium salicylate. She was then challenged with acetaminophen, 325 mg orally.

Results: Approximately 30 minutes after acetaminophen challenge, she developed rhinoconjunctivitis, urticaria, pruritus, cough, and bronchospasm reversed with antihistamines and bronchodilators.

Conclusions: Aspirin sensitivity has not frequently been described in younger age groups. This patient also had several unusual features in that she presented first with sensitivity to acetaminophen that was then followed by aspirin sensitivity. She had urticaria with both aspirin and sodium salicylate; she had combined pulmonary and cutaneous reactions to both acetaminophen and aspirin, which are rarely described; and she had anaphylaxis with low-dose acetaminophen.

Ann Allergy Asthma Immunol 1996;77:473-4.

INTRODUCTION

Acetaminophen is one of the most commonly used antipyretic and analgesic medications and is frequently substituted for aspirin in patients with aspirin sensitivity. In the pediatric population, however, this substitution is not common because aspirin is used infrequently. Recent reports suggest that this substitution is not entirely without risk because of potential aspirin and acetaminophen cross reactivity,¹⁻⁵ although such cross-reactivity is uncommon.^{6,7} Acetaminophen can also trigger anaphylactoid reactions in individuals without known aspirin sensitivity.⁸⁻¹⁰

Many nonsteroidal anti-inflamma-

tory drugs such as aspirin are cyclooxygenase inhibitors. Several animal models have shown that acetaminophen may also possess cyclooxygenase inhibitory activity;^{11,12} however, this relationship continues to be controversial.¹³ The effect of acetaminophen on cyclooxygenase in human lung have yet to be reported.

Settipane and Stevenson³ described three aspirin-sensitive asthmatic patients who underwent double-blind placebo-controlled challenges and reacted to high doses (1000 mg) of acetaminophen with a greater than 20% fall in FEV₁. Two of these patients were desensitized to aspirin and then rechallenged with acetaminophen without reaction suggesting cross reactivity and similar mechanisms (ie, cyclooxygenase inhibition) for reactions to both aspirin and acetaminophen.

High-dose acetaminophen (>650 mg) seems to be necessary to provoke significant bronchospasm in aspirin-sensitive patients. In this case report both cutaneous and pulmonary responses occurred with the usual thera-

peutic dose of acetaminophen (325 mg).

CASE HISTORY

A 13-year-old girl with well-controlled asthma had migraine which in the past had responded without adverse reaction to acetaminophen (325 mg). During a severe migraine, she took 650 mg acetaminophen. Within 10 minutes of ingestion, she developed generalized hives with angioedema and difficult breathing which responded to antihistamines. Approximately 2 months later, the patient, who had never received non-steroidal anti-inflammatory drugs before, ingested aspirin, 325 mg, and within 15 minutes developed generalized giant urticaria lasting three hours. A few weeks later she received ibuprofen (300 mg) and experienced the same reaction as with aspirin.

Several weeks later, Dodd's pill (sodium salicylate, 325 mg, and potassium bicarbonate, 25 mg) was taken and within one hour she developed conjunctivitis, rhinitis, generalized pruritus, and wheezing. Due to the patient's history of migraine and need for analgesics, an acetaminophen challenge was arranged in order to determine objectively whether the patient also had acetaminophen sensitivity.

METHODS

Acetaminophen challenge was instituted following informed consent. Tylenol caplet, 325 mg, (McNeil) was administered orally after performing baseline pulmonary function tests including flow volume loop and monitoring vital signs.

RESULTS

Within 30 minutes of acetaminophen administration, the patient began developing rhinoconjunctivitis and ery-

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Received for publication February 13, 1996.

Accepted for publication in revised form June 24, 1996.

thematous, pruritic patches with wheals occurring on her back, abdomen, and chest. The patient also developed a repetitive cough but no wheezing was detected. Correlating with the clinical reaction was a fall in FVC and FEV₁ of greater than 20%. Pre-acetaminophen challenge FVC was 3.13 L/sec (117% predicted); FEV₁ 2.55 L/sec (104% predicted); and FEF₂₅₋₇₅ of 2.47 L/sec (72% predicted). Post-acetaminophen challenge FVC was 2.49 L/sec (93% predicted); FEV₁ 1.99 L/sec (81% predicted); and FEF₂₅₋₇₅ of 1.87 L/sec (54% predicted). Treatment was instituted with oral cetirizine, an H₁-antihistamine, and inhaled albuterol with resolution of her urticaria and cough, and normalization of her spirometry.

DISCUSSION

This patient experienced adverse reactions to acetaminophen and several different nonsteroidal anti-inflammatory agents (aspirin, ibuprofen, and sodium salicylate). The fact that reactions occurred to both aspirin and ibuprofen is not surprising since both drugs are cyclooxygenase inhibitors.^{13,14} The reactions to acetaminophen and sodium salicylate are more difficult to explain. Sodium salicylate is not known to be a cyclooxygenase inhibitor¹⁴ and there have been only isolated case reports concerning its potential cross reactivity with aspirin. It has been reported that acetaminophen may in high doses crossreact with aspirin due to weak cyclooxygenase inhibition.^{2,4,15,16}

Previous reports have suggested that low-dose acetaminophen (<650 mg) usually provokes only mild adverse pulmonary changes or none at all in patients with aspirin sensitivity.^{2,15,16} A recent case report and literature review indicate that in rare cases, anaphylaxis can occur with low-dose acetaminophen.¹⁷ This current case report illustrates that both significant pulmonary and cutaneous symptoms may occur

with low dose acetaminophen challenge in patients with known aspirin sensitivity and asthma. It is also interesting to note that this patient also experienced combined cutaneous and pulmonary reactions when exposed to aspirin and non-steroidal anti-inflammatory drugs, an extremely rare occurrence.¹³⁻¹⁷

A feature unique to this particular case is the fact that the patient initially reacted to acetaminophen and then subsequently to aspirin rather than vice-versa, which has primarily been reported in the literature.^{1,3,16} This situation would likely be seen more commonly in the pediatric population that now avoids aspirin because of the potential for Reye's syndrome.

In conclusion, low-dose acetaminophen is capable of provoking severe reactions in aspirin-sensitive asthmatic individuals. The degree of risk, however, is probably low when acetaminophen is substituted in aspirin-sensitive patients.

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