

Acetaminophen-Induced Exanthem of the Breasts

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We describe an unusual case of a maculopapular exanthem secondary to acetaminophen use that presented on the breasts and anterior pelvis in regions of pressure from the patient's undergarments. A review of the literature regarding exanthematous drug eruptions secondary to acetaminophen use also is presented.

Cutis. 2012;89:284-286.

Case Report

A 30-year-old woman presented to the allergy/immunology department for an evaluation of a possible allergy to acetaminophen. The patient reported having 2 episodes of an urticarial-like rash after taking oral acetaminophen in childhood. She explained that the rash was not immediate and developed within 6 to 8 hours following acetaminophen ingestion. She denied any associated symptoms or concurrent illness. The rash reportedly resolved within 24 hours without any specific therapy. The patient could not recall her age at the time of the initial episode. The second episode occurred around 11 years of age, and she has not taken acetaminophen since then. She tolerated nonsteroidal anti-inflammatory drugs (NSAIDs) without any complications. At presentation, she was trying to become pregnant and desired to have acetaminophen as a pain medication option.

Her medical history was notable for allergic rhinitis with sensitivity to tree and weed pollen and recurrent spontaneous abortions of unknown etiology. Evaluation for hypercoagulability was unremarkable.

She was a nonsmoker who minimally used alcohol. She had no other known drug or food allergies. Her only medications at the time of initial evaluation were over-the-counter diphenhydramine hydrochloride and pseudoephedrine hydrochloride as needed. Physical examination revealed pale nasal turbinates with mild edema but was otherwise unremarkable.

Given the distant and mild reaction history, an open oral drug challenge to acetaminophen was conducted. After abstaining from antihistamines for more than 5 days, the patient was given oral acetaminophen every 30 minutes in various doses: 50, 100, 200, 325, and 650 mg. She was monitored for 1 hour following the final dose and showed no signs or symptoms concerning for an immediate systemic reaction. However, approximately 3 hours following the final dose, the patient noted the onset of a non-urticarial, erythematous, maculopapular eruption that was symmetric, well-demarcated, and present on her breasts, only in the region of skin in contact with her



Figure 1. Maculopapular exanthem of the right breast, only in the region of skin in contact with the bra; the remainder of the patient's chest was spared.

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The authors report no conflict of interest.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the US Department of the Army, US Department of Defense, or the US Government.

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bra (Figure 1). The rash was only mildly pruritic and she showed no signs or symptoms concerning for anaphylaxis. The following day the rash on her breasts was unchanged, but she had developed a similar eruption on the anterior pelvic region of her panty line, which also was well-demarcated and only present in the region of skin in contact with her undergarment. She had no fever or mucosal lesions. The patient was treated with triamcinolone acetonide ointment and fexofenadine hydrochloride with complete resolution within 4 days.

To confirm that the eruption was secondary to acetaminophen use, an open oral drug challenge was repeated after 4 weeks. The patient developed the same maculopapular exanthem on her breasts in the bra region approximately 20 minutes following the 325-mg dose of acetaminophen. The open oral drug challenge was discontinued and the patient was closely monitored. She did not develop any other symptoms and was discharged from our clinic. The following day she had the same symmetric eruption involving her breasts and anterior pelvis only in the regions of skin in contact with her bra and panty line. A punch biopsy was obtained from the site of the rash on her right breast and tissue examination revealed spongiotic dermatitis as well as perivascular lymphocytic infiltrates with eosinophils consistent with an exanthematous drug eruption (Figure 2). The exanthem resolved within 3 days without any specific therapy.

Comment

Adverse drug reactions to acetaminophen at typical doses are uncommon. Acetaminophen possesses weak cyclooxygenase inhibitor activity, which may explain the drug reactions in aspirin- or NSAID-sensitive patients at higher doses.¹ Acetaminophen has been implicated in acute generalized exanthematous pustulosis, fixed drug eruptions, urticaria and angioedema, Stevens-Johnson syndrome and toxic epidermal necrolysis, and other cutaneous reactions.² Type I hypersensitivity to acetaminophen is rare but has been described.¹

Exanthematous rashes are the most common of all cutaneous drug reactions.³ Amoxicillin is a frequent causative agent. The maculopapular eruptions likely occur through an immunologic, T-cell mediated, type IV hypersensitivity Gell and Coombs reaction,⁴ but the exact pathophysiology is unknown. Although exanthems are common manifestations of drug reactions, they rarely have been reported secondary to acetaminophen use. Stricker et al⁵ reviewed 50 cases of acute hypersensitivity reactions to acetaminophen that were reported to the World Health Organization

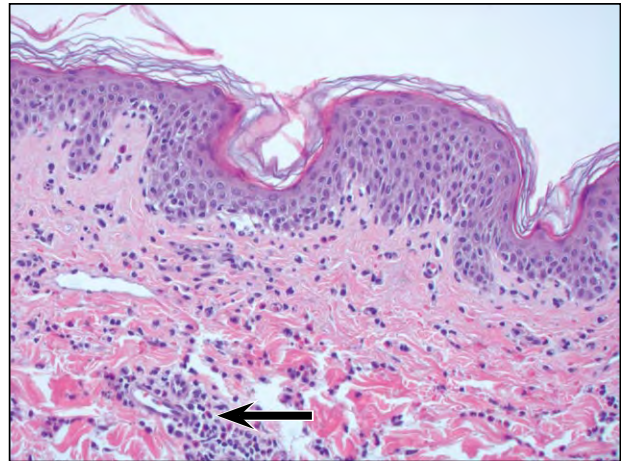


Figure 2. A punch biopsy revealed spongiosis at the dermoepidermal junction and a perivascular lymphocytic infiltrate with eosinophils (arrow)(H&E, original magnification $\times 20$).

Collaborating Centre for International Drug Monitoring in Uppsala, Sweden, in 1985 and noted 12 cases of erythematous or maculopapular rashes. No other details were provided. Matheson et al⁶ reported a case of an infant who developed a case of a maculopapular rash following the ingestion of breast milk from her mother who had taken acetaminophen. The rash occurred on multiple occasions, including while the patient was at the clinic with immediate testing of the mother's breast milk showing elevated levels of acetaminophen.⁶ Rallis et al⁷ evaluated drug eruptions in children treated with various medications for ear, nose, and throat infections, and one patient was noted to have a maculopapular rash attributed to acetaminophen solely based on clinical and historic factors.

In our patient, the clinical appearance of the rash and the presence of eosinophils in the punch biopsy are consistent with a drug-induced exanthem secondary to acetaminophen use. The diagnosis was confirmed by the use of repeated open oral drug challenges. The report of our patient also is unusual because the location of the eruption was confined to the breasts, only in the regions of skin in contact with her bra and her panty line. Because exanthematous drug eruptions can occur in areas of pressure,¹ we speculate that our patient's exanthem had a pressure-related component and thus occurred only in areas of thinner skin that had pressure applied from her undergarments.

Although this cutaneous manifestation of a drug allergy is not life threatening, the low causative dose, cosmetic appearance of the exanthem, and mild discomfort will preclude the use of acetaminophen in

our patient during pregnancy. The patient tolerated NSAIDs well, which will remain her primary pain medication option outside of pregnancy.

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