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Urticaria from caffeine

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Caffeine is a naturally occurring biologic amine found in foods, particularly beverages (coffee, tea, cola drinks, and chocolate). Chemically, it is a methylxanthine, a potent pharmacologic agent, closely related to theophylline and theobromine. Caffeine is the most popular and widely used stimulant drug in the world; it causes habituation and has widespread pharmacologic actions that include the stimulation of the central nervous system and the heart and increased output of gastric acid and urine, as well as a moderate bronchodilator effect.¹ A cup of coffee contains between approximately 50 and 150 mg of caffeine, and the pharmacologically active dose is about 200 mg.

We report a patient who developed urticaria after the ingestion of caffeine-containing beverages.

CASE REPORT

A 53-year-old man, with personal and family history of atopy (hay fever), referred to acute episodes of urticaria after ingestion of coffee, tea, cola drinks, and, eventually,

with chocolate. This "sensitivity" had begun 15 years previously, when, 20 minutes after ingestion of a cup of coffee, he developed itching, erythema, and wheals on his face, neck, and upper trunk. These symptoms reappeared with the same latency and in the same locations on every occasion that he ingested one of the aforementioned beverages or foods. He noted that the larger the amount he drank the more severe the eruption. The urticaria usually resolved in 1 or 2 hours without treatment. He also referred to a 20-year history of aspirin idiosyncrasy, developing generalized urticaria, predominantly on the upper trunk, after ingestion of aspirin. He had never suffered from dyspnea or any other extracutaneous symptom with these substances. By avoiding the ingestion of aspirin-like drugs and caffeine-containing foods, he remained asymptomatic. The patient's serum IgE was 129 IU/ml. Skin prick and intradermal tests with an aqueous solution of pure caffeine (1:60 gm/ml) were negative as well as a leukocyte histamine release test (fluoromatic automatized method) with several fivefold dilutions of this solution. Patch tests with undiluted and 1:10, 1:100, and 1:1000 dilutions in saline were negative at 20 minutes, 48 hours, and 96 hours. On two separate occasions, double-blind, placebo-controlled, oral challenge with caffeine (25 mg) administered in white, opaque, tartrazine-free capsules produced itching and urticaria on the face, neck, and trunk in 20 minutes. Precipitating antibodies could not be demonstrated by double gel diffusion in Ouchterlony gel.

To evaluate the role of endogenous histamine in this reaction, the patient was administered terfenadine (60 mg) 1 hour before administering the caffeine. This pretreatment

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completely inhibited the apparition of urticaria, suggesting the implication of mediator release and H₁-receptor stimulation in the pathogenesis of the reaction.

The possibility of a cross-reaction with other methylxanthines was tested by administration of anhydrous theophylline. Oral challenge with 25 and 300 mg elicited no response.

In contrast, aspirin sensitivity was demonstrated by a positive oral challenge with aspirin, which resulted in generalized urticaria 30 minutes after administration of 30 mg.

DISCUSSION

Allergic-like reactions caused by caffeine are extremely rare. However, the oral challenge tests performed confirm that caffeine was the substance responsible for the appearance of urticaria as well as the exceptional coexistence of caffeine and aspirin sensitivity in our patient. We have no evidence to implicate an immune mechanism as being responsible for this reaction to caffeine, and a pharmacologic mechanism is also very unlikely since xanthines themselves are inhibitors of the release of chemical mediators.² Therefore, a personal susceptibility or idiosyncratic pathway may be the underlying mechanism.

In a previous case of urticaria caused by caffeine studied by our group,³ the prick test was positive, although the passive transfer test (Prausnitz-Küstner)

was negative. There are case reports of urticarial reactions caused by aminophylline,^{4,5} which have been considered secondary to the ethylene diamine portion of the aminophylline molecule.⁵

We have no explanation for the association of caffeine and aspirin sensitivity in this patient. It could be a coincidence, but the similarity of the clinical pictures with both drugs could also be due to the existence of final common pathways.

Finally, we call attention about the importance of considering chemicals that exist naturally in food (e.g., caffeine) as well as food additives in the pathogenesis of allergic and allergic-like reactions to foods.

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