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PAPAIN-INDUCED OCCUPATIONAL RHINOCONJUNCTIVITIS AND ASTHMA – A CASE REPORT

ALERGIA ZAWODOWA WYWOŁANA PAPAİNĄ – OPIS PRZYPADKU

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ABSTRACT

This report presents a case of occupational asthma, rhinitis and conjunctivitis to papain in a 50-year-old herbs and spices packer, with documented increased eosinophilia in induced sputum and in the nasal lavage fluids after a specific inhalation challenge test (SICT) and specific nasal challenge test (SNCT) with this enzyme. Immunoglobulin E-mediated (IgE) sensitization to papain was confirmed by positive results of a skin prick test with specific solution. Specific inhalation and nasal challenge tests demonstrated a direct and significant link between the exposure to this protease and the allergic response from the respiratory system. Additionally, the SNCT induced a severe reaction of the conjunctivae and a significant increase in the count of eosinophils in tears, despite the lack of direct contact of the allergen with the conjunctiva. Med Pr 2016;67(1):109–112

Key words: asthma, occupational allergy, enzyme, rhinitis, papain, conjunctivitis

STRESZCZENIE

W artykule opisano przypadek zawodowej astmy oskrzelowej, alergicznego nieżyty nosa i zapalenia spojówek wywołanych papainą u 50-letniej pakowaczki ziół i przypraw. W badaniu cytologicznym udokumentowano wzrost odsetka eozynofiliów w indukowanej płwocinie i popłuczynach nosowych po swoistej próbie prowokacyjnej wziewnej i donosowej z tym enzymem. Zależną od immunoglobuliny E (IgE) nadwrażliwość pacjentki na papainę potwierdzono dodatnimi wynikami punktowych testów skórnych z roztworem tej proteazy. Wyżej wymienione próby prowokacyjne wykazały istotny związek między ekspozycją na papainę a reakcją alergiczną ze strony układu oddechowego. Ponadto swoista próba prowokacyjna donosowa wywołała wzmożoną reakcję ze strony spojówek i istotny wzrost odsetka eozynofiliów we łzach mimo braku bezpośredniego kontaktu alergenu ze spojówkami. Med. Pr. 2016;67(1):109–112

Słowa kluczowe: astma, alergia zawodowa, enzym, alergiczny nieżyt nosa, papaina, alergiczne zapalenie spojówek

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INTRODUCTION

Papain is an enzyme which is present in papaya plant (*Carica papaya*), and which is commonly used in cosmetic, pharmaceutical, and food industries. The first case report of allergy to papain was described in 1928. A few new cases of occupational papain-induced asthma have been reported since then, but mainly concerning employees of cosmetic and pharmaceutical industries [1–3]. We present a case of a patient with occupational allergy to papain, who after a provocation test, developed allergic rhinitis associated with ocular symptoms.

CASE DESCRIPTION

A 50-year-old, non-smoking female was investigated for suspected occupational asthma and rhinitis in the Department of Occupational Diseases, the Nofer Institute of Occupational Medicine, Łódź, Poland. She had worked as a packer of herbs and spices for 12 years. For the last 3 years she had been suffering from work-related nasal symptoms, while for the last 2 years – from dyspnea and cough. The symptoms had occurred regardless of a season, especially at work when dealing with meat softening salt which had contained papain. The patient had noticed that symptoms had improved

during the weekends and over vacations. She had never been tested for allergy before and had taken no drugs. She had had no family or personal history of atopy. The patient had been working with papain also directly prior to the examination at the department.

Physical examination and laboratory tests revealed no abnormalities. The baseline spirometric (Master-Scope, Jaeger, Germany) values were as follows: forced expiratory volume in 1 s (FEV_1) = 2.88 l (109.4%), forced vital capacity (FVC) = 3.72 l (120.9%), FEV_1/FVC = 77.35, maximal expiratory flow at 50% (MEF_{50}) = 3.24 l/s (82.6%). Skin prick tests (SPT) to common allergens (trees, weed and grass pollens, dust mites, feathers, moulds, dog and cat hair) (Allergopharma, Germany) were negative, while SPT with a solution of papain showed a positive reaction even at a concentration of 0.001% (a 3×20 mm wheal response while the histamine reaction was 3×25 mm). Skin prick tests performed using the same papain solutions were negative in 2 atopic and non-atopic control subjects.

The methacholine challenge test, specific inhalation challenge test (SICT) and specific nasal challenge test (SNCT), first with placebo, then with a papain solution were also performed. A 5-minute SICT with

a 0.01% solution of papain induced an isolated early asthmatic reaction with a 30.4% decline in FEV_1 and a significant increase in the number of eosinophils in the induced sputum.

Additionally, a significant increase in non-specific bronchial hyperreactivity was observed after the SICT (methacholine concentration causing the 20% decrease of FEV_1 (PC20) = 10.3 mg/ml before and PC20 = 4.2 mg/ml after the SICT). During the SNCT, approximately 3 ml of a 0.001% papain solution was administered to the nasal cavity. Immediately after the nasal provocation clinical symptoms of rhinitis and an increased count of eosinophils in the nasal lavage fluid were observed. The SNCT also induced a severe reaction of the conjunctivae and a significant increase in the count of eosinophils in tears (Table 1).

DISCUSSION

In a recent review by Baur and Bakehe, over 100 allergic asthma cases due to papain were summarized [4]. In our case, the clinical history suggested occupational respiratory allergy. All the symptoms appeared after occupational exposure to papain and, similarly

Table 1. Cellular analysis of the patient's sputum, nasal lavage and tear fluid before and after the specific inhalation and nasal challenge test with papain

Tabela 1. Ocena cytologiczna płwociny, popłuczyn nosowych i łez pobranych od pacjenta przed swoistą prowokacją wziewną i donosową z papainą oraz po prowokacji

Time of collecting material Czas pobrania materiału	Cells in collected material Komórki w pobranym materiale [%]					
	epithelial nabłonkowe	neutrophils neutrofile	eosinophils eozynofile	basophils bazofile	limphocytes limfocyty	monocytes monocyty
Sputum / Płwocina						
before SICT / przed SICT	38	31	2	0	1	0
24 h after SICT / 24 godz. po SICT	5	62	5	0	4	0
Nasal lavage / Popłuczyny nosowe						
before SNCT / przed SNCT	23	76	1	0	0	0
4 h after SNCT / 4 godz. po SNCT	13	71	14	1	0	1
24 h after SNCT / 24 godz. po SNCT	25	56	18	0	0	1
Tears / Łzy						
5 min after SNCT / 5 min po SNCT	6	31	2	0	1	0
1 h after SNCT / 1 godz. po SNCT	71	21	6	0	2	0
24 h after SNCT / 24 godz. po SNCT	13	0	0	0	0	0

SICT – specific inhalation challenge test / swoista prowokacyjna próba wziewna, SNCT – specific nasal challenge test / swoista prowokacyjna próba donosowa.

to other reports [1–3,5], the immunoglobulin E-mediated (IgE) sensitization to papain was confirmed with a positive SPT result with a papain solution. In our case, the SICT and SNCT with papain induced allergic responses from the respiratory system and conjunctiva. During the SNCT, not only symptoms of rhinitis occurred but – despite the lack of a direct contact of the allergen with the conjunctiva – conjunctivitis was observed, too. Additionally, high eosinophilia in tears was found, and it correlated with clinical symptoms. It confirms that there are mechanisms determining the coexistence of symptoms of allergic rhinitis and conjunctivitis.

Occupational allergy to papain had been previously described. Tarlo et al. reported the cases of patients with work-related symptoms that correlated with exposure to papain [1]. In the study by Baur et al. occupational exposure to airborne papain induced respiratory, conjunctival and/or cutaneous symptoms in more than a half of the investigated workers [2]. Diagnostic procedures used in that study included: skin prick testing, determination of specific IgE and the SICT with 0.001–0.5 mg of papain, which elicited immediate or dual asthmatic reactions in all symptomatic workers. It has been highlighted that airborne papain has to be considered as a health hazard for workers both because of strong immunogenic potency and a proteolytic activity. Novey et al. reported that atopic employees of a pharmaceutical company had developed pulmonary symptoms and anti-papain antibodies significantly sooner after papain exposure than the others did [6].

On the other hand, duration of exposure had no effect on symptomatology, pulmonary function or immunological response. Soto-Mera et al. reported cases of allergy to papain among beauty salon workers, in the case of whom rhinitis, conjunctivitis, asthma and urticaria had occurred when dissolving tablets of papain, which had been used for cosmetic procedures [3]. Contact urticaria, rhinoconjunctivitis and bronchial asthma due to occupational exposure to papain used to soften cephalopods, which has also been described [7].

Niinimäki et al. presented a case of papain-induced hypersensitivity in a cosmetologist who had experienced conjunctival irritation, rhinorrhea and nose itching associated with the use of an abrasive cream containing papain [8]. The diagnostics included SPT, specific IgE to papain and the SNCT performed by inserting a small piece of cotton moistened with a papain solution. After the challenge, symptoms of rhinitis were observed but there was no mention of conjunctivitis

induced by the challenge. Milne and Brand reported a case of occupational allergy due to papain exposure in a 27-year-old analytical chemist [9]. While working in the laboratory where papain was sifting she noticed eye irritation followed by an increased nasal secretion and almost abrupt onset of asthma. Medical intervention was required.

Little is known about the co-occurrence of ocular symptoms in patients with allergic rhinitis, especially among those with suspected occupational allergy. Single studies about rhinoconjunctivitis have referred it to hypersensitivity to environmental allergens. For example, the relationship between nasal allergen exposure and the prevalence of ocular symptoms has been proven among pollen allergic patients when exposed to allergens on a field with and without a special anti-allergen filters placed inside their noses. The measures taken to prevent allergy symptoms, significantly reduced the signs both of rhinitis and conjunctivitis [10].

CONCLUSIONS

In conclusion, in this particular case we have demonstrated a direct relationship between exposure to papain and an allergic response from the nasal mucosa and conjunctiva. The well documented cellular changes and increased eosinophilia in the nasal and tear fluids after the SNCT have correlated with clinical symptoms. This objective evaluation of allergic disorders is particularly important when we have to distinguish occupational from work-aggravated diseases with symptoms due to irritant workplace hazards.

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