Porcine pancreatic extracts (PPE), which are widely used as a digestive drug in Korea, are composed of $\alpha$-amylase and lipase. Such enzymes are commonly described as occupational allergens. This is the first report of occupational rhinitis caused by PPE developing into occupational asthma in a hospital nurse. She showed strong positive response in the skin prick test (SPT) (5+, wheal ratio of allergen to histamine) and had a high serum-specific IgE level to PPE, but showed a negative response in the methacholine bronchial challenge test (MBT). She had been exposed to PPE intermittently with intermittent medications for rhinitis. Two years later, she presented with rhinitis and additional asthmatic symptoms. In contrast to her first visit, she showed a positive response in the MBT, and developed bronchoconstriction in the PPE-bronchial provocation test (BPT). These findings suggest that inhalation of PPE powder can induce IgE-mediated occupational rhinitis in a hospital setting, which will develop into occupational asthma if avoidance is not complete.

**Key Words:** Pancreatic Extracts; Occupational Rhinitis; Occupational Asthma, Specific IgE

### INTRODUCTION

Porcine pancreatic extracts (PPE), composed of $\alpha$-amylase and lipase, are widely used as a digestive drug in this country; however, they can induce IgE-mediated occupational rhinitis or asthma in bakery workers or those involved in the pharmaceutical industry (1-3). Although it is widely accepted that allergic rhinitis may precede asthma, few studies have reported about occupational rhinitis developing into occupational asthma (4). This is the first case of occupational rhinitis progressing into occupational asthma during a 2-yr follow-up period with chronic exposure to digestive enzymes.

### CASE REPORT

A 31-yr-old female who had dispensed digestive drugs to admitted patients during 6 yr of employment as a university hospital nurse presented to allergy clinic 2 yr ago and complained of rhinorrhea and sneezing, but no asthmatic symptoms, when handling PPE powders. The patient was non-atopic and had no history of medical illness or family history of allergic disease. To evaluate her IgE responses, a skin prick test (SPT) was performed, and strongly positive responses were generated to PPE and $\alpha$-amylase (5+ and 3+ wheal ratios of allergen to histamine, respectively). PPE and other medicinal extracts collected from her workplace were prepared according to the previously described method (5) and used to detect serum-specific IgE by enzyme-linked immunosorbent assay (ELISA). The positive cutoff value for a high level of serum-specific IgE antibody was defined as the mean $\pm$ 3 SD (standard deviations) of the absorbance value from unexposed healthy controls. The patient showed high levels of specific IgE to PPE and $\alpha$-amylase by ELISA (1041 and 1003 absorbance values, respectively). To confirm bronchial sensitization, a methacholine bronchial challenge test (MBT) and a specific bronchial provocation test (BPT) were performed with PPE, and both generated negative responses (Table 1). The patient was thus diagnosed with occupational rhinitis to PPE. Antihistamine and a topical steroid were recommended to control her rhinitis symptoms, and she continued working in the same environment. Two years later, she revisited our allergy clinic complaining of rhinitis and additional asthmatic symptoms. A second SPT showed increased responses to PPE and $\alpha$-amylase (6+ and 6+ wheal ratios of allergen to histamine, respectively), and her serum-specific IgE level was found to be highly elevated by ELISA (720 and 718 absorbance values, respectively). A second MBT demonstrated positive responses at 1.36 mg/mL, and the BPT showed an early asthmatic response after inhalation of PPE.

---

**Seung Youp Shin, Gyu Young Hur*, Young Min Ye*, and Hae Sim Park**

Department of Otolaryngology, Kyung Hee University College of Medicine, Seoul; Department of Allergy and Rheumatology*, Ajou University School of Medicine, Suwon, Korea

Received: 13 April 2007
Accepted: 6 August 2007

Address for correspondence
Hae-Sim Park, M.D.
Department of Allergy and Rheumatology, Ajou University School of Medicine, San-5 Wonchon-dong, Yeongtong-gu, Suwon 442-749, Korea
Tel: +82-31-219-5150, Fax: +82-31-219-5154
E-mail: hspark@ajou.ac.kr

*This study was supported by the Korea Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A055071).
to porcine pancreatic extract. Allergen and histamine (1 mg/mL); PPE-BPT, bronchial provocation test; SPT, skin prick test; A/H, the ratio of the size of the wheal caused by the allergen and histamine (1 mg/mL); PPE-BPT, bronchial provocation test to porcine pancreatic extract.

(Table 1); both tests were performed as previously described (5). Negative responses were recorded for the other drug powders tested.

| Visit       | SPT (A/H) | Specific IgE by ELISA absorbance value (410 nm) | PCE | PPE-β-amylase | PPE-α-amylase | MBT | PPE-BPT |
|-------------|-----------|-----------------------------------------------|-----|---------------|---------------|-----|---------|
| Initial visit | 5+       | 3+                                             | 1.041 | 1.003         | >25            | None | None    |
| 2 yr later   | 6+       | 6+                                             | 720  | 718           | 1.36           | Early |         |

SPT, skin prick test; A/H, the ratio of the size of the wheal caused by the allergen and histamine (1 mg/mL); PPE-BPT, bronchial provocation test to porcine pancreatic extract.

DISCUSSION

This case demonstrates that PPE powder inhalation can induce occupational rhinitis, and furthermore develop into occupational asthma when the causative allergen is not avoided in an exposed nurse working in a hospital. It is commonly accepted that allergic rhinitis precedes the development of asthma, although reports on allergic rhinitis turning into asthma are few, especially in a hospital nurse by drug powder. The patient had been diagnosed as having occupational rhinitis, due to the work-related rhinitis symptoms, strongly positive responses in the SPT, and high serum-specific IgE levels to PPE and α-amylase, but not in the MBT and specific BPT. After 2 yr, she developed occupational asthma, showing the additional symptoms of lower respiratory tract and a positive response on the MBT and specific BPT.

PPE are composed of α-amylase and lipase, which are common components of digestive enzymes. Enzyme allergy has been recognized since the late 1960s (6, 7). It may cause asthma, rhino-conjunctivitis, allergic contact dermatitis, and contact urticaria (8). A community-based study recently reported that enzymes could be a specific occupational risk (9). There have been some reports of occupational asthma induced by these enzymes inhaled during the course of work, predominantly among pharmaceutical industry workers (10-13). In our preceding reports, we detected occupational allergy to these enzymes inhaled during the course of work, predominantly among pharmaceutical industry workers (10-13). In our preceding study, it had been demonstrated that PPE and α-amylase had extensive cross-allergenicity by PPE and α-amylase ELISA inhibition test, and shared one strong IgE binding component by IgE immunoblot study. However, lipase showed minimal inhibition for both PPE and α-amylase ELISA inhibition tests, and a lesser degree of inhibition on lipase ELISA inhibition test (5).

In conclusion, it is important to carefully examine, treat, and follow patients with occupational allergic rhinitis, and remove them early enough from allergen exposure, in order to prevent the disease progressing to asthma.

REFERENCES

1. Losada E, Hinojosa M, Quince S, Sánchez-Cano M, Moneo I. Occupational asthma caused by alpha-amylase inhalation: clinical and immunologic findings and bronchial response patterns. J Allergy Clin Immunol 1992; 89: 118-25.
2. Zeitner A, Jepp S, Wahl R, Kunkel G, Kiethe-Tebbe J. Multiple IgE-mediated sensitizations to enzymes after occupational exposure: evaluation by skin prick tests, RAST, and immunoblot. Allergy 1997; 52: 928-34.
3. Brisman J, Belin L. Clinical and immunological responses to occupational exposure to alpha-amylase in the baking industry. Br J Ind Med 1991; 48: 604-8.
4. Piirila P, Elistander T, Hytonen M, Keskinen H, Tupaesla O, Tuppurainen M. Rhinitis caused by ninhydrin develops into occupational asthma. Eur Respir J 1997; 10: 1918-21.
5. Park HS, Kim HY, Sih YJ, Lee SJ, Lee SK, Kim SS, Nahm DH. Alpha amylase is a major allergenic component in occupational asthma patients caused by porcine pancreatic extract. J Asthma 2002; 39: 511-6.
6. Pepys J, Longbottom JL, Hargreave FE, Faux J. Allergic reactions of the lungs to enzymes of Bacillus subtilis. Lancet 1969; 1: 1181-4.
7. Flindt ML. Pulmonary disease due to inhalation of derivatives of Bacillus subtilis containing proteolytic enzyme. Lancet 1969; 1: 1177-81.
8. Laraqui C, Harouart K, Belanamale I, Benhaymond N, Verger C. Occupational respiratory risks in workers exposed to enzymes in detergents. Rev Mal Respir 1996; 13: 485-92.
9. Zock JP, Cavaile N, Kromhout H, Kennedy SM, Suyner J, Jaen A, Muniozguren N, Payo F, Almar E, Sanchez JL, Anto JM, Kogevinas M. Evaluation of specific occupational asthma risks in a community-based study with special reference to single and multiple exposures. J Expo Anal Environ Epidemiol 2004; 14: 397-403.
10. Dolan TF Jr, Meyers A. Bronchial asthma and allergic rhinitis associated with inhalation of pancreatic extracts. Am Rev Respir Dis 1974; 110: 812-3.
11. Cartier A, Malo JL, Pineau L, Dolovich J. Occupational asthma due to pepsin. J Allergy Clin Immunol 1984; 73: 574-7.
12. Aiken TC, Ward R, Peel ET, Hendrick DJ. Occupational asthma due
13. Park HS, Nahm DH. New occupational allergen in a pharmaceutical industry: serratial peptidase and lysozyme chloride. Ann Allergy Asthma Immunol 1997; 78: 225-9.

14. Bahn JW, Lee JY, Jang SH, Kim SH, Kim HM, Park HS. Sensitization to Empynase® (pronase B) in exposed hospital personnel and identification of the Empynase® allergen. Clin Exp Allergy 2006; 36: 352-8.

15. Petrick MM, Salvin RG. Occupational rhinitis. Immunol Allergy Clin North Am 2003; 23: 193-203.