

Propylthiouracil-induced asthma

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Key words: asthma; hyperthyroidism; propylthiouracil.

Propylthiouracil (PTU) is widely used in the treatment of hyperthyroidism. Many side-effects of the drug have been reported, such as transient granulocytopenia, hepatitis and vasculitis. These adverse effects of the drug are of critical importance in the clinical management of patients. Recognition of possible side-effects and delineation of their pathogenesis are of considerable value. In this report, we present a hyperthyroid patient, who developed asthmatic attacks with PTU treatment.

A 43-year-old Vietnamese woman complained of insomnia, fatigue, poor appetite, heat intolerance, hand tremors and losing weight (12 lbs) over the last 4 months. She had no history of allergy to drugs or food. She denied neither smoking nor drinking alcohol. Her past medical history was unremarkable, except for two C-sections. On physical exam, she was found to have a diffuse enlargement of the thyroid gland. The laboratory data revealed as follows: leucocytes, $7.1 \times 10^3/\text{mm}^3$ (normal: 5–10); triiodothyronine uptake (T_3 -uptake), 41% (normal: 22–37); thyroxine by the radioimmunoassay (T_4 RIA), 19.9 mcg/dl (normal: 5–15); free thyroxine index (FTI), 8.2 (normal: 1.5–4); triiodothyronine by the radioimmunoassay (T_3 RIA), 409 ng/dl (normal: 86–187); thyroid-stimulating hormone (TSH), <0.1 mIU/ml

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(normal: 0.2–5); thyroglobulin (Tg), 28 ng/ml (normal: 0–60); anti-microsomal autoantibodies (AMA), <0.1 U/ml (normal: <0.3); anti-thyroglobulin autoantibodies (ATA), <0.1 U/ml (normal: <0.3). The ultrasonography of thyroid gland revealed a homogenous thyromegaly (right lobe, $5.7 \times 1.6 \times 2.5$ cm and left lobe, $5.2 \times 1.7 \times 2$ cm) and no focal nodule. She was treated with PTU 100 mg, twice a day.

Two months later, she experienced the episodic wheezing and dyspnoea. Her thyroid function tests were as follows: T_3 U of 44.9%, T_4 RIA of 10.9 mcg/dl, T_3 RIA of 240 ng/dl, FTI of 4.9, and TSH of 0.02 mIU/ml. Her leucocytes decreased to $4.3 \times 10^3/\text{mm}^3$. The pulmonary function tests showed an airflow obstruction with forced vital capacity (FVC) of 0.95 l (38.8% predicted) and forced expiratory volume in 1 s (FEV_1) of 0.9 l (43.4% predicted), and there was a partial reversal of the airway obstruction following the administration of inhaled β_2 agonist medication, FVC of 1.4 l (57.1% predicted) and FEV_1 of 1.32 l (63.5% predicted). Her chest X-ray was unremarkable. She was started on oral theophylline, prednisone and inhaled β_2 agonist medications. Her asthma attacks, however, improved since she was rendered in a euthyroid state and discontinued taking PTU. Her thyroid function tests were as follows: T_4 RIA of 7 mcg/dl, T_3 U of 32%, FTI of 2.2, T_3 RIA of 98 ng/dl, TSH of 1 mIU/ml, AMA of <0.1 U/ml, ATA of <0.1 U/ml, and Tg of 11 ng/ml.

The development of asthmatic attacks in our hyperthyroid patient might suggest a relationship between these two diseases. Our previous paper (1) has addressed these problems. Nakazama and Kobayashi (2) found no apparent uniform influence on the severity of asthma in patients with both diseases. Moreover, asthmatic attacks occurred after our patient received PTU treatment which might suggest that PTU might have a role in causing asthma. PTU selectively

accumulates in neutrophils (3) and binds to myeloperoxidase; the result is a change in the haem structure of the enzyme (4). D'Cruz et al. (5) suggested that PTU could alter myeloperoxidase by oxidation in a minority of susceptible persons. The altered enzymes, possibly still complexed with the drug, could stimulate other neutrophils to degranulate and lead to the release of lytic enzymes and toxic species of oxygen. Many side-effects of the drug have been reported in particular pulmonary cavitation, interstitial pneumonitis, eosinophilic pleuritis, alveolar haemorrhagic, and adult respiratory distress-like syndrome (6). Hypersensitivity vasculitis associated with PTU is a well-documented clinical entity. The disease improved after the discontinuation of PTU therapy or the administration of glucocorticoids (or both), as was found in our patient.

In conclusion, the complex occurrence of PTU-induced asthma is rare but possible. These symptoms may be a hypersensitivity phenomenon.

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Accepted for publication 2 September 2003
Allergy 2004; 59:889–890
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References

1. LUONG VQK, NGUYEN THL. Hyperthyroidism and asthma. *J Asthma* 2000;**37**:125–130.
2. NAKAZAWA T, KOBAYASHI S. Influence of thyroidal therapy on asthma symptoms in the patients with both bronchial asthma and hyperthyroidism. *J Asthma* 1991;**28**:109–116.
3. LAM DCC, LINDSAY RH. Accumulation of 2-[^{14}C]-propylthiouracil in human polymorphonuclear leukocytes. *Biochem Pharmacol* 1979;**28**:2289–2296.

4. LEE E, HIROUCHI M, HOSOKAWA M, SAYO H, KOHNO M, KARIYA K et al. Inactivation of pyeloperoxidase by propylthiouracil. *Biochem Pharmacol* 1990;**39**:1467–1471.
5. D'CRUZ D, CHESSER AMS, LIGHTOWLER C, COMER M, HURST MJ, BAKER LR et al. Antineutrophil cytoplasmic antibody-positive crescentic glomerulonephritis associated with anti-thyroid drug treatment. *Br J Rheumatol* 1995;**34**:1090–1091.
6. NGUYEN THL, LUONG VQK, PHAM VB. An antineutrophil cytoplasmic autoantibody associated with a propylthiouracil-induced adult respiratory distress-like syndrome: report of a case and review of the literature. *Endocr Pract* 1998;**4**:89–93.

Adverse reaction to dextromethorphan

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Key words: adverse reaction; dextromethorphan; opiates.

Dextromethorphan is a nonrespiratory depressant opiate derivative used alone or in combination with other compounds as symptomatic treatment of cough and its efficacy is similar to that of codeine (1).

A 24-year-old woman presented at our outpatient clinic for a sensation of bolus in the throat with swallowing difficulty, erythema and hives with audible whistling immediately after the first dose of Romilar® (dextromethorphan hydrobromide), which was resolved after treatment with corticosteroids and antihistaminic agents. She had taken Algidol® (paracetamol and codeine) half an hour before the onset of the symptoms. She had previously tolerated Romilar, paracetamol and codeine without any problems.

An allergy study by prick test with Romilar (dextromethorphan) was positive. A skin prick test (SPT) with Romilar

was also performed in 10 controls, being positive in three of them.

The SPT with paracetamol and codeine was negative. Oral challenge with paracetamol and codeine was well tolerated. Oral challenge was also performed with another opioid agonist, tramadol, which was well tolerated.

After challenge with dextromethorphan (0.5 ml of the Romilar syrup solution), the patient immediately developed four hive lesions on her back that was resolved after antihistaminic treatment.

Given that the results of the challenge test were doubtful because it was not possible to disguise the taste of the preparation and as the adverse reaction was not severe and the patient requested this drug to control her symptoms, we decided to repeat the challenge test.

In the first place, a placebo having identical taste as Romilar was administered and was well tolerated. Then dextromethorphan was administered and after 0.5 ml of the solution, the patient developed generalized erythema with generalized pruritus and decreased blood pressure. Prompt treatment with adrenaline, steroids and antihistamines relieved the symptoms.

Dextromethorphan is used as an antitussive drug with the same efficacy as codeine but with less subjective or gastrointestinal abnormalities. Unlike other opiates, it has no analgesic power. Its toxicity is low and adverse reactions are rare, the most common being those that affect the central nervous system or psychiatric disorders; rash or urticaria type manifestations and anaphylaxis are totally rare (1).

We have not found any reports of allergic reaction to dextromethorphan with positive skin test. There is one case of anaphylaxis (2) due to dextromethorphan in which no skin test was performed and one case of fixed drug eruption with positive oral challenge but with negative epicutaneous test (3).

Opiate derivatives are nonspecific histamine releasers and induce nonallergic drug hypersensitivity (4).

In our case, it is interesting that the patient has tolerated codeine and tramadol, also nonspecific histamine releasers. Because of this, as well as the positivity of the prick and the rareness of reactions of

this type in spite of the wide use of the drug, a mechanism of IgE-mediated drug allergy cannot be ruled out (4).

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Accepted for publication 18 November 2003
Allergy 2004; 59:890

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References

1. BENN J, PECK R. Dextromethorphan: an overview of safety issues. *Drug Safety* 1992;**7**:190–199.
2. KNOWLES S, WEBER E. Dextromethorphan anaphylaxis. *J Allergy Clin Immunol* 1998;**102**:316–317.
3. SAKARI S, SAKARI R. Fixed-drug eruption due to dextromethorphan. *Arch Dermatol* 1990;**126**:970–971.
4. JOHANSSON SGO, HOURIHANE JO, BOUSQUET J, BRUIJZEEL-KOOMEN C, DREBORG S, HAAHTELA T et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy* 2001;**56**:813–824.

Exposure to methyl methacrylate and hypersensitivity pneumonitis in dental technicians

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Key words: dental technician; hypersensitivity pneumonitis; methyl methacrylate.

We report two cases of dental technicians with a diagnosis of hypersensitivity pneumonitis because of inhalation of methyl methacrylate (MMA), occur-

These observations demonstrate the risk of the development of not only pneumoconiosis or asthma, but also an hypersensitivity pneumonitis to MMA.