Coexistence of allergic bronchopulmonary aspergillosis and atopic dermatitis: Is total IgE level useful to identify relapses of allergic bronchopulmonary aspergillosis?

To the Editor,

Allergic bronchopulmonary aspergillosis is a hypersensitivity reaction to *Aspergillus fumigatus* colonisation of the tracheobronchial tree. Atopic dermatitis is a chronic skin disease presenting with relapses and characterised by a disturbance of the epidermal barrier function, which culminates in dry skin, as well as by IgE mediated sensitisation to environmental allergens. ABPA and AD are rare conditions in which an increment in total IgE is a hallmark. So far, no case reporting the coexistence of AD and ABPA has been reported. Herein, we report a case of AD coexistence with ABPA in which a conflict occurred about the role of total serum IgE in the follow-up of treatment for ABPA.

A 49-year-old woman who had suffered from AD for 20 years and asthma for four years was admitted to our outpatient clinic because of uncontrolled asthma. The patient had applied to the emergency room for asthma several times in the last year despite regular use of inhaled beclomethasone/formoterol 200/12 mcg/day and montelukast 10 mg/day. She needed topical steroids and emollients for AD, occasionally with a favourable response.

Physical examination of the chest revealed decreased breathing sounds and diffuse expiratory rhonchi in the bilateral lung zones. On her skin, eczematization, lichenification and xerosis were noticed mainly on the neck and volar surfaces of the forearms. The patient was examined by a dermatologist. The diagnosis of atopic dermatitis was confirmed according to the criteria of Hanifin and Rajka (5). Contact dermatitis and polymorphic light eruption were excluded by the dermatologist. Laboratory evaluation revealed a white blood cell count of 6800/mm³ (eosinophil 13.2%) and a total immunoglobulin (IgE) level of 2527 kU/L. Serum specific IgE against *Aspergillus fumigatus* was 1.6 kU/L (<0.35 kU/L normal range) (Pharmacia, Uppsala, Sweden). Skin-prick tests with *Aspergillus fumigatus* antigen showed a positive reaction for type I hypersensitivity (Histamine: 7×7 mm, aspergillus mix: 3×3 mm) (Allergopharma, Reinbek, Germany). Intradermal tests with *Aspergillus fumigatus* antigen showed a positive reaction (histamine 7×7, aspergillus mix: 15×15). Spirometry showed airway obstruction (FEV1: 69%, FEV1/FVC: 67) with significant bronchodilator reversibility (360 ml [% change 20%]). High Resolution Computed Tomography (HRCT) demonstrated ground glass and nodular infiltrations in different segmental areas. Regarding the differential diagnosis of increased total IgE levels, the patient had asthma and allergic rhinitis. However allergic rhinitis and asthma might not include diseases presenting very high total IgE levels. Parasitic infections which are associated with high elevated total IgE levels were also excluded by documentation of negative stool examination for three occasions. She also had no clinical evidence of other diseases which cause elevated total IgE levels such as gastroenteritis, hyper IgE syndrome, lympho-reticular malignancies, netherton syndrome, HIV infection. CSS syndrome was ruled out due to absence of CSS prodromal period, absence of both extra pulmonary symptoms such as peripheral neuropathy, and a progressive lack of eosinophilia. Based on the clinical and laboratory findings, the patient was diagnosed as ABPA. Oral methylprednisolone (0.5 mg/kg/day) and itraconazole (200 mg/day) were introduced. Two weeks later, the daily doses of methylprednisolone were switched to alternate days for an additional eight weeks. The dose of methylprednisolone was tapered down over the following eight months until a dose of 4 mg/day was reached. The patient was maintained on methylprednisolone for a total of 14 months. Antifungal therapy was continued for 12 months. Clinical improvement was evident with a significant reduction in respiratory symptoms accompanied by a reduction in total IgE (145 kU/L), blood eosinophil count and an improvement in spirometry (Table 1). Recovery was also noticeable on the HRCT taken 14 months after diagnosis. Four months after discontinuation of methylprednisolone, the patient had no asthma symptoms. However, her total IgE level had risen to 1440 kU/L (Table 1). On skin exam-

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**Table 1**

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>After 14 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total IgE (kU/L)</td>
<td>2527</td>
<td>1440</td>
</tr>
<tr>
<td>Blood eosinophil %</td>
<td>13.2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

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*We assure the Editorial Board that this work as seen and approved by all co-authors has not been published previously and is not currently under consideration for publication elsewhere. The authors declare they have no conflict of interest.*
Table 1  Evaluation of total serum immunoglobulin (Ig) E, *A. fumigatus* specific IgE, blood eosinophil count, lung function and HRCT before and after treatment.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>At the end of treatment (14 months)</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, %</td>
<td>101</td>
<td>122</td>
<td>117</td>
</tr>
<tr>
<td>FEV₁, %</td>
<td>69</td>
<td>117</td>
<td>112</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>67</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>Serum IgE, kU/L</td>
<td>2527</td>
<td>145</td>
<td>1440</td>
</tr>
<tr>
<td>Eosinophils, %</td>
<td>13.2</td>
<td>6.4</td>
<td>10</td>
</tr>
<tr>
<td><em>A. fumigatus</em> IgE, kU/L</td>
<td>1.6</td>
<td>–</td>
<td>0.39</td>
</tr>
<tr>
<td>HRCT</td>
<td>Ground glass infiltration and nodular infiltration</td>
<td>No pathological findings</td>
<td>No pathological findings</td>
</tr>
</tbody>
</table>

FVC: forced vital capacity; FEV: forced expiratory volume in 1 s; HRCT: high resolution computed tomography; *A. fumigatus: Aspergillus fumigatus.*

ethic disclosures

Patients’ data protection. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

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Cold-induced urticaria with systemic reactions after hymenoptera sting lasting for 10 years

To the Editor,

A 20-year-old man was referred to our allergy and immunology department with the complaints of intense pruritus, generalised erythema and oedema on the trunk, face and extremities after exposure to cold. He had experienced the same symptoms on cold rainy days. The patient reported that all his cold-related complaints had begun 10 years ago shortly after a common wasp sting on his head, which was limited to mild local reaction. Two years after the wasp sting, he experienced a mild anaphylactic reaction (chest tightness, nausea, dizziness, abdominal pain) while standing in a cold river for fishing. Although the patient was able to prevent himself from cold exposure in his civil life, he was unable to avoid cold during his military service and he experienced systemic reaction with chest tightness, nausea, dizziness, abdominal pain while waiting outside for muster on a cold day. The patient was evaluated by cold contact stimulation test (CST) with an ice cube in a plastic bag (3, 5 and 8 min). The test was positive only at 8 min. Other physical urticaria forms were not observed. Laboratory evaluation included complete blood count, erythrocyte sedimentation rate, C-reactive protein, anti-nuclear antibody, rheumatoid factor, antistreptolysin-O, cold agglutinins, cryoglobulins, complement C4, syphilis, hepatitis B and C and HIV serologies, thyroid hormones, thyroid stimulating hormone, and anti-thyroid peroxidase. All laboratory tests were within normal limits. Bee venom-specific IgE were found class II positive for Apis Mellifera (1.32 kUA/L), and Vespula Spp (1.08 kUA/L).

He was instructed to avoid cold exposure and medical therapy with a second generation antihistamine, desloratadine, was prescribed. After 1 week of antihistamine treatment, his tolerance to cold increased considerably and CST at 8 min was found negative.

Acquired cold urticaria (ACU) induced symptoms are generally restricted to cold-exposed skin areas, however more severe clinical manifestations can be observed in case of extensive cold exposure. Those symptoms may range from generalised urticarial symptoms to systemic reactions affecting respiratory, gastrointestinal or cardiovascular system. ACU is idiopathic in most cases. Insect bite, jellyfish sting, bee and wasp sting and venom immunotherapy are reported as trigger factors for ACU. Although the sensitisation to hymenoptera venom is common, ACU following hymenoptera sting is rarely reported. Although the prevalence of atopic disorders in patients with ACU was reported similar to the general population high rates of atopy in these patients have also been reported.

The pathogenesis of ACU is still unknown. Histamine is released after cold challenge in ACU patients. Increased levels of IgE and functional anti IgE antibodies (IgG and IgM) have been demonstrated in patients with ACU. These may act as a functional autoimmune and histamine-releasing factors described in some patients with chronic idiopathic urticaria.

ACU generally tends to have a chronic course and the mean duration of symptoms ranges between 4.8 and 9.3 years. However, Kalegeromitos et al. have reported four cases of Hymenoptera sting induced ACU. The severity of the symptoms decreased in time and all cases had complete remission in less than one year. However, our case had systemic reaction even after 10 years from Hymenoptera sting. It seems that ACU after Hymenoptera sting may last for several years. These patients must be informed that their disease may not disappear in the short term.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Confidentiality data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Conflict of interest

The authors have no conflicts of interest to declare.

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