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CASE STUDY

Acute allergic reaction and demonstration of specific IgE antibodies against α-1-protease inhibitor

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Acute allergic reaction and demonstration of specific IgE antibodies against α-1-protease inhibitor. F.J. Meyer, M. Wencker, H. Teschler, H. Steveling, J. Sennekamp, U. Costabel, N. Konietzko. ©ERS Journals Ltd 1998.

ABSTRACT: A 44 yr-old female with severe pulmonary emphysema and reduced α-1-protease inhibitor (α_1-PI) serum levels developed an acute anaphylactic reaction following the third intravenous infusion of human α_1-PI which was administered to prevent the progression of pulmonary emphysema. Specific immunoglobulin E-antibodies against human α_1-PI could be demonstrated in the patient's serum using an enzyme allergosorbent test. Because of the risk of further severe anaphylactic reaction, the replacement therapy with α_1-PI was discontinued. Physicians should be aware of this rare complication.

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Alpha-1-protease inhibitor (α_1-PI) deficiency is a hereditary metabolic defect, associated with liver and lung disease [1]. The pathogenesis of pulmonary emphysema in adults with the homozygote form (PiZZ) is thought to be due to an imbalance between antiproteases and proteases. Although the benefit of different chronic replacement modalities with human α_1-PI concentrate in the prevention of emphysema remains to be determined, it is anticipated that this therapy will prevent progression of the lung disease [2–5]. In previous studies, toxicity of the treatment proved to be very low. In the following, a rare complication of an acute allergic reaction during α_1-PI infusion is reported. The symptoms were comparable to the classic description of an acute anaphylactic reaction [6]. Specific immunoglobulin (IgE) antibodies against human α_1-PI could be demonstrated for the first time.

Case report

A 44 yr-old female, an exsmoker since the age of 9 yrs, with severe bilateral pulmonary emphysema was found to have reduced α_1-PI serum levels (39 mg·dL^{-1}; normal 170–330 mg·dL^{-1}). Isoelectric focusing of the serum in agarose disclosed a homozygous α_1-PI deficiency of the phenotype PiZZ. She received the first and second *i.v.* α_1-PI replacement (4 g Prolastin-HS; Bayer, Leverkusen, Germany) without any side-effects. The third infusion was administered 2 weeks later, again allowing >60 min for the application. It caused an acute anaphylactic reaction including nausea, dyspnoea with mild wheezing, systemic hypotension, bradycardia and near unconsciousness. There was no skin rash or oedema. Adequate therapy was started and resulted in complete recovery within a few hours.

Prior to the *i.v.* administration of α_1-PI, laboratory tests showed normal serum concentrations for IgA, IgG, IgM and IgE. Human immunodeficiency virus (HIV) serology was negative and the sedimentation rate, complete blood count, clotting, liver and kidney parameters were normal. There was no history of atopy or allergic reaction. The patient had had no previous administration of blood products.

After the severe adverse reaction laboratory tests revealed an elevated total IgE to 390 U·L^{-1} (four times normal). Specific IgE antibodies against Prolastin-HS were found in the serum of the patient using an enzyme Allergosorbent test (EAST™, Sanofi Diagnostics Pasteur, Chaska, MN, USA) with two different lots of α_1-PI from Bayer (production series) as the antigen. This test uses an enzyme-labelled antiserum to human IgE to replace the ^{125}I-labelled antiserum used in earlier allergoabsorbent tests [7, 8].

A prick skin test with α_1-PI (Prolastin-HS, concentration for infusion: 1 g in 40 mL distilled water) showed no immediate or late skin reaction. An intracutaneous skin test with the same solution in a 1:1,000 dilution was negative, but 1:100 (weal 4 mm, flare 8 mm) and 1:10 dilutions (weal 5 mm, flare 9 mm) were positive.

Because of the risk of further severe anaphylactic reaction, the replacement therapy with α_1-PI was discontinued in this patient.

Discussion

This is the first report of an allergic reaction and the demonstration of specific IgE antibodies following *i.v.* replacement therapy with α_1-PI. Since 1989, 444 emphysematous patients with severe α_1-PI deficiency (PiZZ) and clinically relevant pulmonary emphysema have been substituted under the author's supervision [9]. So far, no serious side-effects

have been encountered [3]. This is consistent with most reports, where no acute reactions to α_1-PI infusion occurred. Others have described adverse reactions, including hypoxaemia/cyanosis, hypotension, chest or back pain, haematoma-like spots, weight loss, transient leukocytosis, eosinophilia, fever, light-headedness, vertigo/dizziness, headaches and fatigue. The side-effects were self-limited, and none required hospitalization or alteration of the treatment [10–14]. In a series of animal studies using rabbits, monkeys, mice and rats, neither acute nor subacute toxicity studies presented any significant adverse effects [15].

In a previously reported adverse reaction caused by α_1-PI, high molecular weight polysaccharides associated with sucrose stabilization were implicated as the causative agent in the suspected lot, but no specific antibody or allergic mechanism was identified [14].

In the present patient, the specific IgE antibodies were not related to a single lot. Serum from the patient was tested for specific antibodies against α_1-PI using two different lots from Bayer (production series) as a source of antigen in the enzyme allergosorbent test and found that the serum reacted with both lots.

This demonstration of IgE antibodies against α_1-PI depends on the use of commercial Prolastin, which might include other blood proteins. The demonstration of antibodies against recombinant α_1-PI would have been more definite. Alternatively, antigenic epitopes could be missing from the recombinant material.

In conclusion, an adverse reaction due to an immunoglobulin E-mediated allergic mechanism may occur during repeated replacement therapy with intravenous α-1-protease inhibitor. Replacement therapy is increasingly being used in diseases other than α-1-protease inhibitor deficiency, *e.g*. cystic fibrosis [16, 17]. The caring physician should be aware of this rare complication.

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