

advisable for young patients with PCD, especially when combined with physical therapy (4).

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C4 deficiency in chronic angioedema

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Key words: angioedema; C4 deficiency.

● HEREDITARY angioedema (HAE) is an autosomal dominant disorder caused by decreased level, or functional deficiency, of the C1 inhibitor protein.

We describe a patient with diminished levels of the C4 and C2 complement components, with episodes of chronic angioedema, and showing a genetic deficiency of C4 protein. The patient was a 46-year-old woman with a 2-year history of episodic angioedema. The parts of the body involved were the eyelids, cheeks, tongue, and upper airway. She also suffered from abdominal attacks with cramp-like pains and vomiting. Skin swellings were very frequent (two or three per month) without apparent cause. There was neither pregnancy nor estrogen administration during these 2 years. The laboratory results were as follows: C4 3.8 mg % (normal range 15–47); C2 <4 mg % (4–24); C3 80 mg % (100–185). All these values had been reproduced at several time points. C1 inhibitor levels and function, C1q, C4bp, AP50, and CH50 were in the normal range, as was IgG, IgM, and IgA. Antinuclear antibodies, rheumatoid factor, cryoglobulins, HB_sAg, Anti-HB_e, Anti-HCV, and immunocomplexes were negative. The complement profile in her family showed normal values in her mother and brother, while C4 was low in her other two brothers and in her three children (9.6–13.4), one of whom had had several episodes of angioedema during puberty. C3 was slightly diminished in her sister

A case of partial genetic deficiency.

and two of her children (82–92). C1 inhibitor, C2, and the functional activity of C1 inhibitor were normal in all her family members. Data from the patient's father were not available because he was dead. The patient was treated with tranexamic acid 500 mg/h, and remained almost asymptomatic.

Our patient had a clinical disorder with characteristics of HAE, including a low C4 and a good response to tranexamic acid. However, the normal levels and function of C1 inhibitor ruled out this disease. A partial genetic deficiency of C4 was observed in several members of her family. In addition, the patient had a low level of C2, and a slight reduction in C3. The latter was also found in some members of her family. These facts suggest an associated deficiency in C4 and C2, which could be explained by the close location of both genes at chromosome 6. The reduction in C3, however, cannot be ascribed to the same reason, because it is placed at chromosome 19. Although a reduction in levels of these complement proteins might be due to activation of the classic pathway, we did not find any evidence of such a process. The patient had neither clinical symptoms nor analytic markers of diseases, such as dermatomyositis and vasculitis, associated with C4 or C2 deficiency.

Recently, HAE with normal C1 inhibitor and its activity has been described in women (1). For this disorder, the authors proposed the term "hereditary angioedema type 3". The presence of diminished C4, and the absence of symptoms depending on high estrogen levels (pregnancy, oral contraceptives, and hormone replacement therapy) exclude such a disease. Llatser & Guillaumet (2) have described a family with C4 and C2 deficiency, and two brothers affected by angioedema.

In conclusion, the association of a clinical process which resembles HAE with a decrease in C4 level is not always caused by a deficiency or dysfunction of the C1 inhibitor component.

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We report the case of a 46-year-old nonsmoker woman with a history of rhinitis and asthma due to grass pollen.

She had kept two hares as house pets for 2 years. Approximately 1 year after acquiring the hares, she presented with nasal and ocular itching, tearing, nasal stuffiness, and persistent asthma attacks. She was treated with inhaled budesonide (1600 µg/day) and formoterol (18 µg/day), but optimal control of asthma was not achieved. When she was examined in our clinic, physical examination, spirometry, and chest radiographs were all normal.

Skin prick tests (SPT) with a battery of common inhalant allergens were positive to grass and olive pollen. After being defatted, dialyzed, and lyophilized, an extract of hare epithelium was prepared in phosphate-buffered saline at 10 mg/ml (protein concentration 3 mg/ml). SPT to this hare extract and rabbit epithelium 5% w/v (C.B.F. Leti, Madrid, Spain) elicited positive skin responses (8- and 6-mm wheals, respectively). SPT to a battery of animal dander and/or urine extracts (C.B.F. Leti) from dog, cat, horse, cow, goat, guinea

pig, hamster, rat, and mouse were all negative. Total serum IgE (Pharmacia, Uppsala, Sweden) was 260 kU/l. Specific IgE antibodies determined by ELISA against hare (0.304 OD) and rabbit epithelia (0.478 OD) were positive, as compared to control sera from five atopic subjects allergic to mites (0.100 OD). Specific IgE (Pharmacia CAP System) measurements were positive against rabbit epithelium (9.42 kU/l) and negative against guinea pig, mouse, rat, and hamster. In the CAP-inhibition assays, IgE reactivity to rabbit epithelium (solid phase) was completely inhibited by hare extract, indicating cross-reactivity between these epithelia. Skin prick and serologic tests to hare epithelium were negative in five atopic and five nonatopic control subjects.

The methacholine inhalation test revealed bronchial hyperresponsiveness (PC₂₀ 0.125 mg/ml). Specific bronchial challenge to hare epithelium extract (0.04 mg/ml) was carried out by the tidal breathing method, and it elicited an isolated early asthmatic response (32% fall in FEV₁ 10 min after challenge). The patient showed a progressive improvement after removal of the hares from the house.

Allergic asthma to pet hares

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Key words: allergic asthma; animal allergens; hare.

• ALTHOUGH rabbits are popular domestic pets, there are few reports on asthma due to this animal (1, 2). The hare (*Lepus europaeus*) is another member of the Leporidae family and, to the best of our knowledge, allergy caused by this mammal has not been previously described.

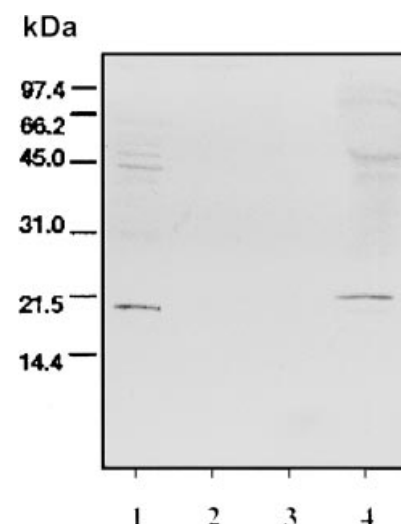


Figure 1. IgE immunoblots of hare (1), dog (2), cat (3), and rabbit (4) epithelium separated by SDS-PAGE under reducing conditions.