

Is House Dust Allergen a Possible Causal Factor for Relapses in Lipoid Nephrosis?

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In three cases of minimal change nephrotic syndrome (lipoid nephrosis), an allergen sensitivity to house dust, cat hair and grass pollen was demonstrated by clinical and biological data. An increase in proteinuria after specific allergen contact and a decrease after withdrawal of the allergens, suggested that the cause was allergenic. Such cases demonstrate the necessity of an etiological investigation of particularly the atopic features in lipoid nephrosis. Results of these investigations can lead to specific therapy in selected cases.

Key words: allergy; house dust; nephrotic syndrome; pollen.

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More than 20 years ago, Fontana et al. (1) suggested a possible role for allergy in minimal change nephrotic syndrome, i.e. lipoid nephrosis (LN) (2, 3). In the most typical published cases, the allergens implicated are either seasonally inhaled allergens such as grass pollen (4, 5, 6, 7, 8) or rare allergens such as bakery dust (9), molds (8) or, in more recent publications, daily ingested food allergens, such as cow milk (10) or eggs (11).

Other common allergens have been mentioned in several published cases but their responsibility cannot be assessed with certainty (1, 6). A systematic investigation of the role of allergy in LN, has shown the apparent association of common allergens, such as house dust (12).

The aim of this study was to evaluate the role of house dust in LN. As this allergy is often undetected because its manifestations are not seasonal we made a systematic search for a house dust sensitisation in our LN patients.

METHODS AND MATERIAL

LN was diagnosed by conventional investigations. Renal biopsies were studied with light microscopy and immunofluorescence for IgG, IgM, IgA, C3 and fibrinogen. Antisera were obtained from Behring Diagnostics.

Symptoms of atopic disease were recorded by means of a detailed questionnaire. Intradermal skin tests for immediate hypersensitivity using inhalant allergen extracts were performed by the usual methods (Pasteur Institute and Stallergen Lab.). The respective concentrations of each allergen were: house dust (1/50,000), *Dermatophagoides pteronyssinus* (DP) (1/10⁴), feathers (1/5,000), dog and cat hair (1/10⁴), molds (1/10³) and grass pollen (1/10⁴). The test was positive when the papula diameter was >8 mm (estimated + to +++). Serum IgE concentration was measured by the radio-immunosorbent test (RIST; Phadebas test - Pharmacia Laboratory). The upper normal limit (geo-

metric mean + 2SD) was 460 IU/ml in our controls. Radioallergosorbent test (RAST) assays were performed for house dust, DP, dog and cat hairs, molds and grass pollen (Pharmacia kits). Positive results were estimated semi-quantitatively as + to +++. Human basophil degranulation tests (HBDT) were performed with the same inhalant allergens (normal < 40%) (13). Nasal or bronchial allergen challenge was used to confirm allergenic association in respiratory symptoms.

To assess the role of house dust in glomerular disease, proteinuria in sensitised LN patients was measured before and after each i.d. and s.c. injection: proteinuria was quantified in milligram/minute (mg/min (3 h sample) or g/day (24 h sample)).

From among 40 LN patients, diagnosed according to histological criteria (12), three patients were selected, because of their house dust sensitivity.

RESULTS

These three cases are individually described. Clinical data are summarized in Table 1.

Case No. 1

A young woman, 30 years old, presented in October 1978 with generalized oedema, massive proteinuria (11 g/day) and a pure nephrotic syndrome: serum albumin was 2.0 g/100 ml, serum cholesterol 345 mg/100 ml, serum creatinine 0.6 mg/100 ml, and blood pressure 90/60. Chest film normal. During hospitalization, proteinuria fell to a stable level of 3–4 g/day. A percutaneous renal biopsy light microscopically showed a normal aspect in all the glomeruli, with negative immunofluorescence leading to the diagnosis of LN (2, 3). Anamnesis revealed rhinitis and asthma, which had appeared at the age of 4–5 years. In 1979, the forced expiratory volume in 1 sec (FEV₁) was 1.74 l (-23%) and bronchial challenge with acetylcholine (120 µg) was positive. Intradermal reactions were +++ for house dust and ++ for dog hair, while candida, grass pollen and molds were negative. Total serum IgE concentration was 200 IU/ml. Specific IgE antibody levels were +++ for *Dermatophagoides pteronyssinus* and + for house dust. HBDT was positive for house dust (71%), DP (85%) and dog hair (100%).

Bronchial challenge was positive for 100 µg DP with a decrease in FEV₁ (-33%). Considerable proteinuria variations occurred after injections of DP or house dust as shown in Fig. 1: proteinuria decreased from 2 to 0.45 mg/min after intradermal skin test and increased from 0.4 to 2.1 mg/min after challenge by s.c. injection of mite (DP) extract. Finally, it increased again from 0 to 4.5 mg/min after challenge by s.c. of a DP house dust extract. Challenge by normal saline caused no significant change in proteinuria (Fig. 1). Disodium cromoglycate therapy and house dust hyposensitization were performed. Proteinuria disappeared after a few weeks, and after 18 months of this treatment the attacks of asthma were clearly less frequent and milder and proteinuria still absent.

Case No. 2

A young man, 17 years old, developed a pure nephrotic syndrome in 1971, with a serum albumin of 1.0 g/100 ml, oedema and pleural effusions. Renal biopsy showed normal glomeruli in light microscopy, and immunofluorescence was negative for IgG, IgM, IgA, C3 and fibrinogen, leading to a diagnosis of LN. Proteinuria disappeared 3 weeks after treatment with prednisone 1.5 mg/kg/day, but because of corticoid dependence treatment was continued for 15 months at a lower dose. After 6 years of complete remission, urinary protein was again detected during a routine control in October 1979 (the last negative result had been observed 6 months before). In November 1979, proteinuria reached 4 g/day. Anamnesis revealed an intermittent and obstructive rhinitis with bilateral conjunctivitis, appearing only after contact with cats. Skin tests were strongly positive (++++) for house dust and for cat hair. Serum IgE concentration was 290 IU/ml. Specific serum IgE was positive for house dust and strongly positive for cat epithelium. HBDT was positive for cat hair (75%) and house dust (76%). Nasal allergen challenges gave positive results for cat hair (75 µg) but were negative for house dust. Proteinuria decreased during hospitalization and increased three fold after skin testing. The effect of these allergen challenges on proteinuria is shown in Fig. 2. After contact with a cat, proteinuria rapidly rose to 4.5 g/d and decreased to 0.4 g/d after withdrawal of the allergenic contact. In March 1980, proteinuria increased up to 30 g/day (no previous contact with cats) and corticotherapy was given. Proteinuria disappeared within a few days. During treatment, however, nasal challenge with house dust led to a temporary proteinuria of 0.20 mg/min lasting a few hours.

Table 1.
Clinical and biological data of the three patients

	Case No. 1	Case No. 2	Case No. 3
Age at onset (years)	30	17	22
Sex	F	M	M
Number of relapses	0	2	2
Diagnosis	lipoid nephrosis	lipoid nephrosis	lipoid nephrosis
Renal biopsy	light microscopy, normal immunohistology, negative	light microscopy, normal immunohistology, negative	light microscopy, normal immunohistology, negative
Proteinuria before treatment	11 g/24 h	10 g/24 h	15 g/24 h
Serum albumin	2.0 g/100 ml	1.0 g/100 ml	1.2 g/100 ml
Atopic manifestations	asthma and rhinitis	seasonal rhinitis and conjunctivitis	seasonal rhinitis
Skin test sensitivity	house dust +++	house dust +++ cat hair +++	grass pollen +++ house dust ++
Serum IgE concentration (RIST)	200 IU/ml	290 IU/ml	1 100 IU/ml
Specific IgE concentration (RAST)	+++ <i>D. pteronyssinus</i> + house dust	+ house dust +++ cat hair	+++ dactylis +++ meadow + house dust
Human basophil degranulation test	71 % for house dust 85 % for <i>D. pteronyssinus</i>	75 % for cat hair 76 % for house dust	not done
Significant variations in proteinuria after allergenic injections	3 positive challenges for house dust and <i>D. pteronyssinus</i> (Fig. 1)	3 positive challenges for house dust and 2 for cat hair (Fig. 2)	1 positive challenge for grass pollen and 1 for house dust
Result and treatment	complete remission: hyposensitization + cromoglycate	complete remission: prednisone + disodium cromoglycate	complete remission: prednisone + disodium cromoglycate

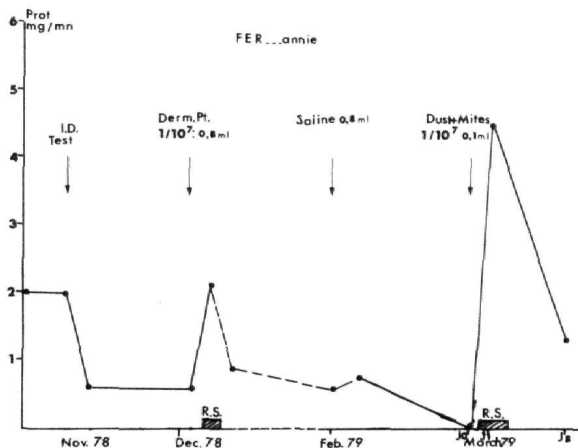


Fig. 1. Case 1. Evolution of proteinuria (mg/min) over a 4 month period in relation to allergen injections. RS = respiratory symptoms.

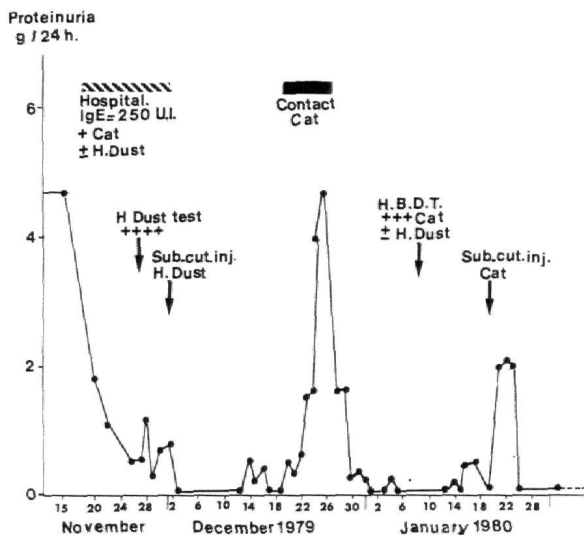


Fig. 2. Case 2. Evolution of proteinuria (g/24 h) over a 3 month period in relation to allergen injections and allergenic contact.

Case No. 3

A young man was affected by hay fever characterized by coryza and conjunctivitis, and by bouts of LN (confirmed by renal biopsy) in May 1969 and June 1973 which responded to corticotherapy. Pollen sensitivity was suggested by the following data: rapid disappearance of proteinuria and coryza when hospitalized in a room with filtered air, in June 1973; onset of a transitory proteinuria after an intradermal test with pollen extracts; recurrence of coryza and strong proteinuria when he returned home in July 1973.

Proteinuria rapidly cleared after conventional steroid treatment, which was stopped in November 1973. In January 1974, after a 6-month proteinuria-free period, an intradermal test was made with house dust extract (Pasteur Institute at 1/5,000) in the course of an investigation for autumnal rhinitis. The test was strongly positive (++++) and was accompanied by a bout of coryza. The following day proteinuria was 2 g/day and rapidly increased to 7 g/24 h. Two weeks later, corticotherapy was initiated (60 mg/day) leading to a rapid disappearance of the proteinuria, which has not reappeared.

DISCUSSION

These dramatic fluctuations in proteinuria following contact with allergens or following their

withdrawal, e.g. the decrease in proteinuria during the first day of hospitalization, strongly suggest that house dust and cat hair, as well as pollen, may be responsible for LN relapses. In contrast to grass pollen these allergens have not yet been reported as possible causal factors in LN (4, 6, 7).

The frequency of sensitivity to such allergens in LN is probably underestimated and could be further defined by systematic investigations of allergy (14). Observed cases in our department, in the last few months, show that these allergens might play a pathogenic role, not only in LN, but also in other glomerular diseases (15). Recently, we were able to demonstrate sensitivity to a specific inhalant allergen (16) in six of 23 N patients, examined for atopic symptoms.

The mechanism by which an allergen penetrating the respiratory or digestive tract provokes proteinuria remains unknown; that it is immunological is not yet certain, but likely (6, 17).

The allergens act mainly by an IgE dependent mechanism. In LN, IgE levels are significantly increased in serum (18, 19, 20), but IgE is not present in the kidney (21, 22).

When an allergen comes in contact with the respiratory or digestive tract, various vasoactive mediators could be released by mast cells and also by macrophages which bear IgE Fc receptors (23, 24). The mediators possibly enter the general circulation and lead to an increase in glomerular permeability. Enzymes, particularly collagenase, can also increase capillary permeability in experimental models (25). Alternatively, the allergens could enter the general circulation, especially if mucosal permeability is increased, and trigger sensitized basophils, inducing the release of vasoactive mediators directly into the general circulation.

The allergen could also encounter specific IgG and form circulating immune complexes. Depending on their size, these complexes could bind C1q, leading to complement activation and the formation of substances increasing capillary permeability (C5a). In addition, anaphylatoxins could act directly by contributing to mast cell and basophil degranulation. This hypothesis is supported by the following arguments: the presence of circulating IgG immune complexes (17, 26); a transitory decrease of C3 after provocation tests (10) and an elevation of C3d during bouts, without a decrease in C3 and C4 (27); the occasional observation of delayed skin responses to various allergens.

Finally, the role of lymphocytes remains to be discussed. After stimulation by a non-specific mitogen, these cells elaborate a vascular permeability factor (28). This may also occur in some cases following contact with specific allergens (29). This factor is known to modify the sialoproteins of glomerular capillary walls *in vitro*, thus furnishing a possible explanation for the onset of proteinuria (30).

The true mechanisms may in fact be multiple, combined in varying proportion and differing from one case to another.

CONCLUSIONS

In three cases of lipid nephrosis, allergen sensitization to house dust, cat hair and/or grass pollen allergens was demonstrated by clinical and biological data. The increase in proteinuria after specific allergenic contacts and the de-

crease after withdrawal suggests that these allergens may be causal factors. The mechanism remains unknown.

Such cases demonstrate the necessity of searching for atopic features in LN. These investigations could result in specific therapy, which may be of value in selected cases.

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