

## Local nasal desensitization provoking systemic illness with proteinuria

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### Summary

We report a case of allergic rhinitis with systemic illness and proteinuria, which was repeatedly provoked by nasal exposure to allergen. Local nasal desensitization resulted in remission of both rhinitis and systemic illness. The disease was associated with systemic complement fixation via the classical pathway.

### Introduction

Cases of nephrotic syndrome temporally associated with attacks of hay fever have been described (Reeves *et al.*, 1975; Thomson *et al.*, 1975). It is tempting to infer a causal relationship, particularly as the illness in some of these cases responded to hyposensitization injections, but causality cannot be considered proven until it has been shown that artificial allergen challenge provokes the disease. Deliberate induction of nephrotic syndrome in man is not acceptable on ethical grounds.

Local nasal desensitization is a method of treating allergic rhinitis in which the offending allergen is sprayed in aqueous solution into the nose (Taylor & Shivalkar, 1972). The dose is adjusted to produce mild rhinitis at the beginning of the course. Ten to twelve doses are given over a period of 4-6 weeks, during which time challenge-induced symptoms usually decrease. Clinical improvement follows in about three-quarters or more of patients (Taylor & Shivalkar, 1972; Mehta & Morrison-Smith, 1975).

We report here an example of local nasal desensitization, the primary purpose of which was to cure disease, but during the course of which allergen-provocation of proteinuria was observed.

### Case report

This young man of 13 had suffered from perennial nasal blockage with rhinorrhoea since the age of 12. Symptoms were associated when severe with fever, malaise and frontal headaches. He had a strong positive immediate skin test to house dust, and a course of hyposensitization injections with this allergen produced some improvement. A second course, however, made his symptoms much worse. He was then referred to

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us, aged by this time 16. He no longer had rhinorrhoea, but suffered severe attacks of nasal obstruction often with nosebleeds, and still had the systemic symptoms. He had never suffered much from sneezing.

The symptoms suggested 'late' responsiveness (Taylor, 1975), confirmed by the virtual absence of any immediate response to house dust, either by skin test or direct nasal challenge. He developed a late response to challenge, maximal 8 hr later, with severe nasal obstruction followed over the next few days by nosebleeds.

He was given a course of local nasal desensitization with 1.5% house dust extract (Bencard Solution for Challenge diluted 100-fold in saline). Blood was taken before, during and after the course for complement studies. A symptom chart was kept and early-morning urine was examined for protein using Labstix (Ames). Daily protein estimations were instituted only after the mid-course of his out-patient attendance.

**Table 1.** Complement studies before, during and after local nasal desensitization. Normal limits for this laboratory are shown in brackets

| Day                                 | CH <sub>50</sub><br>(45-80<br>units/ml) | C <sub>3</sub><br>(100-200<br>mg/100 ml) | I.K. titre<br>(up to 1/2) | C <sub>1q</sub><br>(80-120%) | C <sub>4</sub><br>(60-170%) | GBG<br>(60-170%) |
|-------------------------------------|-----------------------------------------|------------------------------------------|---------------------------|------------------------------|-----------------------------|------------------|
| 0<br>(before treatment)             | 38.5                                    | 130                                      | Neg. at 1/2               | N.D.                         | N.D.                        | N.D.             |
| 15<br>(2 days after fifth<br>dose)  | 39.4                                    | 90                                       | Neg. at 1/2               | 66                           | 58                          | 71               |
| 36<br>(11 days after<br>ninth dose) | 45.5                                    | 150                                      | Pos. at 1/8               | 100                          | 100                         | 100              |
| 367<br>(1 year later)               | 43.9                                    | 115                                      | Pos. at 1/2               | 84                           | 87                          | 94               |

N.D. = not done

Altogether nine doses of spray were taken, at intervals varying from 2 to 4 days.

The first four doses were followed after 5-8 hr by the typical symptoms, nasal blockage and malaise, lasting from 6 hr to 3 days. The fifth dose produced no symptoms but the sixth was followed by 3 days of nasal blockage, malaise and headache, with 30 mg/100 ml proteinuria; the urine having been free of protein before treatment. The seventh caused no trouble but the eighth was followed (though not until 2 days later) by some malaise, and 30 mg/100 ml of proteinuria. The ninth dose was given just as these manifestations were making him feel distinctly unwell and was followed by a very severe attack of nasal blockage, headache and sore throat, with malaise and lethargy sufficient to keep him off school all week, and 8 days proteinuria of up to 100 mg/100 ml. Treatment was stopped, but the illness took another 2 weeks to resolve completely.

Total haemolytic complement levels (CH<sub>50</sub>) were low before and during his treatment and normal at his post-course attendance, at which time (9 days after the height of illness) immunoconglutinin titration, previously negative was positive 1 in 8. C<sub>3</sub>, C<sub>1q</sub> and C<sub>4</sub> levels were reduced during therapy, while the level of glycine-rich-β-

glycoprotein (GBG) was normal. This indicates *in vivo* complement activation via the classical pathway, without significant involvement of the alternative pathway.

Now 1 year later, his rhinitis is greatly improved, and is no longer associated with systemic illness or epistaxis. There is no proteinuria and complement studies are essentially normal.

### Discussion

Association of two phenomena in time does not prove that one causes the other, but the fact that six out of the nine doses of allergen were so precisely followed 5–8 hr later by typical symptoms and signs leads us to attribute this illness to allergen-exposure. Reeves *et al.* (1975), in their description of pollen-associated-nephrosis, noted the presence of C<sub>1q</sub>-precipitable immune complexes in the circulation of two of their patients, and postulated that *in vivo* complement fixation might play a part in pathogenesis. This suggestion is supported by the finding, in this patient, of evidence of classical-pathway complement activation during treatment.

This case highlights the two-edged nature of our therapeutic weapons. One course of injections gave some improvement, while a second produced deterioration. We would speculate that the 'immediate' reactivity (rhinorrhoea) benefited from the injections, but the 'late' symptoms (nasal blockage, sinusitis and possibly the systemic illness) were aggravated. Reports of this kind are not uncommon and we do not now use injection therapy where there is a large 'late' component in the symptomatology.

Local desensitization was also two-edged for this patient. Therapy was proceeding according to plan until he used his spray when he was already suffering symptoms, possibly provoked by natural exposure to allergen, and this was followed by unusually severe illness. This suggests that local nasal desensitization should not be attempted while severe symptoms are already present, and the symptoms following one dose should be allowed to subside before the next is given.

This patient himself alerted us to the possibility of systemic immune-complex disease by stressing the malaise, lethargy and fever that accompanied his rhinitis. Few patients routinely take their temperatures, and doctors tend to underestimate the relevance of the lassitude and malaise that so frequently accompany allergic rhinitis. With this case in mind, one wonders if systemic disease of this kind is commoner and more important than hitherto thought, particularly where 'late' reactivity is prominent.

### References

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