FORMATION OF ALLERGIC REACTIVITY TO WORMWOOD POLLEN IN COMBINED SENSITIZATION TO POLLEN AND BACTERIA

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The principles governing the formation of hypersensitivity of immediate type to wormwood (Artemisia absinthium L.) under conditions of combined (at intervals of 3, 12, and 28 days) sensitization with cells of a vaccine strain of Brucella abortus 19-BA, were studied. The degree of specific allergic reaction to pollen 2, 6, and 12 weeks after the beginning of the experiment was studied by Ovary's passive cutaneous anaphylaxis test, by the indirect degranulation of mast cells of healthy rats, and the general anaphylaxis reaction to intravenous injection of a saline extract of wormwood pollen. In animals with combined sensitization to pollen and brucellas allergy to pollen was formed sooner. The degree of allergic reactivity to the pollen allergen at all times of the investigation was greater in animals with combined allergy than in animals with sensitization purely to pollen. KEY WORDS: sensitization; wormwood pollen; brucellas; combined forms of allergy.

In patients with allergoses hypersensitivity is frequently observed to several heterologous antigens. This form of sensitization is known as combined [2]. Polysensitization is frequently found in bronchial asthma and it often leads to a severe course of the disease [7, 8]. Hypersensitivity to bacteria and pollen simultaneously is often found in patients with allergic rhonosinusopathies [3, 4]. Consequently the important problem arises of the principles governing the development of hypersensitivity to different allergens in combined forms of sensitization. The present writer has found that simultaneous sensitization to microbial antigens and pollen did not lead to any marked interaction [5, 6], whereas in initial sensitization by microbial antigens hypersensitivity to pollen was stimulated. The object of the present investigation was to study the character of the immunoallergic response to pollen antigen in animals sensitized initially with wormwood (Artemisia absinthium L.) pollen and later with Brucella abortus strain 19-BA.

EXPERIMENTAL METHOD

Experiments were carried out on 60 guinea pigs (46 experimental, Ovary's passive cutaneous anaphylaxis test was carried out on 14). The experimental animals were divided into four groups. Group 1 consisted of ten animals sensitized three times on alternate days with wormwood pollen: twice in a dose of 0.5 ml of a 5% solution of pollen in Freund's complete adjuvant subcutaneously, and once with 0.5 ml of a 3% saline extract of the same pollen intraperitoneally (control); Group 2 consisted of 12 guinea pigs sensitized with wormwood pollen (by the same scheme as Group 1) and three days later with brucellas (a single subcutaneous injection of a suspension of 2 billion cells of the vaccine strain Brucella abortus 19-BA; Group 3 – 12 animals sensitized with wormwood pollen, and two weeks with brucellas; Group 4 – 12 animals sensitized with wormwood pollen and four weeks with brucellas.

The animals were tested 2, 6, and 12 weeks after the beginning of the experiment in order to determine hypersensitivity of immediate type to pollen antigen. A 3% saline extract of wormwood pollen, prepared by the method of Cock and Milford [1], was used as the antigen. Circulating homocytotropic antibodies against pollen were determined by Ovary's passive cutaneous anaphylaxis test (PCAT) [9], and the reaction of generalized anaphylaxis to intravenous injection of 0.5 ml of a 3% saline extract of wormwood pollen also was studied. The

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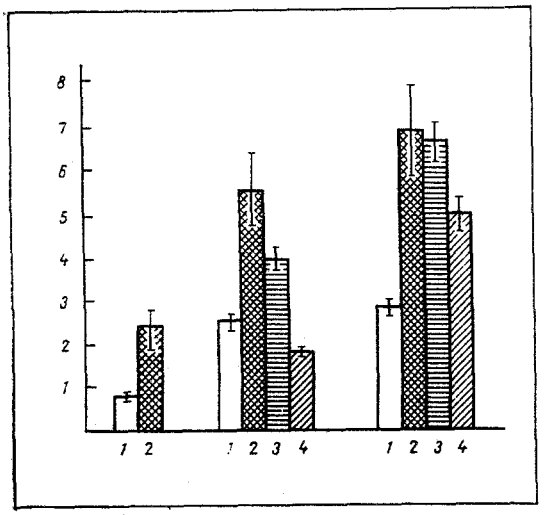

Fig. 1

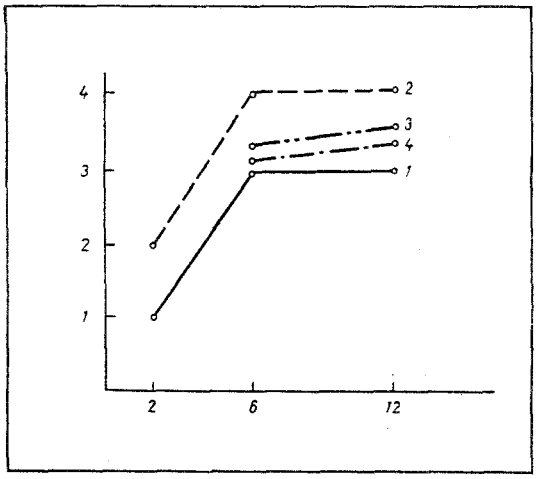

Fig. 2

Fig. 1. Ovary's PCAT in animals with combined sensitization to wormwood pollen and brucellas. Abscissa: 1) wormwood pollen, 2) pollen, brucellas three days later, 3) pollen, brucellas two weeks later, 4) pollen, brucellas four weeks later; ordinate, mean area of stained spot (in cm^2).

Fig. 2. Generalized anaphylaxis reaction in guinea pigs with combined sensitization to wormwood pollen and brucellas. 1) Pollen; 2) pollen, brucellas three days later; 3) pollen, brucellas two weeks later; 4) pollen, brucellas four weeks later. Abscissa, times of testing (in weeks); ordinate, index of anaphylactic shock.

clinical picture of anaphylactic shock was assessed by means of the index of Weigle et al. [11]. The animals' sera were investigated by the indirect mast cell degranulation test [10] on intact rats.

EXPERIMENTAL RESULTS

The degree of specific allergy response to pollen antigen was determined two weeks after sensitization with pollen in the animals of Groups 1 and 2 by means of the PCAT (Fig. 1). In the control animals the area of staining of the spots was small – 0.84 ± 0.09 cm^2 – but in the experimental guinea pigs of Group 2 it was three times larger, namely 2.57 ± 1.01 cm^2. These results indicated that additional sensitization by the microbial allergen stimulated the initial sensitization to the heterologous allergen. In the animals of group 3 and 4, two weeks after injection of pollen no tests were carried out, for they were sensitized to brucellas at that time and later (four weeks). Investigation of the sera of the animals of all four groups six weeks after the beginning of the experiment showed that in guinea pigs with combined sensitization the production of specific antibodies against pollen was at a higher level than in the control. The effect of the microbial allergy as a stimulator of heteroallergy was particularly marked in the animals of group 2, i.e., when the interval between sensitization with pollen and brucellas was shortest.

In the guinea pigs of Group 3 the PCAT to pollen allergen after six weeks was weaker (4.01 ± 0.5 cm^2) than in the animals of group 2 (5.74 ± 0.6 cm^2), but significantly higher than in the control animals (2.68 ± 0.30 cm^2; $P < 0.05$). In the guinea pigs of group 4 no stimulating effect of brucellas was observed on induction of hypersensitivity to pollen; on the contrary, a tendency was actually observed for the initial allergen to be inhibited. Investigation of the sera of animals of the same group later (12 weeks after the beginning of the experiment) revealed a considerable increase in the size of the stained spot (5.2 ± 0.8 cm^2) compared with their size in the control guinea pigs (2.83 ± 0.4 cm^2). The phenomenon of inhibition was clearly temporary. At the same time, in the animals of the other two groups (2 and 3) with combined sensitization, increased production of circulating homocytotropic antibodies determined by Ovary's test was observed. As Fig. 1 shows, in these animals the skin reaction was more marked than in the animals of Group 4, but the difference was not statistically significant. It is interesting to note that in the guinea pigs of all groups the mean area of the same spot at the second time of testing was larger than at the first time ($P < 0.001$). This indicates that the induction of hypersensitivity to pollen in the combined form of allergy, just as in purely pollen allergy, increases until the 40th-84th day.

At all times of investigation the formation of allergies to pollen was studied in the animals of all four groups by means of the general anaphylaxis reaction (Fig. 2). Four or five animals were taken from each group for investigation. The indices of anaphylactic shock in the guinea pigs of Group 2 were higher than in the remaining animals. The indices of the anaphylactic reaction in the guinea pigs of the control group were lower at all times than in animals with combined allergy. These results confirm those of the PCAT and were evidence that in combined forms of allergy to wormwood pollen and brucellas, allergic reactivity to the pollen allergen is stimulated. The results of the mast cell degranulation test, carried out after six weeks with wormwood pollen antigen, indicated stronger allergy in animals with combined sensitization: Group 2) 28.7 ± 2.6%, Group 3) 26.7 ± 4.0%, Group 4) 34.0 ± 2.6%, control) 22.3 ± 2.8%.

The formation of allergic reactivity to pollen allergen in combined forms of sensitization to pollen and microorganisms thus follows a different course from that in pure pollen allergy. In animals sensitized with pollen, additional (3, 12, and 28 days later) sensitization with brucellas led to increased formation of specific allergic reactivity to pollen allergen. Brucellas, like Mycobacterium tuberculosis and certain other microorganisms, under certain conditions and, in particular, when they are introduced into the body together with other allergens, can probably act as adjuvants. This phenomenon of the stimulating action of microbial allergy on initial hypersensitivity of immediate type to a heterologous allergen requires clinical study with the aim of preventing combined forms of hypersensitivity.

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