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Role of Some Infectious Agents in Atopic Dermatitis

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Certain infections such as Kaposi's herpetic eruption, impetigo, recurrent cutaneous herpes simplex and warts are more frequent in subjects with atopic dermatitis. It is likely that the continuous alterations of the skin are more important than immunological factors in increasing the frequency of some infections in subjects with atopic dermatitis. Moreover, these infections do not seem to affect significantly the clinical course of atopic dermatitis. *Key words: Atopic dermatitis; Infections.*

This lecture attempts to answer the following questions: (*a*) Are certain infections more frequent in subjects with atopic dermatitis? (AD) (*b*) If they are, is it because these subjects have a complex immunological disorder or simply because the affected skin cannot defend itself against infectious agents? (*c*) Do these infections affect the clinical course of atopic dermatitis?

First we will refer to the most typical infection that affects children with atopic dermatitis—Kaposi's herpetic eruption. It is not an uncommon infection if we consider the fact that we have observed 20 cases of the disease (1) in the last 2 years. It is caused by herpes simplex, type 1 or 2, and also the virus coxsackie A16 can mimic perfectly the eruption caused by a herpetic virus. Of 20 cases recently observed, 19 arose on preexisting AD and one on preexisting congenital erythrodermic ichthyosis. This fact suggests that Kaposi's herpetic eruption affects subjects with AD more often, because these subjects are carriers of a complex immunological imbalance at the center of which there is probably a T-lymphocyte deficiency.

When we studied the first cases of this disease from an immunological point of view we often found a T-lymphocyte deficiency. This explains why immunostimulating drugs have been used in the treatment of this disease. When we examined the immunological mechanism of this disease in greater depth, and above all when we repeated immunological tests at various stages of the illness, we saw that the problem was not as simple as had appeared at first sight.

Eight out of twenty cases showed an initial deficiency of T-lymphocytes and an increased T-helper/T-suppressor ratio in the early stage of herpetic eruption. Seven out of these eight cases, when tested at the resolution stage of the disease, showed normal levels of T-lymphocytes. A 6-year-old boy, affected by HyperIgE syndrome, was the only case of persistent T-lymphocyte deficiency. From a clinical point of view, the child presented a severe herpetic eruption complicated by a deep keratitis which caused blindness of the right eye. Furthermore, it was established that this child had a recurrence of herpetic eruption 2 years later.

In three out of twenty cases a T-lymphocyte deficiency was observed only during the resolution phase of the infection. Finally, in nine out of twenty cases it was not possible to detect any T-lymphocyte deficiency. On the other hand, increased levels of total IgE were demonstrated in all cases during the first days of the infection, whereas IgE levels decreased in all cases after 15 days, during the resolution phase of the infection. The behaviour of IgE does not seem to be linked to T-lymphocyte deficiency; IgE behaviour is consistent and predictable, whereas T-lymphocyte deficiency varies considerably. Nor

does there appear to be a clear link between the seriousness of the infection and the severity of AD: we observed mild cases of AD complicated by severe herpetic eruption.

The fact that in most cases herpetic eruption affects subjects with AD does not mean that the eruption affects them because they are immunocompromised. It probably affects them because AD is the most frequent facial dermatitis in the first 2 years of life, the period that generally coincides with the first contact with the herpes virus: the infection is generally transmitted by a kiss from a parent affected by recurrent labial herpes simplex. On the other hand, herpetic eruption can, though this is rare, complicate other dermatoses, such as erythrodermic ichthyosis, that are not associated with T-lymphocyte deficiency.

We treated six cases of this serious infection with acyclovir: even starting the therapy on the day that the specific lesions first appeared, new vesicles continued to appear for 2 to 3 days as did the constitutional symptoms. Eczema vaccinatum, a disease we have not seen for many years, is another severe complication of AD. A 17-year-old girl had AD since the first months of life with slight but uncommonly (5) located lesions (on the scalp and groin). At the age of three she developed severe generalized vaccinia eruption which endangered her life. She still bears multiple scars left by this episode. The patient, who has notable T-lymphocyte deficiency and reduced levels of IgM (9 mg/100 ml), suffers from recurrent bronchitis, suppurative middle ear infection, multiple intestinal parasitoses, chronic rhinitis and bronchial asthma. She is also affected by multiple warts which arose 10 years ago and recurrent labial herpes simplex which gives rise to deep atrophic scarring.

We also tried to discover whether the commonest infections of childhood are more frequent in atopic children. In order to answer this question, we carried out an epidemiological survey on 2514 children in nursery schools in Bari: the incidence of AD in this control population was 2.6% and the incidence of asthma/rhinitis was 8.5%. Furthermore, we examined the incidence of AD and asthma/rhinitis subjects in our patients suffering from the commonest infections of childhood, such as bullous impetigo, recurrent cutaneous herpes simplex and warts (Table I). Subjects with AD showed an increased susceptibility to these cutaneous infections, especially bullous impetigo, whereas the percentage of subjects with asthma/rhinitis was similar to that encountered in normal controls. On the other hand, when we examined the incidence of AD and asthma/rhinitis in a group of 352 children with very frequent respiratory infections (more than 5 every year) we found that subjects with asthma/rhinitis were more susceptible to these infections, whereas the percentage of subjects with AD was similar to that encountered in normal controls.

The conclusions to be drawn from our results confirm that certain infections are more frequent in AD subjects. The increased frequency of cutaneous infections does not seem to be linked in most cases to T-lymphocyte deficiency; it is likely that the persistent

Table I. *Incidence of the commonest infections in atopic children*

		Atopic dermatitis		Asthma/rhinitis	
	No. of cases	No. of cases	%	No. of cases	%
Bullous impetigo	306	42	13.7	23	7.5
Recurrent cutaneous *H. simplex*	144	12	8.3	11	7.6
Warts	209	9	4.3	18	9.1
Controls[a]	2 514	66	2.6	212	8.4

[a] 2514 children attending nursery schools in Bari.

alteration of the affected skin plays a more important role. The same is also true of the persistent alteration of the respiratory apparatus, leading to the increased susceptibility to respiratory infections in subjects with asthma/rhinitis.

In order to answer the third question, whether or not infections affect the clinical course of AD, we will refer to the commonest infection of AD subjects, impetigo, usually caused by staphylococcal or mixed infection. Even though itching causes continuous excoriation of the skin in all cases, impetigo occurs in roughly 10% (3) of our AD subjects, more frequently in cases with pompholyx-like lesions located on the feet or in cases with congested or exudating lesions: the latter generally occur on the face in the first year of life. In these cases a tendency to relapse can be frequently observed. If the infectious cause of this complication is not recognized, the clinical conditions of these children worsen significantly. Regional adenitis is quite frequent where as abscesses of the lymph nodes are seldomen countered.

It is likely that in certain cases persistent staphylococcal infections may aggravate the clinical course of AD, especially in the first years of life. Staphylococcal infection may exacerbate AD directly through an increased inflammation of the skin. Specific IgE antibodies (2, 4) against staphylococcus may also worsen the inflammation through an allergic reaction. On the other hand, in most cases it is unlikely that infections play a fundamental role in the clinical course of AD.

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