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Inverse association between positive tuberculin tests and positive allergy skin tests in children

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Abstract

Background The association between *Mycobacterium tuberculosis* infection and atopy remains controversial. Reaction to tuberculosis infection is mediated by Th-1 immune responses whereas allergic reactions are mediated by Th-2 immune response. In patients with atopic syndrome who also suffer from tuberculosis infection, the Th-2 response will be suppressed and allergy manifestations will decrease. Therefore, it is important to determine the appropriate allergy test and to predict outcome after completing tuberculosis treatment.

Objective To evaluate the influence of a positive tuberculin test on skin test results in diagnosing atopic disease.

Methods A cross sectional study was conducted in the pediatric allergy outpatient clinic, Soetomo Hospital, Surabaya, Indonesia between 2004 and 2007. Eighty-five patients were enrolled in this study. The tuberculin test was performed on all patients with allergy. The allergy test was carried out by performing a skin scratch test.

Results There was a weak inverse correlation between positive tuberculin tests and positive allergy skin tests in children (house dust mite, food and pet allergies). The correlation between a positive tuberculin test and house dust mite allergy test was r: -0.364 (P=0.001; α=0.01). The correlation between the tuberculin test and food allergies was r: -0.420 (P=0.001; α=0.01). The correlation between the tuberculin test and pet allergies was r: -0.344 (P= 0.001; α=0.01).

Conclusions A positive tuberculin test is weakly correlated with positive allergy skin test results, suggesting that it is appropriate to do allergy skin testing even in children with a positive tuberculin test. **[Paediatr Indones. 2009;49:7-10]**.

Keywords*: allergy, skin test, tuberculin test, inversed association*

The prevalence of allergic disorders has been increasing over the last 30 years.[1] Epidemiological studies have yielded conflicting results for the association between *M. tuberculosis* infection and atopic disease in children. Shirakawa *et al*[2] reported an inverse association between tuberculin responses and atopic disorders in Japanese children suggesting that BCG immunization, subclinical exposure to *M. tuberculosis* without clinical disease, or host characteristics may influence the lymphocyte balance with decreased atopy as a result.

Sarinho *et al*[3] found smaller BCG scars in asthmatics than in non-asthmatics four-year-old Brazilian children who were given the BCG vaccine when they were newborns. Von Mutius[4] reported an inverse relationship between national tuberculosis rates (World Health Organization) and the prevalence of asthmatic symptoms in subjects from Europe, USA, Canada, Australia and New Zealand.[4,5] Alm and Strannegaerd have shown that neither BCG vaccination nor atypical mycobacterial infections are correlated with atopy.[6]

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We hypothesized that a positive tuberculin test is inversely associated with positive allergy tests (house dust mite, food, and pet allergies) in children. The objective was to determine the effect of a positive tuberculin test on skin test results in the diagnosis of atopic disease.

Methods

This cross-sectional study was conducted between 2004 and 2007 at Soetomo Hospital, Surabaya, Indonesia. There were 85 children enrolled in this study. To be included, atopic children had to show clinical evidence and history of allergic diseases. We excluded exclusion subjects with known immune compromising disease (malnutrition; immunosuppression by disease or drugs; viral infections such as measles, mumps, varicella, and influenza, or administration of live-virus vaccines), active tuberculosis, and refusal to participate. Informed consent was given by all parents.

Skin scratch tests to common allergens (house dust mite, cats and dogs, eggs and shrimps) were performed on the forearm of each subject after collection of questionnaire data. Histamine (10 mg/ml) was used as the positive control and normal saline as the negative control. A skin test result was considered positive if the wheal was larger than or equal to the wheal of the positive control after 15 minutes.

The tuberculin test was performed by injecting 0.1 ml PPD RT 23 2TU intradermally by an experienced person who was not informed of the children's atopic status. The transverse diameter of the induration was measured after 2–3 days by the same person. A positive tuberculin test was defined as an induration of 10 mm or more.

We also investigated risk factors for atopic diseases, such as family history of atopy and characteristics of homes. Statistical analysis was performed using a two tailed Pearson correlation test.

Results

There were 85 study subjects enrolled in this study. The characteristics of the children are given in **Table 1**. All of them were on follow-up at Pediatric Allergy Immunology Clinic at Soetomo Hospital, Surabaya, Indonesia. Positive tuberculin test was recorded in 18 patients (21%).

The mean of tuberculin indurations size was 1.79 (SD 0.411) mm. There was inversed association between tuberculosis infection and allergy manifestation in children (house dust mite, food, and pet allergy). The correlation between tuberculin test and house dust mite allergy was r=-0.364 (P<0.001). The correlation between tuberculin test and food allergy was r=-0.420 (P<0.001). The correlation between tuberculin test and pet allergy was r=-0.344 (P=0.001). The relations of tuberculin indurations size in children with house dust mite, food, and pet allergy was found to be similar.

Positive family history was more common in atopy patients. Positive skin tests were more common in children with negative tuberculin test (**Table 2**).

Table1. Characteristics of study subjects

Characteristic	N = 85	Percentage
Age		
<12 months	10	12
1-6 year	37	44
>6 year	38	44
Gender		
Male	49	58
Female	36	42
Family history		
Positive	70	82
Negative	15	18
House dust mite		
allergy	70	82
Positive	15	18
Negative		
Food allergy		
Positive	72	85
Negative	13	15
Pet allergy		
Positive	66	78
Negative	19	22
Tuberculin test		
Positive	18	21
Negative	67	79
BCG scar :		
Positive	68	80
Negative	17	20

Table 2. Characteristics of patients with house dust mite, food, and pet allergy

		HDM* allergy		Food allergy		Pet allergy	
		Yes	No	Yes	No	Yes	No
Gender	Male	37	12	39	10	35	14
	Female	33	3	33	3	31	5
Positive family history	Yes	61	9	61	9	57	13
	No	9	5	11	3	9	5
Tuberculin test	Positive	10	8	10	8	9	9
	Negative	60	7	62	5	57	10
BCG scar	Positive	57	11	58	10	53	15
	Negative	13	4	14	3	13	4

*HDM=house dust mite

Discussion

This study demonstrates a significant weak inverse association between tuberculin test and allergy skin test in children. This is not consistent with study group from Japan; Shirakawa *et al*[2] hypothesized that a decline in the prevalence of tuberculosis might be an underlying factor in the rise in the prevalence of atopic diseases in recent decades, suggesting that *M. tuberculosis* infection reduces the expression of allergy, as was found in Japanese children. The explanation of this discrepancy maybe because of different subjects. Study in Japan used tuberculosis infection, whiles ours used tuberculin positive patients.

This study also shows slight decreased skin test reactivity in allergic children with positive tuberculin test, suggesting that tuberculin test may not suppress allergic sensitization. Different mechanisms could explain these findings. Chronic infections such as tuberculosis may down regulate atopic response through the induction of regulatory cells and production of anti-inflammatory cytokines. *M. tuberculosis* infection is a potent inducer of T-helper 1 (Th1) responses which inhibit T-helper 2 (Th2) responses.[7] Positive tuberculin test in our study may not always tuberculosis infection.

Ozmen reported that some viral, bacterial, fungal, and protozoa infections lead to secretion of IFN-α from Th 1 cells; thus inhibiting IgE synthesis through B lymphocytes. Therefore, these infections induce the secretion of Th 1 cytokines, which cause the immune response to shift into Th 1 type. *Mycobacteria* is specifically known for strongly stimulating the Th 1 response. Attenuated *Mycobacterium tuberculosis* vaccination may suppress the development of atopy by secreting IFN-α and interleukin (IL)-2. Not having tuberculosis and other infectious diseases may lead to absence of an inhibitory effect on Th 2 immune mechanisms; thus an increase in the rate of allergic diseases in developed countries.[1]

Unlike infections, in atopic disease Th 2 cells are stimulated through allergen stimulation and synthesize IL-4, which leads to IgE secretion from B lymphocytes. In such people, the immune response has shifted to Th 2 type and the Th 1 response has been suppressed. According to this hypothesis, atopic response and delayed-type hypersensitivity to tuberculin are two different series of reactions, antagonist to each other. The tuberculin response is therefore expected to decrease in allergic diseases.[8-10]

In conclusion, there is a weak inverse association between skin test reactivity in allergic children with positive tuberculin test. This study can help to determine the appropriate allergy test even in children with positive tuberculin test.

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