BRONCHIAL ASTHMA AND CHLAMYDIA PNEUMONIAE ANTIBODIES IN CHILDREN AGED 4–8 YEARS IN OLOMOUC DISTRICT

František Kopřiva^a, Jaroslava Szotkowská^b, Martin Zápalka^a

^a Department of Pediatrics, Faculty of Medicine, Palacky University, 775 06 Olomouc, Czech Republic

^b Department of Immunology, Faculty of Medicine, Palacky University
e-mail: Kopriva@fnol.cz

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BACKGROUND. Although several studies have demonstrated an association between infection with Chlamydia pneumoniae and asthma, these were mainly limited to exacerbation of symptoms in adults with known asthma

OBJECTIVE. We investigated the role of C. pneumoniae infection in 149 atopic children with chronic cough and asthma, comparing them with 241 control non-atopic subjects presenting at Olomouc hospital between 1999 and 2003 with non-specific symptoms (temperature above normal (subfebrile), abdominal pain, arthralgia, and other symptoms).

METHODS. The levels of C. pneumoniae-specific antibodies were measured using Chlamydien-rELISA kits (Medac, Hamburg, Germany).

RESULTS. In a group of 83 atopic children with chronic cough, IgM and IgG antibodies to C. pneumoniae were demonstrated in 20 children (24 %). Among children with bronchial asthma, positive antibody was present in 29 children (44 %; /p=0,052/); of this number, 24 (36 %; /p=0,06/) had IgM and IgG antibodies while 5 children (8 %) had IgA and IgG antibodies against C. pneumoniae. A group of non-atopic children with non-specific symptoms included 38 children (16 %) with antibody positivity; 27 children (11 %) with IgM and IgG antibodies and 11 children (5 %) with IgA and IgG antibodies against C. pneumoniae.

CONCLUSIONS. Asthma in children was associated with elevated levels of IgM and IgG antibodies to C. pneumoniae.

INTRODUCTION

Chlamydia pneumoniae is common intracellular respiratory pathogen, and although many infections are believed to be asymptomatic, a growing body of evidence suggests an association between C. pneumoniae infection and asthma in some individuals¹. For the clinician, the diagnosis of C. pneumoniae infection may be difficult because of the lack of widespread availability of diagnostic facilities for either organism identification or serologic testing, and because of controversies surrounding serodiagnostic criteria. The association was first described by

Hahn et al., who reported wheezing in 9 out of 19 adult patients with serologic evidence of current or recent C. pneumoniae infection². In another study 11 % asthmatic and 5 % control children found to have positive cultures for C. pneumoniae³. Although some results were controversial, several studies confirmed these findings^{4,5,6}. Our study aimed to investigate the current situation in the seroprevalence of C. pneumoniae infection in Olomouc district in a group of atopic children with chronic cough and asthma compared with a control group of non-atopic children with non-specific symptoms, i.e., temperature above normal, abdominal pain, arthralgia, fatigue.

Table 1. Characteristics of atopic a non-atopic children (n = 390, median 5 years)

	Atopic children			Non-atopic children
		Cough	Bronchial asthma	
Boys	88	49	35	170
Girls	61	34	31	71
n	149	83	66	241

Non - atopic patients with subfebrile, abdominal pain, arthralgia, fatigue

MATERIALS AND METHODS

We conducted a retrospective study including 390 children (258 boys and 132 girls) aged 4–8 years (median, 5 years) examined in a pediatric outpatient unit and hospitalized in the Department of Pediatrics of Palacky University School of Medicine and University Hospital in Olomouc (Czech Republic) 1999–2003 period (Table 1). Each child had a detailed history taken and total serum immunoglobulin E (S-IgE) levels determined. Atopic children had a positive skin test (wheal $\geq$ 3 mm) to at least one of the most common aeroallergens from our area (house-dust-mites, grass pollen, birch pollen, cat and dog dander, and mold mixture). Ineligible for the study were children with congenital respiratory tract anomalies and those with a serious respiratory disease, e.g., cystic fibrosis.

A total of 149 atopic children (88 boys and 61 girls):¹ 83 children (55.7%) referred for examination with non-productive chronic cough, predominantly night-time cough persisting for more than three weeks;² 66 pediatric patients (44.3%) with persistent mild bronchial asthma (according to GINA 2002), had levels of antibody against *C. pneumoniae* determined using ELISA and Chlamydia-ELISA kits (Medac, Hamburg, Germany).⁷

S-IgE levels were determined by nephelometry. S-IgE values of 150 IU/ml, determined in our laboratory, are considered a significant marker of allergy. All atopic children had total S-IgE levels higher than 150 IU/ml.

The same investigations were undertaken in a control group of non-atopic 241 (170 boys and 71 girls) children with subfebrile, abdominal pain, arthralgia, fatigue. None of these control children showed S-IgE levels over 150 IU/ml.

Our data were analyzed statistically using contingency table and χ square test.

RESULTS

Among our 149 atopic children with chronic cough, 20 (24%) with chronic cough were shown to have IgM and IgG antibodies against *C. pneumoniae*. Among children with bronchial asthma, positive antibodies were present in 29 children (44%; / $p=0.052$ /); of this number 24 children (36%; / $p=0.06$ /) had IgM and IgG antibodies while 5 children (8%) had IgA and IgG antibodies against *C. pneumoniae* (Table 2, 3).

In the group of 241 non-atopic children with non-specific symptoms, positive antibodies were found in 38 children (16%), i.e. 27 children (11%) with IgM and IgG antibodies and 11 children (5%) with IgA and IgG antibodies against *C. pneumoniae*.

Table 2. Number of examined children with chronic cough, bronchial asthma, non-specific symptoms and proportion of positive anti-Chlamydia Ab

	Total/number of positive Ab	% of positive Ab	p
Chronic cough	83/20	24	0,639
Bronchial asthma	66/29	44	0,052
Non-specific symptoms, non-atopic patients	241/38	16	

Ab – antibody

Non – atopic patients with subfebrile, abdominal pain, arthralgia, fatigue

Table 3. Number of children with positive anti-Chlamydia Ab in individual groups

	IgM + IgG	IgA + IgG	IgM + IgG IgA + IgG	p
Chronic cough	20 (24%)	0	20 (24%)	0.68
Bronchial asthma	24 (36%)	5 (8%)	29 (44%)	0.06
Non-specific symptoms, non-atopic patients	27 (11%)	11 (5%)	38 (16%)	

Non – atopic patients with subfebrile, abdominal pain, arthralgia, fatigue

DISCUSSION

Chlamydia pneumoniae is a ubiquitous Gram-negative bacterium, an obligate intracellular parasite with a unique developmental cycle, and a common respiratory pathogen in children as well as adults⁸. Many infections are believed to be asymptomatic. Wheezing and cough are common features of chlamydial lung infections. The mechanism of this apparent association between *C. pneumoniae* infection and asthma is not clear, but presumably relates to chronic bronchial inflammation. Increased production of IL-1, IL-6, TNF- α and granulocyte macrophage-colony stimulating factor (GM-CSF) has been demonstrated in bronchial epithelial cells infected with *C. pneumoniae*. Inflammation in the airways in asthmatics is associated with healing processes resulting in scar formation and tissue remodeling, which seems to be present in almost all asthmatics whatever the severity, duration, or etiology of the asthma. *C. pneumoniae* may be one contributory factor in the development of irreversible changes in the airways. It has been suggested that bronchial hyper-reactivity may be caused by anti-*C. pneumoniae* IgE antibodies (implying allergic sensitization)⁹.

Our study supports the association between *C. pneumoniae* infection and asthma in children. One possible explanation is the finding of an association between variants of the alleles for mannose-binding lectin responsible for the increased incidence of *C. pneumoniae* infection in asthmatic children¹⁰. Cook et al. found that elevated levels of IgG antibody to *C. pneumoniae* were significantly associated with severe chronic asthma and this association was not modified by potential confounding factors¹¹. The presence of short-lived IgA antibodies has been proposed to indicate chronic infection or reinfection, whereas stable elevated levels of more long-lived IgG antibodies may reflect suffer infection in the past or chronic infection. The study by Black et al. showed an association of the severity of asthma and the mean IgG and IgA titers with *C. pneumoniae* infection¹². Results of our study indirectly confirm the conclusions drawn in the above papers. A new diagnostic option is polymerase chain reaction (PCR).

If these associations are important, can we identify individuals at risk for asthma? The answer is: possibly, in the future. To survive within a macrophage, chlamydiae must not elicit a TH1-type CD4 lymphocyte response, such as would be promoted by interferon- γ .¹³ Individuals with particular HLA class II genotypes might therefore be at a higher risk of chronic *C. pneumoniae*-associated disease¹⁴.

Persistent or recurrent *C. pneumoniae* may both initiate the inflammatory process in some individuals, and amplify the inflammation in patients with early mild asthma leading to permanent changes in the airways and chronic disease. Macrolides are antibiotics with both antimicrobial and antiinflammatory activities and thus their use in asthmatic patients could lead to reduction of the airways inflammation and therefore improvement of symptoms

and pulmonary function. Further studies are needed to examine the role of macrolides in asthma therapy. *C. pneumoniae* may persist in the lung after treatment¹⁵.

An association does not mean causality and it is possible that *C. pneumoniae* is coincidental in the bronchi of asthmatic children without playing a contributory role in the amplification of inflammation and progression of asthma.

We conclude that asthma in children was associated with elevated levels of IgM and IgG antibodies to *C. pneumoniae*. Our results are consistent with the hypothesis that *C. pneumoniae* infection may be involved in the development of asthma.

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