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Does Chlamydia pneumoniae *play a role in the pathogenesis of abdominal aortic aneurysm?*

Rola *Chlamydia pneumoniae* w patogenezie tętniaka aorty brzusznej

Chlamydia pneumoniae is a newly described human pathogen, belonging to genus *Chlamydia*. It causes a range of respiratory tract diseases, including pharyngitis, sinusitis, bronchitis, pneumonia, and asthma. Serologic and epidemiological studies have shown that the organisms are widespread geographically, and that epidemics occur in four, six and 10 years cycles [7].

IgG antibody to *C. pneumoniae* is rarely detected in children up to five years of age, but is present in half of adult population. IgG antibody increases with age so that it is found in almost all subjects aged 70 years. Seroconversion usually occurs between eight and 16 years of age and there is higher rate of infection among men than women [2, 6].

Fundamental in chlamydial pathogenesis is the tendency of this organism to cause recurrent and chronic inapparent infections. The persistence of elevated antibody titers is generally considered to be a sign of chronic infection. Constant presence of short-lived IgA antibodies has been proposed to indicate chronic infection, whereas constantly elevated levels of more long-lived IgG antibodies may reflect recurrent infections in the past. IgM antibodies are considered to indicate primary acute infection [9].

Apart from being a respiratory pathogen, C. pneumoniae has been associated serologically with coronary heart disease and myocardial infarction [3, 13, 14].

Recently studies have been conducted to investigate the association between serologic evidence of infection with *C. pneumoniae* and occurrence of abdominal aortic aneurysm (AAA) [1, 11].

The aim of our study was to evaluate the frequency of *Chlamydia pneumoniae* infection in AAA patients by measuring *C. pneumoniae*-specific serum IgG, IgM and IgA levels.

MATERIALS

Patients

19 AAA patients (3 F, 16 M), mean age 70.5 years (55–79) have participated in the research. All patients have been operated for AAA at the Department of Vascular Surgery, University School of Medicine in Lublin. The indications for surgery were: aneurysm size larger than 4.5 cm (4.5–8.0 cm), or the presence of clinical symptoms. All procedures were elective. All patients were non-diabetic, current smokers or ex-smokers and have had hypertension (I or II class according WHO). 6 patients had a history of myocardial infarction and 3 of stroke. The specimens were collected from January to June 2000.

Controls

20 controls subjects, matched for age and sex (4 F, 16 M) without clinical signs and symptoms of cardiovascular and pulmonary disease took part in our study.

METHODS

Microimmunofluorescence method was applied. Chlamydia pneumoniae Micro-IF test (Labsystems, Finland) was used according to manufacture's instructions. Sera analysed for *C. pneumoniae* IgM and IgA were diluted in IgG blocker (Labsystems, Finland) to remove possible interference with IgG.

According to the reference data, the following criteria have been adopted:

1. chronic (persistent) infection: IgG =1:128 and IgA =1:32, IgM=0
2. acute infection: IgG =1:512, IgM =1:8, IgA=0.
3. infection in the past/contact with pathogen IgG =1:128

Statistical analysis was carried out using SPSS for Windows. A p-value of 0.001 was taken as indicative of statistical significance.

RESULTS

Serologic markers for chronic *Chlamydia pneumoniae* infection were detected in 100% (19/19) AAA patients and in 20% (4/20) healthy controls. Seven patients had specific IgG titres of =1:512 and IgA titres =1:64, twelve IgG titres =1:128 and IgA titres =1:64. The titres of specific IgG antibodies (=1:128) and IgA (=1:64) to *Chlamydia pneumoniae* were significantly higher than in control population of the same age ($p<0.001$).

DISCUSSION

Recent discoveries implicating bacteria in conditions such as peptic ulcer disease (*Helicobacter pylori*) and chronic arthritis resembling rheumatoid arthritis (*Borrelia*

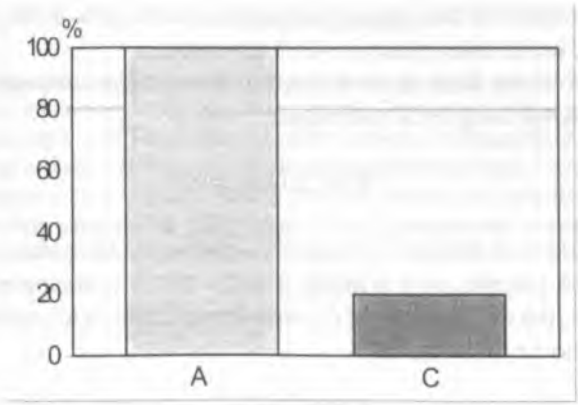

Figure 1. Chronic *C. pneumoniae* infection in AAA patients (A) and healthy controls (C)

burgdorferi) have led to increasing acceptance of the concept that a microbial cause will be found for many chronic inflammatory diseases of previously unknown origin [8]. Since the first observation of the association between *C. pneumoniae* and heart diseases in 1988, an increasing amount of evidence has indicated that *C. pneumoniae* is associated with many more diseases than originally expected [9]. Recently AAA has been added to the list of diseases associated with *C. pneumoniae* infection. The studies published to date confirmed this association [1, 11]. In our pilot study serologic markers for *C. pneumoniae* infection were detected in all patients with AAA. They had specific IgG and IgA antibody titres which reflect chronic infection. Our results are in accordance with those obtained by other authors.

The pathogenesis of abdominal aortic aneurysms (AAA) is still not fully understood, but involves a variety of complex interacting factors. The abdominal aortic aneurysm is formed over several years and is characterised by weakening and dilatation of the aortic wall. It is characterised by a marked inflammatory infiltrate throughout the aortic wall. A positive correlation has been shown between elastolytic activity and invasion of the aortic wall by white blood cells. Activated macrophages appear to play a crucial role in their production of elastase in AAA [11, 12, 15].

Over the last few years both seroepidemiological studies and studies of atherosclerotic lesions throughout the arterial tree have revealed associations between signs of *C. pneumoniae* infection and atherosclerotic lesions in cardiovascular disease. A *C. pneumoniae* infection in respiratory tract may spread systemically by means of phagocytosis of the bacteria in lungs by alveolar macrophages. It has been suggested that the infected macrophages may enter the systemic circulation. Finally, the macrophages may enter the vessel wall as a response to local inflammation on the basis of oxidised LDL cholesterol in the extracellular matrix. The findings suggest that humoral immune reactions to *C. pneumoniae* may play an important role in vascular endothelial injury, which is believed to be of importance for the development of atherosclerosis [4, 5, 10].

It has been postulated that similar mechanisms participate in the process of aortic wall destruction, which takes place in AAA formation.

The next step in our study is an attempt to detect *C. pneumoniae* DNA in aortic wall changes in AAA using PCR technique.

CONCLUSIONS

Serologic markers of chronic *C. pneumoniae* infection have been present in 100% of examined AAA patients, so it is highly possible that it participates in AAA pathogenesis. However, the detailed role of *C. pneumoniae* in the AAA pathogenesis should to be elucidated in further studies.

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STRESZCZENIE

Celem pracy była ocena częstości występowania serologicznych markerów infekcji *C. pneumoniae* u chorych z tętniakiem aorty brzusznej (TAB). Oznaczono miano przeciwciał anty–*C. pneumoniae* w klasie IgG, IgM i IgA, metodą mikroimmunofluorescencji, u 19 chorych z TAB i 20 osób z grupy kontrolnej. Serologiczne markery przewlekłej infekcji *C. pneumoniae* stwierdzono u 100% chorych z TAB i u 20% osób zdrowych. Różnica ta była istotna statystycznie. Wyniki naszych badań wskazują na potencjalną rolę *C. pneumoniae* w patogenezie tętniaka aorty brzusznej.