Chlamydia trachomatis and inflammatory bowel disease - a coincidence?

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Summary

Serological tests of 35 patients suffering from inflammatory bowel disease were compared to those of 35 healthy controls. The tests were performed using the indirect immunoperoxidase assay.

Ninety-three per cent of 15 patients with Crohn's disease had IgG antibodies against *Chlamydia*, compared to 26% in the control group. In the 20 patients with ulcerative colitis, 45% had IgG antibodies against *Chlamydia*, compared to 10% in the control group. High serum titres of IgG antibodies were found in most of the patients with inflammatory bowel disease, mainly with Crohn's disease, while weak reactions appeared in most of the controls in which antibodies were detected. These results suggest a high incidence of *Chlamydia* infection in the studied patients with inflammatory bowel disease, especially in those with Crohn's disease. The possible association between *Chlamydia trachomatis* and inflammatory bowel disease is discussed.

Introduction

The aetiology and pathogenesis of inflammatory bowel disease (IBD) are still unknown. The possibility that at least part of these diseases could be caused by specific transmissible agents was suggested many years ago[1]. The eventual association between Crohn's disease and *Chlamydia trachomatis* was suspected because granuloma and fistula formation are common expressions of both. A few investigations have been made in the past with contradictory results[2-8]. In the present study we have investigated this possible association by searching for antichlamydial antibodies in the serum of patients diagnosed as IBD and compared the results with healthy controls.

Patients and methods

Serum samples were obtained from 15 patients with Crohn's disease and 20 patients with ulcerative colitis. Patients with Crohn's disease were diagnosed on the basis of characteristic symptomatology, and clinical and radiological findings. The diagnosis of ulcerative colitis was made by radiological, endoscopic and biopsy criteria. Details of age, sex, history, disease activity and medical or surgical treatment were recorded for each patient. Control serum samples were obtained from 35 healthy subjects, who were interviewed to ensure that they represented a healthy population and who were matched for age and sex.

The serum samples were coded and tested blind for the presence of antichlamydial IgG and IgA antibodies using the indirect immunoperoxidase assay (IPAzyme Chlamydia Kit; Savion Diagnostics Ltd, Beer Sheva, Israel). Elevated titres of specific IgG and IgA antibodies can serve as a marker for *C. trachomatis* present or past infection.

The results achieved in both groups were compared and the statistical significance was assessed by Student's *t*-test.

Table 1. Serology for Chlamydia

	No of patients	*IgA*	*IgG*
Crohn's disease	15	5 (33%)	14 (93%)
Controls	15	1 (6%)	4 (26%)
		P=0.1-0.05	P<0.0025

Table 2. Serology for Chlamydia

	No of patients	*IgA*	*IgG*
Ulcerative colitis	20	1 (5%)	9 (45%)
Controls	20	0	2 (10%)
		P=0.15-0.20	P=0.01

Results

Five of 15 patients with Crohn's disease (33%) had IgA antibodies to *C. trachomatis*, compared to one in the control group (6%). This difference was not statistically significant (P=0.1-0.05, Table 1). IgG antibodies were detected in 14 patients with Crohn's disease, (93%) compared to four subjects in the control group (26%) and this difference was clearly significant (P<0.0025, Table 1).

In the group with Crohn's disease, the IgG titres were 1/64 in six patients, 1/128 in two, 1/256 in four and 1/1024 in the other two. In the control group, they appeared at level 1/64 in all the positive four individuals.

In the ulcerative colitis group, IgA antibodies were found in one patient and none in the control group, but IgG antibodies were positive in nine patients (45%) and only in two controls (10%). These results were statistically significant (P=0.01, Table 2).

Among the patients with ulcerative colitis, the IgG titres were 1/64 in four, 1/128 in three, and 1/256 in the other two. In the two positive controls, the levels were 1/64 in one, and 1/128 in the other one.

Regarding the IgG antibodies in the whole group of patients with inflammatory bowel disease (Crohn's disease+ulcerative colitis), there were a significant number of positive results (62.8%) when compared to

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the control group (20%) ($P<0.0005$). Furthermore, higher titres were detected among the inflammatory group than in the positive controls.

Discussion

Crohn's disease was first described in 1932[1] and since then, there has been a marked rise in the incidence of the disease which can not be attributed only to genetic or dietary aetiology or to greater recognition of the disease. Aetiology and pathogenesis of ulcerative colitis is obscure and there is substantial evidence suggesting that an environmental transmissible agent may play a role in both diseases[9-13]. This possibility is also supported by the observation that an IgM lymphocytotoxic antibody, which is present in about half the patients with inflammatory bowel disease, also occurs within those who live close to them at a significantly greater frequency than in controls[14].

Since Crohn had failed to transmit the disease by injecting tissue homogenate of patients with IBD, to healthy laboratory animals, many pathogens have been suggested as being causatives of IBD: *Mycobacterium paratuberculosis*, *Eubacterium contortum*, *Peptostreptococcus*, *Yersinia enterocolitica*, *Clostridium difficile*, *Campylobacter jejuni*, *Bacteroides fragilis*, *Pseudomonas* and others[18]. The search after an infecting agent was encouraged by the similarity between Crohn's disease and other inflammatory diseases of the bowel in men and animals caused by these agents.

We want to focus attention on *C. trachomatis*. This obligatory intracellular parasite has great invasiveness and affinity for lymphatic tissue and can cause a broad spectrum of systemic and urogenital diseases in men and animals.

There is clinical and histological similarity between Crohn's disease and lymphogranuloma venereum which is caused by *C. trachomatis* (immunotypes L1, 2 and 3). Indeed this similarity between Crohn's disease and lymphogranuloma venereum, and especially the anorectal version of the disease, enhanced some authors to try to find any aetiologic association between *Chlamydia* and IBD. Tomenius *et al.*[15] in 1963, demonstrated a positive Frei test in seven of eight patients with the disease. Schuller *et al.*[2], in 1979, reported the presence of antibodies against *Chlamydia* of lymphogranuloma venereum type in 69% of patients with Crohn's disease, and Cevenini *et al.*[3] in 1980, found antichlamydial trachomatis antibodies in 85% of patients with Crohn's disease, and in 39.4% of patients with ulcerative colitis. It was very tempting to suggest that *Chlamydia* really causes IBD, although these results were not supported by other reports[4-8]. As suggested by Elliot *et al.*[8], the reasons for the discrepant findings of the various groups of investigators could be due to their testing a different patient population or by variations in performing the test.

Quinn *et al.*[16] were successful in setting up an experimental model of inflammatory bowel disease in monkeys, by inoculating *C. trachomatis*. The primates developed rectal granulomas identical to those found in Crohn's disease. In calves, oral administration of *Chlamydia* resulted in infections of the distal ileum and the regional mesenteric lymph nodes[17].

In our present investigation we have documented a significantly higher presence of antichlamydial IgG antibodies in patients with inflammatory bowel disease, in comparison to healthy controls. This type of antibody formation suggests long standing antigenic stimulation and, as pointed out by Schuller *et al.*[2] it is tempting to speculate that *Chlamydia* may play a role in IBD. A possible explanation is that some patients, clinically misdiagnosed as Crohn's disease or ulcerative colitis, have an underlying chlamydial infection with similar clinical, endoscopic and radiological appearances. Investigation of chlamydial antibodies in the serum must be done in order to establish the correct diagnosis and to define specific therapy. Another explanation is based on the hypothesis that the antichlamydial antibodies in the serum, reflect intestinal invasion secondary to mucosal barriers damaged by the inflammatory process[18]. James *et al.*[19] suggested that IBD, and especially Crohn's disease, may be due to an immunoregulatory abnormal response to antigens present in the mucosal environment. In this sense, *Chlamydia* may act as an aetiologic agent that starts the pathological process that finally results in IBD, or alternatively, may play a role as an aggravating factor in a bowel previously damaged by a non-infectious disease.

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Forthcoming events

Searching for New Horizons in Non-Invasive Technology: The Next Decade
3-4 February 1990, San Francisco, California
Further details from: Extended Programs in Medical Education, University of California, Room C-124, San Francisco, CA 94143-0742, USA

Colorectal Disease in 1990: An International Exchange of Medical and Surgical Concepts
15-17 February 1990, Fort Lauderdale, Florida
Further details from: The Cleveland Clinic Educational Foundation, Dept of Continuing Education, 9500 Euclid Avenue, TT31, Cleveland, OH 44195-5241, USA

First Breton Workshop of Autoimmunity
9-10 March 1990, Medical School, Brest, France
Call for abstracts: deadline 31 January 1990
Further details from: Professor P Youinou, Immunologie, CHU, BP 824, F 29285 Brest Cedex, France

1990 International Association for the Study of Pain Congress
1-6 April 1990, Adelaide, South Australia
Further details from: Loisa E Jones, BS, Executive Officer, ISAP, 909 NE 43rd St., Suite 306, Seattle, WA 98105-6020, USA

35th General Assembly of the International Union against Venereal Diseases and the Treponematoses: Sexually Transmitted Diseases in the Age of AIDS
-11 May 1990, Royal Society of Medicine, London
Further details from: Dr R D Mann, The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE

Techniques & Applications of Molecular Biology: a Course for Medical Practitioners
9-12 April 1990, University of Warwick
Further details from: Dr Rachel Strachan, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL

Tenth Instructional Course on Tinnitus and its Management
11 April 1990, Nottingham University
Further details from: Mrs J P Willoughby, Course Secretary, MRC Institute of Hearing Research, University of Nottingham, University Park, Nottingham NG7 2RD

World Conference on Lung Health
20-24 May 1990, Boston, Massachusetts, USA
Deadline for abstracts: 1 November 1989
Further information from: American Lung Association, 1740 Broadway, New York, NY 10019-4374, USA

Second Greek/Australian International Medical & Legal Conference
25 May to 1 June 1990, Rhodes, Greece
Further details from: Secretariat, ICMS, PO Box 29, Parkville, Victoria, Australia 3052

XX Congress of the International Society of Internal Medicine
17-21 June 1990, Stockholm, Sweden
Further details from: ISIM 90, Congrex, PO Box 5619. S-11486 Stockholm, Sweden, Phone +46-08 32 69 00

Medical Informatics Europe 90: Health Added Value
20-23 August 1990, Scottish Exhibition and Conference Centre, Glasgow
Call for papers: deadline 1 December 1989
Further details from: Congress Secretarial, Meeting Makers. 50 Richmond Street, Glasgow G1 1XP

East-Coast Conference on Biomechanics
26-28 August 1990
Call for papers: please send one page abstract by 1 February 1990
Further details from: Professor H S Ranu, Department of Biomechanics, Nycom, New York Institute of Technology, Old Westbury, New York 11568, USA

Women's National Cancer Control Campaign
The Women's National Cancer Control Campaign is seeking the services of women doctors nationwide to help with their screening programmes to check for breast and cervical cancer. The Campaign arranges screening programmes at workplaces and town centres, either on the customer's own premises or in the Campaign's mobile units, which are paid for by employers and sponsors. Although much of the screening undertaken by the Campaign is industrial, there are also successful public programmes which help to reach women who might not normally be screened, and ensure that they are now registered on their local Health Authority's recall system.

The WNCCC screening programme offers the following services to each woman attending: a cervical smear test; a breast examination by manual palpation; an internal pelvic examination; and basic instruction in breast self examination.

There is a constant demand for female doctors with experience in this field. Hence it is essential that we maintain a comprehensive network of female doctors and nurses nationwide, so that staffing the units is made as efficient as possible. Women doctors who are interested in working for the Campaign for even one session (morning or afternoon) in their own areas should contact Rosemary Main at WNCCC, 1 South Audley Street, London W1Y 5DQ. (Tel: 01-499 7532). Details of pay and conditions are available on application.