

Chlamydia and the Curtis-Fitz-Hugh syndrome

S DAROUGAR,* T FORSEY,* J J WOOD,† J P BOLTON,† AND A ALLAN†

From the *Subdepartment of Virology, Institute of Ophthalmology, and the †Department of Surgical Studies, Middlesex Hospital, London

SUMMARY Ten women with acute right upper-quadrant abdominal pain but negative results for biliary investigations had a current or past history of pelvic inflammatory disease. A diagnosis of the Curtis-Fitz-Hugh syndrome was made and was confirmed in five patients by laparoscopy.

Neisseria gonorrhoeae was not isolated from the cervical and urethral swabbings of seven patients tested. *Chlamydia trachomatis* was isolated from the endocervical canal in one of six patients examined. Of sera from nine patients tested by a micro-immunofluorescence test, nine and six samples respectively showed type-specific IgG and IgM antibodies against *C trachomatis* serotypes D-K. Type-specific IgG and IgA antibodies were also detected in the cervical and urethral discharge of two out of five patients and in the peritoneal aspirate of two. The presence of high titres of IgG or IgM in sera and IgG or IgA in the local discharges of our patients suggests that *C trachomatis* was probably the cause of the CFH syndrome.

Introduction

Acute right upper-quadrant (RUQ) abdominal pain associated with perihepatitis, pelvic inflammatory disease (PID), and sexually transmitted infection, eponymously known as the Curtis-Fitz-Hugh (CFH) syndrome, has been recognised for many years.^{1,2} It is indistinguishable clinically from acute biliary disease² and can occasionally lead to unnecessary operation. *Neisseria gonorrhoeae* is usually considered to be the cause of inflammation,^{2,3} but recent studies^{4,5} suggest that the syndrome may be associated aetiologically with chlamydial genital infection.

We present the results of investigations for chlamydial infection on 10 patients who were diagnosed as having the CFH syndrome. Details of clinical, radiological, ultrasound, and other laboratory investigations on these patients are described elsewhere (J J Wood *et al*, unpublished data).

Patients and methods

CLINICAL HISTORY

Ten women, complaining of acute RUQ abdominal pain associated with anorexia, nausea, and abdominal tenderness, were admitted to the

Middlesex Hospital, London, over a period of nine months. Their ages ranged from 16 to 40 years (table I). In all cases the provisional clinical diagnosis was of acute biliary disease. The results of liver function tests and biliary tract investigations, including ultrasound examination, cholecystogram (in five patients), and intravenous cholangiogram (in one patient), showed no abnormalities. None of these investigations demonstrated or suggested the presence of gall stones. Because of the negative results and either a past history of PID or the presence of symptoms or signs of PID, the clinical diagnosis in these patients was changed to the CFH syndrome.

LAPAROSCOPY FINDINGS

Laparoscopy, performed on five patients to investigate the pelvic disease, showed "violin string" adhesions between the liver capsule and the anterior abdominal wall, which are typical of the CFH syndrome.^{1,3} These adhesions were all injected, fibrinous, and separate from the area of the gall bladder. In the remaining five patients, laparoscopy was not considered necessary for the diagnosis or management of the pelvic disease, hence the typical adhesions of the CFH syndrome were not confirmed. The clinical features in conjunction with the negative results of the biliary investigations were, however, highly suggestive of the CFH syndrome.

CULTURE

Specimens taken from the cervix and urethra by swabbing were cultured in modified Thayer-Martin

Address for reprints: Professor S Darougar, Subdepartment of Virology, Institute of Ophthalmology, Judd Street, London WC1H 9QS

TABLE 1 Results of clinical, microbiological, and serological investigations in 10 women suspected of having Curtis-Fitz-Hugh syndrome

Patient No	Age (years)	RUQ pain	History of PID	Current PID	Biliary investigations	Laparoscopy findings	Culture results for:		Antichlamydial antibodies	
							Gonococci	Chlamydia	Serum	Local fluid
1	31	+	+	+	N	Perihepatitis	-	-	+	-
2	16	+	-	+	ND	Perihepatitis	ND	ND	+	+
3	24	+	+	+	N	Perihepatitis	-	-	ND	+
4	25	+	+	+	N	Perihepatitis	-	ND	+	ND
5	40	+	-	+	N	Perihepatitis	-	+	+	ND
6	23	+	+	-	N	ND	ND	ND	+	ND
7	24	+	+	+	N	ND	-	-	+	-
8	23	+	-	+	N	ND	-	-	+	+
9	18	+	-	+	N	ND	ND	ND	+	ND
10	18	+	+	+	N	ND	-	-	+	-

+ Positive; - negative; N = normal; ND = not done

medium for the isolation of gonococci. Swabbings also collected from the endocervical canal for the isolation of chlamydia were placed in vials containing 2SP transport medium⁶ containing 3% v/v fetal bovine serum and transported to the laboratory at the Middlesex Hospital within a few hours, where they were stored at -70°C . Methods of culture in McCoy cells treated with IUDR and identification of chlamydial inclusions by an iodine staining technique have been described.⁷

DETECTION OF ANTICHLAMYDIAL ANTIBODIES
Blood samples were taken by venepuncture and the serum separated. Peritoneal fluid was collected by aspiration at laparoscopy. Discharges from the cervix and urethra were collected by saturating special cellulose sponges.⁸ These specimens were transported to the Institute of Ophthalmology, where they were tested for antichlamydial antibodies by a modified micro-immunofluorescence test.⁹ Serum was examined for the presence of type-specific antichlamydial IgG at a starting dilution of 1/16 and IgM at a starting dilution of 1/8. Local discharges and peritoneal fluid were tested for antichlamydial IgG and IgA at starting dilutions of 1/8.

Results

Results of investigations are shown in tables I and II.

CULTURE

N gonorrhoeae was not isolated from the cervical or urethral specimens of any of the seven patients tested. *C trachomatis* was isolated from the genital tract of one of six patients tested.

ANTICHLAMYDIAL ANTIBODIES

Type-specific antibodies against *C trachomatis* serotypes D-K (causing genital infection) were detected in the sera of all nine patients tested (tables I

and II). Eight of these had IgG at a titre $\geq 1/64$ and six had IgM at $\geq 1/8$ suggesting active infection with *C trachomatis*⁸ (table II). In one patient (No 5), whose serum was mistakenly treated with EDTA, IgG was present at a titre of 1/32 and no IgM was detected, but *C trachomatis* was isolated from her genital tract. Type-specific antibodies against *C trachomatis* serotypes D-K were detected in the cervical discharge of two out of five patients and in the peritoneal aspirate of the two patients tested (table II). No antibodies were detected against *C trachomatis* serotypes A-C (causing hyperendemic trachoma) or against the lymphogranuloma venereum serotypes or against *Chlamydia psittaci*.

Discussion

The 10 cases of the CFH syndrome reported here were identified over nine months and formed approximately 10% of all admissions for suspected acute biliary disease during this period, which suggests that the CFH syndrome is more common than has previously been realised.

Failure to isolate gonococci in the patients tested suggested that this agent was unlikely to be the cause of the disease in most of our patients. *C trachomatis* was isolated from the genital tract of one of six patients tested, and all had raised levels of antibodies against *C trachomatis* serotypes D-K in serum or local discharge (tables I and II). In previous studies of the CFH syndrome *C trachomatis* was isolated from the genital tract in all four patients tested.^{5 10} The lower isolation rate of *C trachomatis* in this study may be related to the chronicity and the mildness of the concurrent PID or lower genital tract infection. Recent studies have shown that in mild or chronic chlamydial infections of the eye or genital tract chlamydial isolation rates are generally very low compared with those in severe infections.^{11 12}

TABLE II Antichlamydial antibody titres against *C trachomatis* serotypes D-K in 10 patients with suspected or confirmed Curtis-Fitz-Hugh syndrome

Patient No	Serum		Cervical fluid		Urethral fluid		Peritoneal fluid	
	IgG*	IgM	IgG	IgA	IgG	IgA	IgG	IgA
1	256	16	0	0	0	0	ND	ND
2	128	0	ND	ND	ND	ND	256	0
3	ND	ND	256	128	256	128	64	0
4	128	8	ND	ND	ND	ND	ND	ND
5	32†	0	ND	ND	ND	ND	ND	ND
6	64	0	ND	ND	ND	ND	ND	ND
7	256	32	0	0	0	0	ND	ND
8	256	32	8	0	0	8	ND	ND
9	256	64	ND	ND	ND	ND	ND	ND
10	256	32	0	0	0	0	ND	ND

*Reciprocal end point titre

†Serum was treated with EDTA

ND = not done

Raised levels of type-specific antichlamydial IgG were detected in the sera of nine patients tested (table II) at titres of $\geq 1/64$ in eight and of $1/32$ in one, from whose genital tract *C trachomatis* was isolated. In the one patient whose serum was not tested (patient 3), high titres of antichlamydial antibodies were found in cervical and urethral discharges and in her peritoneal aspirate. Type-specific antichlamydial IgM was detected in the sera of six out of nine patients, who also had IgG titres of $\geq 1/128$. Our previous studies^{8, 13} have shown that the presence in serum of IgG at titres of $\geq 1/64$ or of IgM at titres of $\geq 1/8$ correlates well with clinical and microbiological diagnoses of active ocular or genital chlamydial infections.

Type-specific antichlamydial antibodies were detected in the cervical and urethral discharges of two out of five patients and in the peritoneal aspirate of the two patients tested. The presence of antichlamydial IgG or IgA at titres of $\geq 1/8$ in local discharges (tears or cervical discharge) is closely associated with acute chlamydial infections.^{8, 13} These antibodies have been found in the tears of 75% of patients with active trachoma¹⁴ and in those of 85% of patients with isolation-positive paratrachoma (TRIC ocular infection)¹³ and in the cervical secretions of 74% of women with isolation-positive chlamydial infections of the cervix.⁸

The titres of type-specific IgG and IgM found in the sera of the patients in the present study are markedly higher than those found in women with uncomplicated cervical chlamydial infection⁸ but are similar to those found in women with PID^{15, 16}; they correspond well with previous findings in the CFH syndrome.^{4, 5}

After preliminary investigations, five patients were treated with a course of ampicillin and metro-

nidazole, but none showed any marked relief of their RUQ abdominal pain. After high titres of antichlamydial antibodies had been detected, these patients were treated with a five-week course of tetracycline and responded well.

We consider, in agreement with other workers, that *C trachomatis* is a major cause of lower genital tract infection and PID. Because of the close association between CFH and inflammatory disease of the genital tract, it is reasonable to assume that *C trachomatis* can also play an important role in the development of this syndrome.

The laboratory work was supported by a grant from the Department of Health and Social Security. The authors are grateful to Dr B H O'Connor for his assistance in organising this project.

References

1. Curtis AH. A cause of adhesions in the right upper quadrant. *JAMA* 1930; **94**: 1221-2.
2. Fitz-Hugh T jun. Acute gonococcal peritonitis of the right upper quadrant in women. *JAMA* 1934; **102**: 2094-6.
3. Stanley MM. Gonococcal peritonitis of the right upper part of the abdomen in young women. *Arch Int Med* 1946; **78**: 1-13.
4. Müller-Schoop JW, Wang SP, Munzinger J, Schlapfer HU, Knoblauch M, Ammann RW. *Chlamydia trachomatis* as a possible cause of peritonitis and perihepatitis in young women. *Br Med J* 1978; **i**: 1022-4.
5. Wolner-Hanssen P, Weström L, Mårdh P-A. Perihepatitis and chlamydial salpingitis. *Lancet* 1980; **i**: 901-4.
6. Gordon FB, Harper IA, Quan AL, Trehan JD, Dwyer RStC, Garland JA. Detection of *Chlamydia (Bedsonia)* in certain infections of man. I Laboratory procedures: comparison of yolk sac and cell culture for detection and isolation. *J Infect Dis* 1969; **120**: 451-62.
7. Wentworth BB, Alexander ER. Isolation of *Chlamydia trachomatis* by use of 5-iodo-2-deoxyuridine-treated cells. *Appl Microbiol* 1974; **27**: 912-6.
8. Trehan JD, Darougar S, Simmons PD, Thin RN. Rapid diagnosis of chlamydial infection of the cervix. *Br J Vener Dis* 1978; **54**: 403-8.

9. Treharne JD, Darougar S, Jones BR. Modification of the micro-immunofluorescence test to provide a routine serodiagnostic test for chlamydial infection. *J Clin Pathol* 1977;**30**:510-7.
10. Paavonen J, Valtonen VV. *Chlamydia trachomatis* as a possible cause of peritonitis and perihepatitis in a young woman. *Br J Vener Dis* 1980;**56**:341-3.
11. Darougar S, Woodland RM, Forsey T, Cubitt S, Allami J, Jones BR. Isolation of *Chlamydia* from ocular infections, In: Hobson D, Holmes KK, eds. *Nongonococcal Urethritis and Related Infections*. Washington DC: American Society for Microbiology 1977;295-8.
12. Alani MD, Darougar S, Burns DCMacD, Thin RN, Dunn H. Isolation of *Chlamydia trachomatis* from the male urethra. *Br J Vener Dis* 1977;**53**:88-92.
13. Darougar S, Treharne JD, Minassian DC, El-Sheikh H, Dines RJ, Jones BR. Rapid serological test for diagnosis of chlamydial ocular infections. *Br J Ophthalmol* 1978;**62**:503-8.
14. Treharne JD, Dwyer RStC, Darougar S, Jones BR, Daghfous T. Antichlamydial antibody in tears and sera, and serotypes of *Chlamydia trachomatis* isolated from school children in Southern Tunisia. *Br J Ophthalmol* 1978;**62**:509-15.
15. Treharne JD, Ripa KT, Mårdh P-A, Svensson L, Weström L, Darougar S. Antibodies to *Chlamydia trachomatis* in acute salpingitis. *Br J Vener Dis* 1979;**55**:26-9.
16. Simmons PD, Forsey T, Thin RN, *et al.* Antichlamydial antibodies in pelvic inflammatory disease. *Br J Vener Dis* 1979;**55**:419-21.