

Case report

Isolation of *Chlamydia trachomatis* from the liver of a patient with prolonged fever

M DAN, L D J TYRRELL, AND G GOLDSAND

From the Division of Infectious Diseases, Department of Medicine, The University of Alberta, Edmonton, Alberta, Canada

SUMMARY *Chlamydia trachomatis* was isolated from liver biopsy specimens on two separate occasions in a young, sexually inactive patient with a 10 month history of recurrent episodes of fever, chills, and abdominal pain. Liver function tests showed a five fold increase in alkaline phosphatase, and a 20 fold increase in 5'-nucleotidase. Liver histology changes consisted of mild inflammatory infiltrates in the portal tracts. Treatment with doxycycline was followed by complete recovery. We are not aware of any previous report describing isolation of this organism from the liver parenchyma, or of *C trachomatis* infection presenting as fever of obscure origin.

The spectrum of diseases caused by *Chlamydia trachomatis* is constantly expanding. These obligate intracellular bacteria have long been recognised as the causative agents of trachoma, and more recently have been associated with a variety of sexually transmitted and neonatal infections.¹ Sporadic reports have also associated this micro-organism with otitis media in children,² adult pneumonia,³ mediastinal lymphadenitis,⁴ and endocarditis.⁵

We report herein what appears to be the first instance of *C trachomatis* isolation from liver tissue of a patient with prolonged fever.

Case report

A 16 year old boy was admitted to the University of Alberta Hospital with a 10 month history of recurrent episodes of fever, chills, night sweats, abdominal pain located at the right lower quadrant, and a 10 kg weight loss. Physical examination disclosed a pale youngster who appeared to be chronically ill, and had an oral temperature of 38.3°C. Small, mobile and soft lymph nodes were palpated bilaterally at the axillary areas. A grade 2/6 systolic ejection murmur was heard at the left sternal border. Initial laboratory tests revealed a haemoglobin concentration of 10.9 g/dl; WBC count, 10 800/mm³ with normal differential; ESR, 56/h; alkaline phosphatase, 186 U/l

(normal, 90 U/l); and a moderate increase in alpha and gamma globulins. Albumin, alanine aminotransferase, aspartate aminotransferase, bilirubin, urinalysis, and chest roentgenogram were all normal.

Cultures of blood and urine, PPD skin test, VDRL, and serologic tests for infection by Epstein-Barr virus, cytomegalovirus, hepatitis B virus, and *Brucella*, were all negative.

An investigation for 'fever of unknown origin' was initiated: echocardiogram, roentgenograms of the gastrointestinal tract, intravenous pyelography, radionuclide scans of bone, liver and spleen, and computer assisted tomography of the abdomen were all normal. Because both a gallium citrate 67 scan and ultrasonography indicated possible pathology in the right pelvis, however, a laparotomy was carried out. Several matted, firm lymph nodes were discovered in the mesentery and the porta hepatis. The liver and spleen appeared normal, no other pathology was observed, and a normal appendix was removed. Histologic examination of a lymph node specimen revealed non-specific inflammation.

The patient continued to be febrile up to 40°C, and experienced abdominal pain and night sweats. Because of increasing concentrations of alkaline phosphatase (513 U/l), and raised 5'-nucleotidase (55 U/l; normal, 2.5 Bodansky U/l), a liver biopsy was done. Mild, non-specific inflammatory changes were observed mainly in the portal tracts, and an isolated granuloma was identified. Cultures of the

Address for correspondence: Dr Dan, Infectious Diseases Unit, The E Wolfson Hospital, Holon 58100, Israel.

Received for publication 9 April, 1987.

specimens for bacteria (including *Yersinia*, *Brucella*, and *Mycobacteria*), fungi, and viruses, were negative. Unexpectedly, *Chlamydia trachomatis* was isolated from the liver tissue on McCoy cell culture. To discount the possibility of laboratory contamination, liver biopsy was repeated, and *C trachomatis* grew again from the second specimen. On inquiry, the patient denied any previous sexual activity. No perirectal findings or genital ulcers were noted, and cultures of urethral, rectal, and conjunctival swabs did not produce *Chlamydia*. A three week course of oral doxycycline, 100 mg bid, was initiated. His condition improved gradually: fever and abdominal pain subsided, liver function tests, haemoglobin and ESR values returned to normal, the patient gained weight and felt much better. A third liver biopsy, carried out more than one month after completion of doxycycline therapy, showed chronic inflammation and a single granuloma. Culture of the liver specimen for *Chlamydia* and other micro-organisms was negative this time.

Serologic tests for *Chlamydia* (CF), done on serum specimens obtained 10 and 14 months after doxycycline treatment, showed a constant titre of 1:8. Examination of sera by the Western immunoblot technique showed a high titre of antibody (IgG) against several chlamydial proteins, representing a pattern compatible with systemic lymphogranuloma venereum infection.

On follow up, two years after recovery, the patient has continued to do perfectly well with no laboratory abnormalities.

Discussion

The suggestion that prolonged fever in the present case was caused by *C trachomatis*, is based on the following facts. *Chlamydia trachomatis* was repeatedly isolated from hepatic tissue, after exhaustive investigation failed to document any other etiology. The prolonged disease promptly resolved after a therapeutic course with an antibiotic active against *Chlamydia*. The fact that isolation of the pathogen was not accompanied by a change in specific antibody titres may represent late sampling, after resolution of the active phase response.

The natural history and duration of untreated chlamydial infection are not well documented. Several authors have suggested, however, that disease may persist for long periods in a mild or latent form. Such a chronic infection has been documented for as long as 20 years.⁶ The role of *Chlamydia* in this case is, therefore, not precluded by the prolonged course of illness.

The only previously reported association of *C trachomatis* with liver disease is in Fitz-Hugh-

Curtis syndrome, a perihepatitis accompanying acute salpingitis, in which the pathogen has been isolated from the liver capsule.^{7,8} We are not aware of any previous communication reporting the isolation of *C trachomatis* from liver parenchyma.

The clinical picture of our patient fulfills the criteria of 'fever of unknown origin'. More specifically, it almost perfectly correlates with a description from a recent review of the subject,⁹ according to which bacterial hepatitis may present with fever lasting from weeks to months. The liver may or may not be enlarged and/or tender; however, serum concentrations of alkaline phosphatase are usually raised. The organisms recovered from the liver of patients with this syndrome have included *Propionibacterium acnes*, viridans streptococci, and *Actinomyces israeli*. Our case differs from this description only in the causative agent. Indeed, major textbooks^{10,11} do not mention *C trachomatis* among the numerous micro-organisms that can cause prolonged fever, although another chlamydia, *C psittaci*, is recognised in this setting.

Chlamydia trachomatis infection should be included in the differential diagnosis of 'fever of unknown origin' syndrome in young adults.

The authors thank Errol Presad for performing the *Chlamydia* cultures, and Dr Wanda M Wenman for the serologic studies.

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