CHRONIC ACTIVE HEPATITIS IN INTRAVENOUS DRUG ABUSERS MAY BE DELTA AGENT INFECTION ASSOCIATED

A. G. Shattock, Yvonne Arthurs, G. D. Doyle and J. F. Fielding*

Department of Medical Microbiology, University College, Dublin;
Department of Medicine and Gastroenterology and Department of Pathology,
The Charitable Infirmary. Jervis Street, Dublin 1.

Summary

TWENTY-SEVEN parenteral drug abusers had serum tested for delta antigen and antidelta antibody and had liver biopsies performed. All four patients with chronic active hepatitis were delta positive. This study suggests that delta agent infection increases the risk of progression of intravenous drug abuse associated liver disease to chronic active hepatitis.

Introduction

Since the delta agent was first identified by Rizzetto and his colleagues in 1977 there has been much speculation regarding its nature and significance. The delta agent appears to be an RNA virus which is dependent on hepatitis B surface antigen (HB_sAg) for its replication (Rizzetto *et al,* 1980). Chronic HB_sAg carriers appear to be most at risk of developing delta infection (Smedile *et al,* 1981). Chronic delta infection has been shown to be associated with progressive liver disease (Rizzetto *et al,* 1977). In order to determine whether such liver disease was related to the delta agent per se or to the co-existant hepatitis B virus (HBV) we performed liver biopsies on twenty-seven parenteral drug abusers who had serum tested for delta antigen and antidelta antibody. We report here the histological findings in those who were delta positive and those who were delta negative.

Patients and Methods

Twenty-seven parenteral drug abusers admitted to hospital for liver biopsy during the period from January 1st to August 31st 1981 are included in this study. All patients were referred to us from the Drug Advisory and Treatment Centre by its Medical Director, Dr. M. G. Kelly.

Patients had the following laboratory investigations performed:– full blood count, platelet count, prothrombin time, serum bilirubin, serum alanine and aspartate transaminase, alkaline phosphatase, serum proteins and albumin. Serological tests for hepatitis B virus included HB.Ag (RIA Ausria II Abbott), anti HB_s (immunodiffusion, Shattock, 1974). Patients positive for HB_sAg were also tested for HB_s antigen and anti HB_8 by semi-microdiffusion in 0.7% agarose in barbitone buffer at pH 8.6, with double filling of wells with serum samples concentrated a minimum of four fold with polyacryl gel (Lypogel Hawksley) (Shattock, 1982). Hepatitis B core antibody (anti HB_s) was also tested (RIA "Corab" Abbott or EIA "Corezyme" Abbott). Serum was tested for delta antigen and anti delta antibody by Dr. Rizzetto using his own radioimmunoassay technique (Rizzetto *et al,* 1979), and by enzymeimmunoassay in Dublin (Shattock and Morgan, 1983).

Liver biopsies were performed using a Menghini needle. Histological diagnosis was made in accordance with the criteria suggested in a Review by an International Group (1977). The liver histology of those with serum evidence of delta infection was compared with that of those without serum evidence of delta infection.

---

* Requests for Reprints to Dr. John Fielding, The Charitable Infirmary, Jervis St., Dublin 1.

This article is a reproduction of that published in: Irish Journal of Medical Science, 153(1), 1984, pp.17-19. Pagination may not match that of the original.

Results

Of the twenty-seven patients studied thirteen had serological evidence of delta infection; fourteen did not have delta antigen or anti delta antibody. The mean age, sex and mean duration of intravenous abuse in both groups are tabulated in Table I. Of the thirteen delta positive patients twelve were HB_sAg positive and one had anto HB_s. Of the fourteen delta negative patients ten were HB_sAg positive, three were HB_sAg negative but had anti HB_s and one had no marker of HBV detected in her serum.

TABLE I

Age, sex and duration of abuse in parenteral drug abusers.

Patient group	Number of Patients	Mean age	Sex	Mean duration of i.v. abuse
Delta infection	13	20.5 years (Range 16-27 years)	11 Male 2 Female	37.5 months (Range 24-120 months)
No Evidence of Delta infection	14	21 years (Range 12-29 years)	11 Male 3 Female	32 months (Range 6-84 months)

Of the thirteen delta positive patients four had chronic active hepatitis, seven had chronic persistent hepatitis and two had acute hepatitis. No patient in the delta negative group had chronic active hepatitis; eleven had chronic persistent hepatitis and three had acute hepatitis. These findings are summarised in Table II.

Discussion

Serological evidence of delta infection was found in thirteen of 27 drug abusers tested. Four of these patients had evidence

TABLE II

Histology in delta positive and delta negative patients.

Liver histology	Delta positive patients 13	Delta negative patients 14
Chronic active hepatitis	4	0
Chronic persistent Hepatitis	7	11
Acute hepatitis	2	3

of chronic active hepatitis. None of the fourteen patients without evidence of delta infection had histologically diagnosed chronic active hepatitis. Although the numbers involved were small, both groups appear comparable with regard to age, sex and duration of parenteral abuse. Thus delta agent infection may be associated with the progression of intravenous drug abuse associated liver disease to chronic active hepatitis.

These findings are similar to those of Rizzetto and his colleagues (1979) who documented the histological findings in a group of Italian non drug abusers with anti delta antibody in their serum. Of forty-two patients thirty-five had active liver disease which progressed to cirrhosis in nine and hepatoma in three. Five patients had chronic persistent hepatitis. In the same paper he records that of seven patients from New Jersey with anti delta antibody five had biopsy proven chronic active liver disease and one had chronic active liver disease diagnosed on the basis of a six year history of raised enzymes. Unlike the Italians,

these patients from New Jersey were either parenteral drug abusers or haemophiliacs who required multiple blood transfusions. The frequency of chronic active hepatitis among Rizzetto's patients was much higher than that found in either group documented in this study; the majority of our patients had chronic persistent hepatitis. Whilst there is a continuum of histological abnormality between chronic active and chronic active and chronic persistent hepatitis (Scheuer, 1977), the precise diagnosis usually becomes apparent on repeat biopsy six months after the initial biopsy. All four patients with chronic hepatitis in this study had at least two liver biopsies with evidence of chronic active hepatitis.

Parenteral drug abusers have a high risk of acquiring delta infection (Raimondo *et al,* 1982) and because of decreased immunocompetence may have difficulty clearing delta infection in the same way as they have difficulty clearing delta infection in the same way as they HB_sAg (Editorial, Lancet 1982). Parenteral drug abusers may thus be at increased risk of developing chronic active hepatitis. Whether the delta infection also increases the risk of the later development of hepatoma as suggested by Rizzetto *el al* (1979) can only be answered by a long term follow up study.

References

Editorial. 1982. Delta agent—A virus in disguise ? Lancet i, 259-260.

Raimondo, G., Smedile, A., Gallo. L., Balbo, A.,

Ponzetto, A. and Rizzetto, M. 1982. Multicentre study of prevalence of HBV associated delta infection and liver disease in drug addicts. Lancet i, 249-251.

Review by an International Group. 1977. Acute and chronic hepatitis revisited. Lancet ii, 914-919.

Rizzetto, M., Canese, M. G., Arico. S., Crivelli, O., Trepo, C. N., Borino, F. Verme, G. 1977. Immunofluirescence detection of a new antigen antibody system (Delta/Anti Delta) Associated with the hepatitis B virus in the liver and the serum of HB_sAg carriets. Gut 18, 997-1003.

Rizzetto, M., Canese, M. G., Gerin. J. L., London, W. T., Sly. D. L. and Purcell, R. H. 1980. Transmission of hepatitis B virus associated delta antigen to chimpanzees. J. Infec. Dis. 141, 590-602.

Rizzetto. M., Shik, J. W. K., Gocke, D. J., Purcell, R. H., Verme, G. and Gerin, J. L. 1979. Incidence and significance of antibodies to delta antigen in hepatitis B virus infection. Lancet ii. 986-990.

Scheuer. 1977. Chronic hepatitis. A problem for the pathologist. Histopathology 1, 5-19.

Shattock, A. G. 1974. Hepatitis associated (Australia) antigen in Republic of Ireland. A preliminary report. Irish J. Med. Sci. 143, 162-167.

Shattock, A. G. 1982. Unpublished work—Department of Medical Microbiology, University College, Dublin.

Shattock, A. G. and Morgan, B. B. 1983. Sensitive enzyme-immunoassay for the detection of delta antigen and anti delta using serum as the source of delta antigen. J. Med. Virology, in press.