Syphilis and chronic liver disease

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With the advent of the antibiotic era and the improvement in serological diagnostic techniques, there has obviously been a need to reappraise the clinical aspects of syphilis. Karmi, Thirkettle, and Read (1969) reported the results of such a study on the relationship between patients with cirrhosis and syphilitic infection. For many years the consensus of opinion was that a relatively high proportion of patients with cirrhosis also had syphilis (Stokes, Beerman, and Ingraham, 1944). More recently Karmi and others (1969) summarized the results of ten series and came to the conclusion that 10 to 20 per cent. of patients with cirrhosis were likely to have syphilis. The great bulk of the clinical cases on which these studies were based had in fact presented before the advent of antibiotic therapy, but Karmi and his associates found the incidence of syphilis among patients with cirrhosis of the liver in the Bristol area to be still in the region of 10 per cent., 20 years after the introduction of penicillin therapy. We felt that it would be interesting to carry out a further evaluation of the relationship between syphilis and cirrhosis in our population.

Patients and methods

A total of 49 patients was investigated. They had been attending the liver clinic at the Royal Victoria

Hospital, Belfast, and their hepatic function was already being investigated by one of us (V.J.M.). A Wassermann reaction and Kahn, Reiter protein complement-fixation, and FTA-ABS tests were carried out on serological samples from all patients. Any patient who had clinical, epidemiological, or serological evidence of possible syphilitic infection had further blood samples tested at a reference laboratory. The FTA-ABS test was performed as previously described (Mahoney, Harris, McCann, Kennedy, and Dougan, 1972). As a check on our own techniques, samples from ten other patients chosen at random were also sent to the reference laboratory. Their results were in complete agreement with ours.

Results

Table I shows that there appears to be a preponderance of patients with active chronic hepatitis in the series. This reflects the clinical interests of the gastroenterologists involved. Of the 49 patients six had homogeneous positive FTA-ABS tests. Three of these six had positive TPI and RPCF tests. Two of the six who had positive FTA-ABS tests but no other clinical, epidemiological, or serological evidence of syphilis have been previously reported as examples of probable false positive FTA-ABS tests (Harris, McCann, Kennedy, and Fulton, 1974). The relevant data on the remaining four patients is outlined in Table II (overleaf).

Received for publication October 16, 1973
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TABLE I *Results of tests for syphilis in 49 patients with chronic liver disease*

Diagnosis	Sex			FTA-ABS		TPI		RPCF	
	Male	Female	Total	Positive	Negative	Positive	Negative	Positive	Negative
Active chronic hepatitis	7	17	24	0	24			0	24
Cryptogenic cirrhosis	3	6	9	1 ^a	8	0	1	0	9
Alcoholic cirrhosis	9	2	11	4	7	3	1	4	7
Primary biliary cirrhosis	0	2	2	0	2			0	2
Cirrhosis and rheumatoid arthritis	0	3	3	1	2	0	1	0	3
Total chronic liver diseases	19	30	49	6	43	3	3	4	45

^aThis patient also had a history of syphilis

TABLE II *Clinical and serological particulars of four men found to have definite syphilis*

Patient no.	Serological tests			Previously treated	Clinical syphilis	History of syphilis
	TPI	FTA-ABS	RPCF			
1	Neg.	Pos.	Neg.	Yes ^a	No evidence	Yes ^a
2	Pos.	Pos.	Pos.	No	No evidence	No
3	Pos.	Pos.	Pos.	No	No evidence	No
4	Pos.	Pos.	Pos.	Yes	No evidence	Yes

^aThis patient appeared to be unaware that he had received bismuth injections for syphilis and the information was obtained from the records of another hospital

Discussion

There is now an increasing awareness of the relationship between sexually-transmitted disease and overt hepatic disease. While the classical hepar lobatum is now rare, there have recently been reports describing the hepatitis occurring during secondary syphilis as being associated with an abnormally high alkaline phosphatase level and a clinical picture reminiscent of infective hepatitis (Lee, Thornton, and Conn, 1971). There may be concurrent nephrosis or some other manifestation of secondary syphilis (McCracken, Hall, and Pierce, 1969). The histological picture appears to be distinct from that of infectious hepatitis (Baker, Kaplan, Wolfe, and McGowan, 1971) and the condition responds extremely well to penicillin therapy (Sobel and Wolf, 1972). Hepatitis B has recently been shown to behave in an epidemiological manner consistent with its being a sexually-transmitted disease (Fulford, Dane, Catterall, Woof, and Denning 1973). Cytomegalovirus infection, which appears to behave in a similar manner (Harris, 1974), has been associated with hepatitis (Walker and Tobin, 1970). Perihepatitis can occur during gonococcal septicaemia, posing a difficult diagnostic problem (Kimball and Knee, 1970) unless other manifestations of the septicaemic process are also present.

Many workers have felt that cirrhosis associated with syphilis was probably a sequel of 'syringe jaundice'. A more likely explanation in the light of recent knowledge would appear to be that cirrhosis will occur as a sequel of hepatitis in certain patients, and that such patients may have developed the hepatitis as the result of sexual transmission of the causative agent. They may also have acquired syphilis at the same time or at another time. It is well known that patients with one sexually-transmitted disease have a greater than average chance of also having another such disease.

It is relevant that only one of the four patients who definitely had syphilis (Table II) was aware of the diagnosis, and that none of the four had any characteristic clinical signs indicating such infection. It would appear, therefore, that there is still a

relationship between chronic liver disease and syphilis, but it cannot be easily ascertained whether this is a direct or an indirect relationship. Table I clearly shows that the patients diagnosed as having definite syphilis were thought to have either cryptogenic or alcoholic cirrhosis. If the patients with active chronic hepatitis and primary biliary cirrhosis are omitted, the incidence of definite syphilis among the remaining patients would be four out of 23, *i.e.* 17 per cent. Although the numbers involved are small, it is of significance that both Karmi and others (1969) and ourselves have observed that all the patients with both syphilis and cirrhosis are male. When the two series are considered together, ten men among 98 patients with chronic liver disease were found to have syphilis, *i.e.* 10 per cent.

Certain of the hepatic lesions of acute virus hepatitis can progress to cirrhosis (Prior and Friedman, 1973) and most probably some of the ten men acquired their cirrhosis in this manner. Little appears to be known of the after-effects of adult hepatitis due to cytomegalovirus or of hepatic involvement during gonococcal septicaemia. Whatever the cause of the association of syphilis with cirrhosis, routine serological testing of all cirrhotic patients, particularly if they are male, is warranted.

Summary

A series of 49 patients with chronic hepatic disease was investigated for evidence of syphilitic infection. Four male patients were found to have definite syphilis. The possible reasons for the association are considered. The relationships between chronic hepatic disease and sexually-transmitted diseases, such as syphilis, hepatitis B, disseminated gonococcal infection, and cytomegalovirus infection, are discussed.

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Syphilis et affection hépatique chronique

SOMMAIRE

On recherche la preuve d'une infection syphilitique sur une série de 49 malades atteints de maladie hépatite chronique. On trouva des signes établis de syphilis chez quatre malades hommes. On considère les raisons possibles de cette association. On discute la relation entre une maladie hépatique chronique et les malaises sexuellement transmises telles que la syphilis, l'hépatite B, une infection gonococcique généralisée et une atteinte à cytomégalo-virus.