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Liver histopathology in patients with concurrent chronic hepatitis C and HIV infection

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Abstract To investigate the influence of human immunodeficiency virus (HIV) coinfection on preexisting long-term chronic C hepatitis (HCV) 68 liver biopsies from 22 HIV/HCV-coinfected, 13 HIV- and 33 HCV-monoinfected patients and 71 livers obtained at autopsy from 26 HIV/HCV-coinfected and 45 HIV-monoinfected patients were studied by histo- and immunohistochemistry. All HIV patients had reached the advanced stage of immunodeficiency (stage III CDC), except for 3 haemophiliacs (stage II CDC). HCV infection was associated with a higher degree of portal, periportal and lobular inflammation – regardless of whether there was concurrent HIV infection. HIV/HCV coinfection was associated with a significantly higher rate of granulocytic cholangiolitis than HCV and HIV monoinfection ($P < 0.05$), a histological feature uncommon in C hepatitis. In HIV/HCV coinfection cholestasis was a predominant histological feature. HCV monoinfection and HCV/HIV coinfection were associated with the highest fibrosis index. In HIV/HCV coinfection centrilobular fibrosis was significantly more marked than in HCV monoinfection ($P < 0.05$), suggesting an HIV-associated fibrogenic effect. Patients with chronic C hepatitis showed a significantly increased rate of posthepatitic cirrhosis compared with the patients without HCV infection ($P < 0.05$). At autopsy, 10 of the 20 HIV/HCV-coinfected haemophiliacs had developed cirrhosis because of chronic C hepatitis, whereas cirrhosis was found in only 2 of 6 HIV/HCV-coinfected non-haemophiliacs (1 case of chronic B and C hepatitis, and 1 case of chronic alcohol abuse). No cirrhosis was observed in the 45 autopsy patients with HIV monoinfection. The findings suggest that HIV coinfection aggravates the course of preceding long-term chronic C hepatitis by a more marked (centrilobular) fibrosis. HIV/HCV-coinfected patients are threatened by a higher rate of posthepatitic cirrhosis – particularly in multitransfused haemophiliacs – and cholestatic hepatopathy.

Key words Human immunodeficiency virus · Liver · Hepatitis C · Haemophilia

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Introduction

Since hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are transmitted by similar routes [39], many haemophiliacs substituted with clotting factor concentrates were infected with both HIV and HCV in the years before 1984, when donor screening and viral inactivation procedures were not carried out [1, 2, 8, 14, 17]. The effects of HIV coinfection on preexisting hepatitis C virus-related liver disease have not been extensively studied histomorphologically. On the basis of preliminary sporadic observations, an accelerated progression of chronic C hepatitis – followed by symptomatic liver cirrhosis – has been suggested in HIV coinfection [27, 28]. Recent clinical cohort studies revealed that multitransfused HCV/HIV-coinfected adult haemophiliacs are at a considerably higher risk for liver failure, with a cumulative incidence of 9% after 10 years of HIV infection, than HCV-monoinfected individuals [14]. HCV-RNA levels were significantly higher in HIV-positive (HIV+) than HIV-negative (HIV–) multitransfused haemophiliacs, suggesting an increased HCV replication rate in HIV coinfection [15]. The aim of the present study was to find out whether HIV coinfection alters the histopathological findings in liver disease caused by chronic HCV infection. Differences between haemophiliacs and non-haemophiliacs were also sought.

Materials

A total of 68 liver biopsies (1989–1995) were studied (from 56 men and 12 women, 12–67 years, mean 37 years, of age): 22 patients had HIV/HCV coinfection (21 men and 1 woman, ages 22–67 years, mean 34 years), 13 patients had HIV monoinfection (12 men and 1 woman, 24–54, mean 36) and 33 patients had HCV monoinfection (23 men and 10 women, 12–59 years, mean 42 years).

Table 1 Epidemiological data of patients with HIV/HCV coinfection and with HIV or HCV monoinfection (68 liver biopsies and 71 autopsies)

	HIV+HCV+ (n=22)	HIV+ (n=13)	HCV+ (n=33)
Biopsies			
Age (mean)	22–67 (34)	24–54 (36)	12–59 (42)
Sex (m/f)	21/1	12/1	23/10
Autopsies	(n=26)	(n=45)	
Age (mean)	23–52 (36)	24–62 (37)	
Sex (m/f)	25/1	42/3	

The group of HIV/HCV-coinfected patients (n=22) consisted of 15 haemophiliacs (14 with haemophilia A, 1 with haemophilia; 22–49 years, mean 30 years) and 7 non-haemophiliacs (28–67 years, mean 39 years). All HIV+/HCV+ haemophiliacs were anti-HBs positive without any evidence of chronic B hepatitis (HBsAg-negative, HBeAg-negative). Two HIV+/HCV+ non-haemophilicas were also anti-HBs positive, and 1 suffered from chronic B hepatitis. Of the 13 HIV-monoinfected patients, 3 – all non-haemophiliacs – were anti-HBs positive, and 1 of these had developed chronic B hepatitis.

The 33 patients with HCV monoinfection were 20 haemophiliacs (haemophilia A; 12–58 years, mean 41 years) and 13 non-haemophiliacs (24–59 years, mean 43 years). There were 15 haemophiliac patients who were anti-HBs positive, and 1 suffered from chronic B hepatitis. Only one non-haemophiliac was positive for anti-HBs antibodies (Table 1).

The time from serological diagnosis of HIV infection to biopsy ranged from 6 months to 12 years (mean 5.4 years). All HIV patients were obviously in the advanced stage of immunodeficiency (stage III according to the Center for Disease Control, CDC), with CD4+ cell counts of <100/mm^3 in the majority of cases (30) and between 100 and 200/mm^3 in 3 cases, except for 2 haemophiliacs

Table 2 Histomorphological scoring parameters

1. Modified Knodell's histological activity index (HAI)

Portal inflammation (range 0–4)	Score
None	0
Mild – sprinkling of inflammatory cells in <1/3 of portal tracts (PT)	1
Mild to moderate – confluent inflammatory cells in about 1/3 of PT	2
Moderate – numerous inflammatory cells in 1/3–2/3 of PT	3
Marked – dense inflammatory infiltrates in >2/3 of PT	4

Periportal piecemeal necrosis (PMN) (range 0–6)	Score
None	0
Minimal – one or few tongues in single PT	1
Mild – few tongues in <1/3 of PT	2
Moderate – piecemeal necrosis involving <50% of circumference of most PT	3
Marked – PMN involving >50% of circumference of most PT	4
Severe – portal-portal bridges of PMN	5
Very severe – plus septal PMN	6

Lobular necro-inflammatory changes (range 0–10)	Score
None	0
Mild – spotty/confluent necrosis/inflammation (SN/I) in <1/3 of lobules	1
Moderate – SN/I in 1/3–2/3 of lobules	3
Marked – SN/I in >2/3 of lobules and/or bridging portal-central necrosis	6
Severe – pan- or multilobular confluent necrosis	10

Total HAI score (range 0–20)

2. Lymphoid follicles (range 0–3)

	Score
None	0
Mild – <1/3 of PT	1
Moderate – <2/3 of PT	2
Severe – >2/3 of PT	3

3. Fibrosis index (range 0–5)

	Score
None	0
Portal fibrosis only	1
Beginning periportal fibrosis	2
Septal fibrosis	3
Incomplete cirrhosis	4
Complete cirrhosis	5

4. Centrilobular fibrosis (range 0–3)

	Score
None	0
Mild	1
Moderate	2
Severe	3

5. Cholangiolitis absent/present 0/1

6. Cholestasis absent/present 0/1

in stage II (CDC), who had CD4+ cell counts between 200 and 400/mm^3. HCV infection (i.e., non-A, non-B hepatitis before 1989) was documented for at least 15 years in haemophiliacs and for at least 10 years in non-haemophiliacs.

Liver specimens from autopsies of HIV-infected patients (1982–1995) were studied (67 men, 4 women, 23–62 years, mean 37 years). Risk factors were haemophilia (20 cases), homosexuality (23 cases) and intravenous drug abuse (4 cases). In 24 patients a risk factor was not identified.

The autopsy patients included 26 who were HIV/HCV coinfected (25 men and 1 women, 23–52 years, mean 36 years): 20 haemophiliacs (23–49 years, mean 34 years) and 6 non-haemophiliacs (24–52 years, mean 42 years). All haemophiliacs showed anti-HBs antibodies and no evidence of chronic HBV infection or chronic B hepatitis. Three non-haemophiliacs had a chronic HBV infection proved serologically (anti-HBs antibody and HBs/HBe antigen positive).

Autopsy showed HIV monoinfection in 45 cases (42 men and 3 women, 24–62 years, mean 37 years). These patients included 8 who were anti-Hbs positive and one who had suffered from chronic HBV infection (Table 1).

HIV infection was documented serologically 4 weeks to 9 years (mean 4.5 years) before death (haemophiliacs 2–9 years, mean 6.2 years; homosexuals 4 weeks to 9 years, mean 3.4 years; drug addicts 3–7 years, mean 5 years; and patients without any risk factor 1–7 years, mean 3.8 years). All autopsy patients but 1 died in an advanced stage of immunodeficiency (stage III CDC) with a CD4+ cell count <100/mm^3; 1 haemophiliac (stage II CDC) had a CD4+ cell count >200/mm^3.

HCV infection was documented for at least 12 years in haemophiliacs and for at least 10 years in non-haemophiliacs.

Methods

All specimens were fixed in 4% buffered formaldehyde and embedded in paraffin. For routine staining hematoxylin and eosin, Verhoeff's-van-Gieson, Sirius red, iron stain, periodic acid-Schiff reagence (PAS) and Leder's chloracetate-esterase were used. The immunohistochemical reactions were detected with the standard avidin-biotin-peroxidase (ABC) method using a polyclonal antibody to hepatitis B core antigen (HBcAg), a monoclonal antibody directed to the hepatitis B surface (HBsAg) antigen (Dakopatts, Copenhagen, Denmark) and a polyclonal antibody against ubiquitinized proteins (Dakopatts) for the detection of Mallory hyalin.

A modified Knodell's histological activity index (HAI) [22] was used to define the grade of inflammation and the extent of fibrosis (Table 2). Additional histological variables (specified in Table 2) were assessed separately and graded semiquantitatively. The histomorphological analysis was done by two independent observers.

The comprehensive histological diagnosis was made in accordance with the modified international classification [10, 35]. The mean scores for each variable of the different subgroups of biopsies and autopsies were evaluated statistically by the Kruskall-Wallis Test or the Chi-square test, P-values lower than 0.05 being considered significant.

Serological HCV assays were performed by a "second generation" enzyme-linked immunosorbent assay (ELISA, Ortho) and/or a four-antigen recombinant immunoblot assay (RIBA 2, Chiron, Emeryville, Calif.). HCV-RNA was tested by the polymerase chain reaction (PCR).

Results

In both biopsies and autopsy specimens, HCV infection was associated with significantly ($P < 0.05$) more severe portal, periportal and lobular inflammation (as summed up in the HAI) than was seen in specimens from patients without HCV infection – whether or not there was HIV coinfection.

Lymphoid aggregates or follicles (Fig. 1a) were observed predominantly in the presence of HCV monoinfection: in 20 cases to a mild degree, to a moderate degree in 4 and in 1 patient to a severe degree (Table 3). These occurred only in isolated (3) patients with HIV co- or monoinfection and then to a mild degree. Lymphoid aggregates or follicles were not observed in any autopsy case (Table 4). However, in HCV infection with concurrent HIV infection the portal and periportal inflammatory infiltrates contained far more neutrophil granulocytes (Fig. 1b) and fewer lymphocytes than the infiltrates in HCV monoinfections (Tables 3, 4).

There was no significant difference in inflammatory activity between haemophiliacs and non-haemophiliacs.

In both biopsy and autopsy specimens, HCV infection was accompanied by a significantly higher fibrosis index ($P < 0.05$) than was seen in cases without C hepatitis (Tables 3, 4). The fibrosis index was also higher (not significant) in HCV-positive haemophiliacs than in HCV-positive non-haemophiliacs – regardless of whether or not HIV infection was also present.

In both biopsies and autopsies centrilobular fibrosis (Fig. 1c) was also significantly ($P < 0.05$) more pronounced in cases with HCV infection than in those without HCV infection (Tables 3, 4). In addition, in the biopsies from HIV/HCV-coinfected haemophiliacs there was significantly ($P < 0.05$) more marked centrilobular fibrosis than in those from haemophiliacs with HCV monoinfection.

In the biopsies the rate of posthepatitic cirrhosis (Fig. 1d) caused by chronic C hepatitis was similar with HIV/HCV coinfection and HCV monoinfection, and it was observed predominantly in haemophiliacs (HIV/HCV, 3/15; HCV, 6/20). Only 1 non-haemophiliac with HIV/HCV coinfection developed posthepatitic cirrhosis as a result of C hepatitis (in combination with chronic hepatitis B infection) (Table 3).

The high rate of posthepatitic cirrhosis with HIV/HCV coinfection – particularly in haemophiliacs – was much more impressive in the autopsy specimens. HIV/HCV coinfection was accompanied by a very high rate of posthepatitic cirrhosis (46.2%), whereas none of the patients without HCV infection had died with liver cirrhosis. Half (10/20) of all haemophiliacs who had died were found at autopsy to have developed posthepatitic cirrhosis, caused by chronic C hepatitis (8) or by chronic C hepatitis in combination with chronic B hepatitis (2). In 2 cases the cirrhosis of the liver had already been documented by a preceding biopsy. Liver failure attributable to liver cirrhosis was the leading cause of death in 6 haemophiliacs. In contrast, only 2 of the HCV-infected non-haemophiliacs suffered from posthepatitic cirrhosis; this was due to C hepatitis in combination with chronic B hepatitis in 1 case and to chronic alcohol abuse in the other (Table 4).

In both biopsy and autopsy specimens, granulocytic cholangiolitis (Fig. 1e) and intracanalicular and intracellular cholestasis (Fig. 1e) were most frequently observed in the presence of HIV/HCV coinfection, being significantly ($P < 0.05$) more frequent than with HIV or HCV

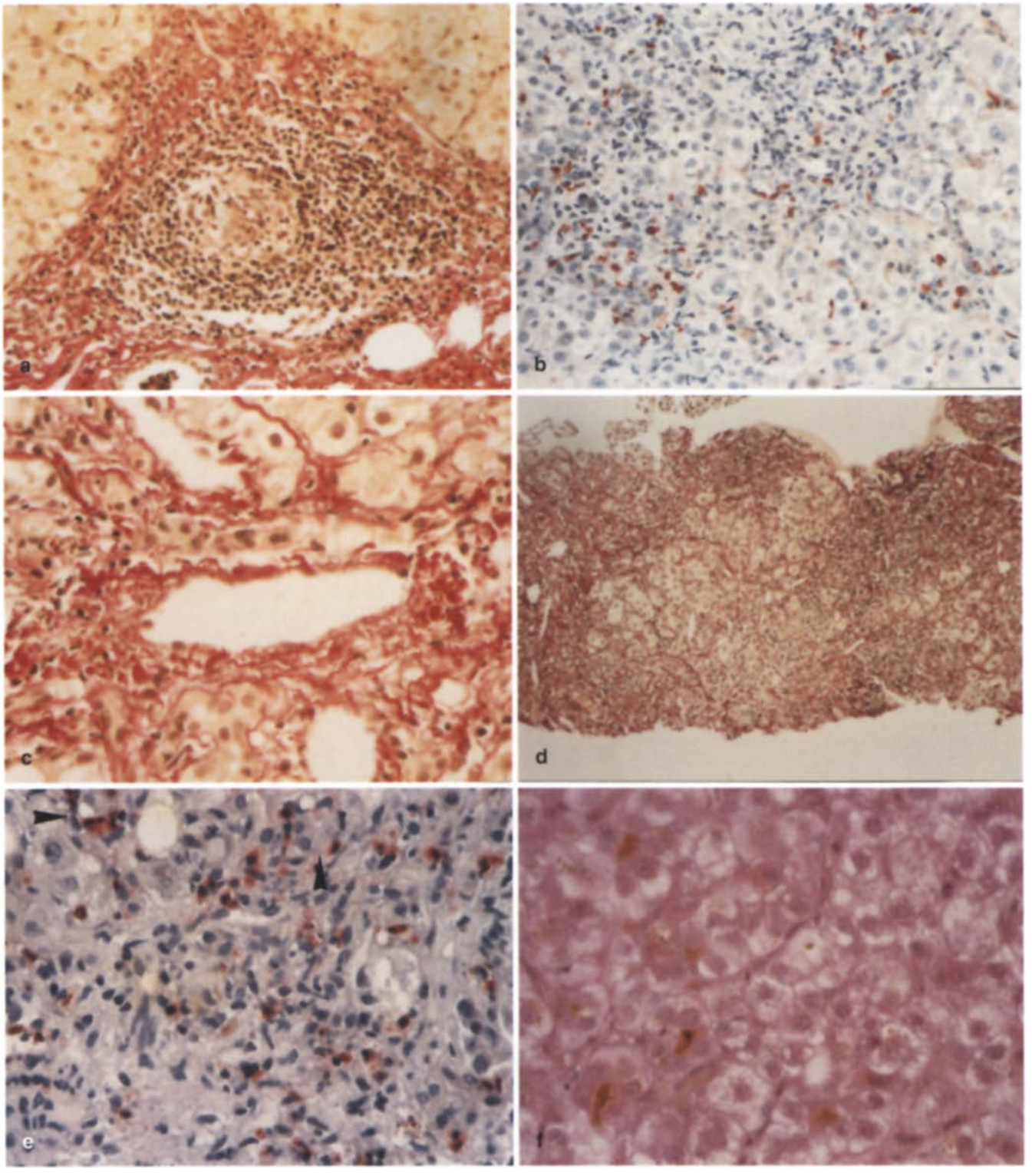

Fig. 1a–f Chronic hepatitis C with concurrent HIV infection. **a** Mild chronic hepatitis C with periportal fibrosis and portal lymphoid follicle. Verhoeff's van Gieson, ×25. **b** Predominantly granulocytic infiltration of the portal and periportal region in chronic HCV/HIV coinfection. Leder's chloracetate-esterase, ×25. **c** Centrilobular fibrosis in HCV/HIV coinfection. Verhoeff's van Gieson, ×40. **d** Progressive cirrhosis in chronic HCV/HIV coinfection with pericellular fibrosis. Verhoeff's van Gieson, ×10. **e** Predominantly granulocytic infiltration of the portal and periportal region with discrete granulocytic cholangiolitis (*arrows*). Leder's chloracetate-esterase, ×40. **f** Severe intracanalicular and intracellular cholestasis in chronic HCV/HIV coinfection. H&E, ×40

monoinfection. There was no difference between haemophiliacs and non-haemophiliacs in this (Tables 3, 4). Cholangitis was not observed in any case.

The degree of cholestasis did not seem to be influenced by fibrosis. This was exemplified in a 29-year-old HIV/HCV-coinfected biopsy patient, who developed liver failure in combination with severe cholestasis, whereas liver fibrosis was observed only to a very mild degree.

Liver involvement in disseminated opportunistic infections was seen in specimens from 15 HIV patients (7

Table 3 Comparative histological analysis of 68 liver biopsies of patients with HIV/HCV coinfection and with HIV or HCV monoinfection

Histology (range)	HIV+ HCV+ (*n*=22)	HIV+ (*n*=13)	HCV+ (*n*=33)
Inflammation			
Portal (0–4)	2*	1*	3*
Periportal (0–6)	1*	0*	1
Lobular (0–10)	2*	0*	1
HAI score (0–20)[a]	5*	1*	5*
Lymphoid follicles (0–3)	0	0	1
Fibrosis (0–5)	2*	0	2*
Fibrosis centrilobular (0–3)	2*	1*	
Cirrhosis	4 (18.2%)*	0 (0%)*	6 (18.2%)*
Cholangiolitis	10 (45.5%)*	0 (0%)*	4 (12.1%)*
Cholestasis	13 (59.1%)*	3 (23.1%)*	1 (3%)*

* $P < 0.05$ (by Kruskall-Wallis test)
[a] Modified Knodell score; median are listed

Table 4 Comparative histological analysis of 71 liver autopsies of patients with HIV/HCV coinfection and HIV monoinfection

Histology (range)	HIV+ HCV+ (*n*=26)	HIV+ (*n*=45)
Inflammation		
Portal (0–4)	2*	1*
Periportal (0–6)	1*	0*
Lobular (0–10)	1*	0*
HAI score (0–20)[a]	5*	1*
Lymphoid follicles (0–3)	0	0
Fibrosis (0–5)	3*	1*
Fibrosis, centrilobular (0–3)	2*	1*
Cirrhosis	12 (46.2%)*	0 (0%)*
Cholangiolitis	18 (69.2%)*	2 (4.4%)*
Cholestasis	22 (84.6%)*	13 (28.9%)*

* $P<0.05$ (Kruskall-Wallis test)
[a] Modified Knodell score; medians are listed

biopsies and 8 autopsies). The pathogens included mycobacteria (*Mycobacterium avium intracellulare* in 5 biopsies and 3 autopsies, and 2 biopsies with *Mycobacterium tuberculosis*); cytomegaloviruses and *Pneumocystis* (2 autopsies each) and *Cryptococcus* (1 autopsy) were also seen, but microsporidiosis was not observed. Liver infiltrates of HIV-associated neoplasms occurred in 4 cases of Kaposi's sarcoma (1 biopsy and 3 autopsies) and 1 of large B-cell lymphoma (autopsy). In 3 biopsies toxic liver damage due to antibiotic therapy and in 1 biopsy panarteriitis nodosa with liver involvement was observed. Intracytoplasmatic Mallory's hyalin, identified immunohistochemically by antibody against ubiquitinized proteins, was detected only in very few hepatocytes of 1 biopsy and 4 autopsies (1 with clinically documented chronic alcohol abuse and subsequent liver cirrhosis).

Steatosis of a mild to moderate degree was a constant morphological finding in biopsies and autopsies, with no significant difference between the subgroups.

In our study HIV-monoinfected patients showed a significantly ($P < 0.05$) higher liver weight (mean 1900 g, SEM 535 g) than HIV/HCV-coinfected patients (mean weight 1595 g, SEM 322 g).

Discussion

After cloning of hepatitis C virus (HCV) RNA and the development of an assay to detect antibodies against a major gene product of that virus [9–11], it was shown that 60–90% of patients suffering from sporadic, post-transfusional and parenterally transmitted non-A non-B hepatitis were positive for serum markers of HCV infection [11]. HCV infection is a major cause of virally induced chronic hepatitis, particularly in haemophiliacs. Up to 90% of this risk group have HCV antibodies [3, 9, 12–21]. At least 50% of those infected with HCV have biochemical evidence of chronic hepatitis, and up to 20% develop chronic active hepatitis or cirrhosis over extended periods of follow-up [3, 8, 15, 19, 22, 23]. Systematic histopathological studies on a possible additional effect of HIV infection on the course of HCV-induced liver disease have not been reported.

The present comparative analysis of the well-defined subgroups – HIV positive or negative, with or without HCV coinfection, and with or without haemophilia – allowed us to work out the effects of these different parameters on liver histomorphology.

As was to be expected, patients with HCV infection with or without HIV coinfection show significantly greater inflammatory activity in the portal fields, the mesenchymal/parenchymal interface and the lobules than do patients with HIV infection alone.

In the liver biopsies under study, HCV-infected patients with HIV coinfection showed slightly less intense portal lymphoid inflammatory infiltrates than their HIV-negative counterparts and did not have lymphoid portal aggregates or follicles, which are a characteristic and frequent histopathological finding in chronic C hepatitis [21, 24–26, 35]. This reduction of lymphoid infiltrates may be due to the advanced disturbance of immune response in the late stage of acquired immunodeficiency in these patients with CD4+ cell counts below 100/mm^3 in nearly all cases. Furthermore, these findings underline the supposition that the HCV-related hepatitis is based mainly on immunomediated mechanisms [27, 28], by analogy with chronic B hepatitis with and without HIV coinfection [7, 29–31]. In our groups the risk factor of haemophilia obviously had no significant influence on the inflammatory activity caused by HCV infection.

Remarkably, the portal and periportal infiltrates in HIV/HCV-coinfected patients were different from those in HIV-negative patients not only quantitatively (in their score values) but also qualitatively (in their cellular components). In contrast to the patients with HCV monoinfection, the HIV/HCV-coinfected patients showed a predominantly granulocytic portal infiltration in combination with a mild granulocytic cholangiolitis, which is an unusual pattern of inflammation in classic chronic active C hepatitis [20, 21, 24, 33, 35]. This finding suggests a yet unexplained HIV-associated effect on the inflammatory pattern in chronic C hepatitis. Cholestasis might be responsible in part for the granulocytic cholangiolitis [32]. In some of the autopsy specimens in which ductular cholestasis was found the cholangiolitis might have been caused by underlying sepsis.

Comparative morphological analysis of the different biopsy subgroups revealed that progressing HCV infection is mainly responsible for the degree of liver fibrosis in HIV/HCV-coinfected patients. The fibrosis index in chronic hepatitis C was slightly higher in haemophiliacs than in non-haemophiliacs. This finding might be due to the longer course of the HCV infection in the haemophiliacs (>15 years vs >10 years in non-haemophiliacs), and perhaps to different modes of infection (reinfections in haemophiliacs, particularly by non-heat-treated coagulation factor concentrates with high viral burden and different HCV subtypes).

The significantly more pronounced reticular centrilobular fibrosis with HIV/HCV coinfection than with HCV monoinfection in the biopsy group is of special interest, since this pattern of fibrosis is unusual in classic chronic C hepatitis. It suggests an independent fibrogenic effect of HIV infection, which might be one possible causative factor in the acceleration of liver disease in the final stage of HIV infection.

The progression of fibrosis in HIV/HCV coinfected patients is reflected impressively in autopsies. Half the autopsied HIV/HCV-coinfected haemophiliacs had developed posthepatitic cirrhosis, which was the leading cause of death in the majority (6/10) of cases. The duration of HCV and HIV infection in the haemophiliacs of our study is in good agreement with the data from the prospective clinical cohort study of Eyster et al. [14], which showed fatal liver failure in 9% of HCV/HIV-coinfected haemophiliacs 10–20 years after HCV infection. From our morphological findings, it seems that fatal liver failure in HIV/HCV-coinfected haemophiliacs may be explained by cirrhosis resulting from chronic C hepatitis, possibly accelerated by the fibrogenic effect of HIV infection in the final stages of the disease. In this context, chronic hepatitis B infection cannot be regarded as a causative factor in inflammation, fibrosis and cirrhosis, because only 1 non-haemophiliac in the biopsy group and 3 non-haemophiliacs in the autopsy group suffered from chronic B hepatitis. An influence of other mechanisms, such as differing therapeutic regimens, opportunistic infections or malignancies, did not appear to be relevant to the causation of the progressive inflammatory and fibrosing liver disease observed.

Cholestasis, which was present in the majority of our HIV/HCV-coinfected patients, is not a usual finding in C hepatitis [20, 21, 24, 26, 35]. According to recent clinical observations [34] severe cholestasis in HIV/HCV-coinfected immunodeficient patients indicates a high risk of developing liver failure within a short period of time. The incidence and degree of cholestasis does not seem to be associated with progressive inflammatory changes or advanced fibrosis. A possible relation between cholestasis and the degree of immunodeficiency could be assumed from biopsy and autopsy findings in a HIV/HCV coinfected homosexual (CD4+ cell count <50/mm^3) who presented clinically with icterus and died shortly afterwards of liver failure. Prefinal biopsy and autopsy revealed marked cholestasis but only minimal inflammatory changes and almost no fibrosis of the liver. Serious cholestatic HCV-related liver disease can develop under different conditions of immunodeficiency. Fatal hepatitis C infection and cholestatic hepatopathy have been described in heart transplant recipients receiving heavily immunosuppressive therapy [36] and in patients with hereditary primary hypogammaglobulinaemia [37]. These findings underline the accelerating effect of severe immunodeficiency on the course of HCV infection. As in hepatitis B virus infection, the replication rate of HCV is accelerated in the late stage of concomitant HIV infection [6, 7]. A direct cytopathic effect of HCV on the hepatocytes in immunodeficiency [4, 5, 6, 34, 38] might result in infection of degenerating liver cells by HCV. However, up to now a relevant cytopathic effect on HCV antigens expressing hepatocytes has not been demonstrated immunohistochemically [39].

HIV-monoinfected livers examined at autopsy had a significantly greater weight than did those affected by HIV/HCV coinfection. These findings are in contrast to those in a recent report [14], according to which hepatomegaly was not found with HIV infection but was present in the majority of cases of HIV/HCV coinfection.

In summary, histomorphological analysis of liver tissue from HIV/HCV-coinfected and HIV- or HCV-monoinfected patients clearly shows that preceding long-term chronic hepatitis C may be aggravated by HIV coinfection, as a result of accelerated centrilobular fibrosis. The course of liver disease in HIV/HCV-coinfected patients is mainly determined by cirrhosis caused by C hepatitis – particularly in multitransfused haemophiliacs – and by HCV-associated cholestatic hepatopathy in the late stage of immunodeficiency. Liver biopsy might help in estimation of the risk of liver failure, which is a particular threat to HIV/HCV-coinfected patients.

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