Clinical Aspects of Liver Diseases

34 Chronic hepatitis

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1 Definition

Chronic hepatitis is *not an entity*, but a heterogeneous group of diseases of varying aetiology, pathogenesis, degree of activity and stage of progression. Thus, like acute hepatitis, this condition constitutes a *syndrome.* • The joint *histological picture* comprises predominant portal inflammation and subsequent periportitis (= interface hepatitis) with different degrees of focal, periportal, zonal or confluent liver cell necrosis, and progredient fibrosis. • *Duration* is long: chronic inflammatory liver diseases persist for more than 6 months. • *Prognosis* is doubtful. This condition may progress through a common final stage to cirrhosis, HCC or liver failure, but also to defective healing, whereby stationary liver fibrosis persists.

2 Historical review

► About 70 years ago (1932), the term **latent liver damage** was coined by H. KALK, who, without any knowledge of morphological findings, was the first clinician to attempt a classification of different chronic liver diseases into clinical groups. • This interpretation was the basis for G. v. BERGMANN's definition of **latent hepatopathy** (1936) (s. p. 74); the clinical observations made by him at that time indeed correspond closely to the picture of chronic hepatitis. • Based on clinical findings in eight patients, E. POLACK observed the transition of acute epidemic hepatitis into **chronic hepatitis** as early as 1937. • *Later, in 1942, K. ROHOLM et al. reported on the histological progression of acute hepatitis to chronic hepatitis in an extensive study involving twelve patients and even monitored the further course up to the development of cirrhosis.* • In 1942 A. KORNBERG used the nomenclature **chronic latent liver damage** following jaundice; F. GEBHARDT et al. (1944) reported on **posthepatitic residual damage** and M. D. ALTSCHULE et al. (1944) on **chronic latent hepatitis** following catarrhal jaundice. The occurrence of **late posthepatitic liver damage** was substantiated by W. VOLWILER et al. (1948). (quot. 18) • From 1947 onwards, H. KALK provided more basic knowledge about **chronic hepatitis**, which he considered to be a chronic interstitial inflammation (according to R. RÖSSLE). By means of laparoscopy, H. KALK distinguished between **four stages:** (*1.*) *large red liver*, (*2.*) *large white liver*, (*3.*) *large multicoloured liver*, and (*4.*) *large multicoloured tuberous liver*. (quot. 18)

3 Histology

3.1 Classification (1968)

Based on the different histological criteria, chronic hepatitis was subdivided in 1968 into (*1.*) **chronic persistent hepatitis** (CPH) (a term coined by H. F. SMETANA as early as 1954) and (*2.*) **chronic active hepatitis** (CAH) (E. G. SAINT et al., 1953) with a *mild* (type A) and a *severe* (type B) course. (7) In this context so-called **chronic necrotizing hepatitis** can be integrated. (24) (s. fig. 34.6) (s. tab. 34.1) • This classification was further refined by the additional differentiation into **chronic lobular hepatitis** (CLH) (H. POPPER et al., 1971) and **chronic septal hepatitis** (CSH) (M. A. GERBER et al., 1974). (10) CLH and CSH are deemed to be variants of chronic persistent hepatitis. CPH exhibits septum formation with a clear inflammatory reaction, yet without piecemeal necrosis. The prognosis for CSH is poorer than that for CLH. • **Chronic minimal hepatitis** shows sparse hyaline necrosis and slight portal cellular infiltrations. Generally, these alterations remain unchanged for years. Morphologically, this term corresponds to so-called *non-specific reactive hepatitis* (V. DESMET, 1986). These reactions are of an inflammatory nature and can be attributed to primarily extrahepatic disease or to focal intrahepatic space-occupying lesions. (s. p. 392) • Occasionally, more severe inflammatory signs can be witnessed in CPH due to increased viral replication and immune reactions. This form was described as minimally active, chronic hepatitis (L. BIANCHI, 1986). (2) Thus, even CPH can develop into CAH.

Initially, this classification, which was based on well-defined **histological criteria**, proved useful – especially since reliable serological or immunological differentiation was not possible at that time. It should be mentioned that the differentiation of CLH was, however, not generally accepted – although this condition is frequently seen in chronic hepatitis C. (12, 18, 24, 26) (s. tabs. 34.1)

1. Chronic persistent hepatitis (CPH) (s. figs. 34.1, 34.2)
Variants:
- chronic lobular hepatitis (CLH)
- chronic septal hepatitis (CSH)

► chronic minimal hepatitis

2. Chronic active hepatitis (CAH) (s. figs. 34.3–34.5)
- type A = mild course
- type B = severe course
- chronic necrotizing hepatitis (s. fig. 34.6)

↓ Fibrosis ↓

Posthepatitic cirrhosis
type I: rapid development (within 6–24 months, ca. 10%)
type II: chronic progressive development
type III: slow periodic development "CAH with cirrhotic transformation"

Tab. 34.1: Schematized morphological classification of chronic hepatitis and its potential to develop into fibrosis and cirrhosis

3.2 Histological criteria

The histological criteria of chronic hepatitis are (*1.*) liver cell damage, (*2.*) inflammatory infiltration, and (*3.*) fibrosis formation. These chronic inflammatory reactions affect firstly the portal field, then the periportal region (i. e. zone 1) and finally the liver lobule. Such reactions constitute a dynamic process, whereby the intensity of the above-mentioned criteria as well as their topographical distribution pattern in the portal, periportal and azinar area vary considerably. (14, 16)

(*1.*) **Portal inflammation:** *Portal hepatitis* reveals varying inflammatory activity. It is common to all forms of