Clinical Aspects of Liver Diseases

23 Acute concomitant viral hepatitis

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A multitude of viruses can affect the liver as a large, filtrating and reacting organ, and subsequently cause concomitant viral hepatitis in the course of an existing systemic viral infection. Laboratory and histological findings in this case are determined by the type of pathogen, including its particular hepatotropic character, and by the immune status or reactivity of the affected organism. Concomitant viral hepatitis does not generally cause symptoms, which is why it is often recognized purely by chance due to slight to moderate elevations in transaminases; minor increases in bilirubin or cholestasis-indicating enzymes are rarely detectable. Nevertheless, rather severe courses with vast hepatocellular necrosis can occur in patients with a weakened immune response. • In infancy, concomitant viral hepatitis is frequently accompanied by a predominant cholestasis syndrome. On the one hand, an infant liver can be damaged by virus infections of a severe and even fatal course, yet on the other hand, it displays an astonishing capacity for regeneration and is indeed capable of restoring destroyed liver structures.

1 Secondary hepatotropic viruses

The most important virus species with regard to their ability to cause concomitant inflammatory reactions of the liver are (*1.*) herpesviruses, (*2.*) rubella viruses, (*3.*) Coxsackie viruses, and (*4.*) paramyxoviruses. (s. tab. 23.1)

1. Herpesviruses	
– Epstein-Barr virus	D E
– Herpes simplex virus 1, 2	D E
– Human herpesvirus 6, 7, 8	D E
– Varicella-zoster virus	(D)
– Cytomegalovirus	D E
2. Togaviruses	
– Rubella virus	D E
– Spring-summer encephalitis virus	D E
3. Picornaviruses	
– Coxsackie virus	D E
– ECHO virus	D E
4. Paramyxoviruses	
– Measles virus	E
– Parotitis virus	(D)
– Giant-cell hepatitis virus	D E
5. Adenoviruses	(S D E)
6. Human parvovirus B19	
7. HIV	laboratory test +

Tab. 23.1: Secondary hepatotropic viruses which can cause viral hepatitis. • In Germany, **obligation for notification** is given in cases of suspicion (S), disease (D) or exitus (E). This can, however, vary from country to country. *If in doubt*, contact the Public Health Department!

1.1 Herpesviruses

Out of a group of approximately 40 herpesviruses (containing DNA, 100 nm in length), the following are classified as secondary hepatotropic: (*1.*) Epstein-Barr virus (types A, B), (*2.*) herpes simplex virus, (*3.*) herpesvirus-6, (*4.*) varicella-zoster virus, and (*5.*) cytomegalovirus.

1.1.1 Infectious mononucleosis

"Pfeiffer's glandular fever" (E. Pfeiffer, 1889) or "infectious mononucleosis" (T.P. Sprungt et al., 1920) is caused by the human herpesvirus 4 (= EB virus 4), which was discovered by M.A. Epstein, B.G. Achong and Y.M. Barr in 1964.

Infectious mononucleosis is a generalized reticuloendothelial infection, mainly found in adolescents and young adults. The total endemic infection rate in the more advanced age groups is 80–100%. • This condition is transmitted by close physical contact ("kissing disease"), sexual contact and blood transfusion. The incubation period of the orally transmitted virus is 8–21 days (up to 7 weeks). This is followed by a prodromal stage with headaches, tiredness and atypical fever. The clinical picture is defined by (chiefly cervical) swollen lymph nodes (95–100%), tonsillitis (> 80%), splenomegaly (> 50%), exanthema, mucosal petechiae in the oral cavity (30–50%) and leucocytosis with very large numbers of lymphomonocytoid cells. These "atypical lymphocytes" (W. Schultz, 1922) are activated T cells. Gallbladder wall thickening is found by sonography. (17)

In about 50% of cases, **hepatitis mononucleosa** with hepatomegaly (10–25%) develops, displaying an increase in transaminases of 10–20 times the normal value. (13, 15) Jaundice is witnessed in 5–10% of cases, usually due to autoimmune-based haemolysis. (2, 4, 5) There is a distinct elevation of LDH and alkaline phosphatase. (7) Hence, the following enzyme constellation can be evaluated as the *biochemical triad* of hepatitis mononucleosa:

LDH	↑↑↑	**(90–95%)**
AP	↑↑	**(75–90%)**
GPT, GOT	↑	**(60–90%)**

The *Paul-Bunnel test* (J.R. Paul, W.W. Bunnel, 1932) is positive from the 4th to 10th day in about 75% of cases. Serological proof of acute infection can be successfully obtained by way of *anti-EB virus IgM*. The virus DNA is revealed by PCR. • *Hepatic lesions* are already found as from the 5th day and are most distinct between the 10th and 30th day of the disease. Portal/periportal and sinusoidal infiltrations of partially beaded lymphomonocytoid cells frequently appear in the form of small