Symptoms and Syndromes

17 Hepatorenal syndrome

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► ***The coexistence of a liver and kidney disease is a frequent clinical event.*** • In fact, reports in the literature date back more than 100 years (F. Th. Frerichs, 1861; K. W. H. Nothnagel, 1874; P. J. Moebius, 1877; A. Weil, 1886). As early as 1863, A. Flint observed the coexistence of cirrhosis with ascites and oliguria, although autopsy revealed the kidneys to be normal. In animal experiments, M. Pawlow (1893) was able to show the occurrence of albuminuria after the placement of a portacaval anastomosis. Jaundice mainly developed parallel to renal damage. Richardière (1890) coined the term "hépatonéphrite" to describe this clinical picture. (49) In 1911 both P. Clairmont et al. and F. Steinthal reported for the first time on renal failure with fatal outcome following surgery on the bile ducts for obstructive jaundice. This renal failure in biliary obstruction was described by F. C. Helwig et al. in 1932 as *"liver-kidney syndrome"*. (27)

The term **"hepatorenal syndrome"** was introduced by P. Merklen in 1916 and taken up by W. Nonnenbruch in 1939. The following description is still largely accepted today: *"A combination of anatomically defined liver disease with a sometimes severe restriction in the function of the kidneys, which display few, if any, morphological changes. Liver disease can be the outcome of hepatocellular damage of any type, i. e. it can be toxic or infectious and originate from cirrhosis or cancer."* (44)

1 Definition

The hepatorenal syndrome (HRS) is a functional, oliguric, progressive, in principle reversible, circulation-related kidney failure occurring in severe liver disease and portal hypertension and increasing liver insufficiency − assuming there are indeed no other causes of the renal insufficiency.

► This syndrome is, in fact, prerenal kidney failure − yet *without response to an adjustment of the effective plasma volume,* i. e. expansion of the intravasal volume does not influence the renal function. This functional renal failure is due to extreme intrarenal vasoconstriction and reduced perfusion in the area of the renal cortex, whereby the blood supply to the medullary parts of the kidney is largely normal. The extrarenal circulation is undisturbed (arterial vascular resistance and vascular filling as well as cardiac output are normal). In cases of cirrhosis, systemic vasodilation becomes increasingly prevalent, together with hyperdynamic circulatory disturbance. In clinical terms, the ultimate outcome is pronounced sodium and water retention with oliguria and excretion of practically sodium-free urine − without or with only slight (< 500 mg/dl) proteinuria.

2 Pathogenesis

The frequent **coexistence** of the *hepatorenal syndrome*, *ascites* and/or *hepatic encephalopathy* suggests that similar pathogenetic mechanisms are responsible for these three intricate developments.

2.1 Biochemical factors

The numerous biochemical substances that may be considered with regard to hepatic encephalopathy or ascites have been outlined in detail. (s. tabs. 15.2; 16.5) • Similarly, an extensive synopsis of pathogenetically effective biochemical factors can be drawn up for HRS as well. All of them ultimately interfere − directly or indirectly − with the renal retention or excretion of sodium and/or the balance between vasodilation and vasoconstriction. RAAS is markedly activated. (5, 28, 33, 41, 62, 64, 65) (s. tab. 17.1) • Vasodilative factors under discussion include bilirubin, bile acids, nitrogen monoxide (NO), false neurotransmitters, calcitonin peptide (25) as well as platelet-activating factor (PAF). In more recent studies, considerably higher plasma values of the vasoconstrictor leukotrienes (C4 and D4) (41) and endothelin 1 and 3 (42) were detected.

	Liver	Plasma	Kidneys/Urine
Angiotensinogen synthesis	↓		
Kininogen synthesis	↓		
Renin breakdown	↓		
Angiotensin II breakdown	↓		
Aldosterone breakdown	↓		
Endotoxin breakdown	↓		
Vasopressin breakdown	↓		
Renin (62)		↑	
Angiotensin II		↑	
Aldosterone		↑	
Endotoxin		↑	
Noradrenaline		↑	
Vasopressin		↑	
Endothelin 2 and 3 (42)		↑	
Leukotriene C_4 and D_4 (41)		↑	
Calcitonin peptide (25)		↑	
Antidiuretic hormone (ADH)		↑	
Kallikrein		↓	
Bradykinin (62)		↓	
Atrial natriuretic factor (ANF)		↓	
Renin			↑
Angiotensin II			↑
Aldosterone			↑
Endothelin			↑
Thromboxane A_2 (65)			↑
Leukotriene E_4			↑
Prostaglandin E_2 (65)			↑
Prostacyclin			↑
Bradykinin			↑

Tab. 17.1: Synopsis of the activity of biochemical factors in the liver, plasma and kidneys or urine relating to the hepatorenal syndrome (with some references)

2.2 Haemodynamic factors

Hepatorenal syndrome is characterized by pronounced vasoconstriction of the renal cortex with tortuosity and narrowing of the interlobular and arcuate arteries. The blood supply to the renal cortex may be almost totally interrupted and, at the same time, the blood flow is diverted into areas containing cortical vessels