THE HEPATORENAL SYNDROME (HRS)

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INTRODUCTION

Progressive oliguric renal failure commonly complicates the course of patients with advanced hepatic disease (1,2). While this condition has been designated by many names including "functional renal failure", and "the renal failure of cirrhosis", the more appealing albeit less specific term "hepatorenal syndrome" has been utilized commonly to describe this syndrome. For the purposes of this discussion, the hepatorenal syndrome may be defined as unexplained progressive renal failure occurring in patients with liver disease in the absence of clinical, laboratory, or anatomic evidence of other known causes of renal failure.

A. Clinical Features

A review of the clinical features of HRS reveals marked variability regarding both the clinical presentation and clinical course (1,2). In the United States, the HRS occurs usually in cirrhotic patients who are alcoholic, although cirrhosis is not a sine qua non for the development of HRS. HRS may complicate other liver diseases including acute hepatitis and hepatic malignancy (3,4,5). Renal failure may develop with great rapidity, often occurring in patients in whom normal serum creatinine levels have been previously documented within a few days of onset of HRS. Recently, Arieff (6) has suggested that the serum creatinine may be a poor index of renal function in patients with chronic liver disease, often masking markedly reduced GFR's. Implicit in such a formulation is the concept that HRS represents a progression in patients who already have markedly impaired renal function.

Numerous reports have emphasized the development of renal failure following events which reduce effective blood volume including abdominal paracentesis, vigorous diuretic therapy and gastrointestinal bleeding, although it can occur in the absence of an apparent precipitating event. In this context, several careful observers have recently noted that HRS patients seldom arrive in the hospital with preexisting renal failure. Rather, HRS seems to develop in the hospital, raising questions as to whether events in the hospital might precipitate this syndrome (1).
Virtually all HRS patients have ascites which is often tense and clinical stigmata of portal hypertension are usually present. The degree of jaundice is extremely variable. Although the majority of reports suggest that the HRS occurs in patients who manifest evidence of severe hepatocellular disease, it is quite apparent that the HRS can occur with minimal jaundice and with little evidence of severe hepatic dysfunction.

The majority of patients have a modest decrease in systemic blood pressure, but significant hypotension occurs usually as a terminal event. Most patients die within three weeks of onset of azotemia, although rare patients have survived for several months with mild azotemia (8).

HRS patients manifest a rather characteristic urine excretory pattern, voiding urine which is practically sodium-free and retaining the capacity to concentrate urine to a modest degree.

B. Pathogenesis

Several lines of evidence have lent strong support to the concept that the renal failure in HRS is functional in nature. Despite the severe derangement of renal function, pathologic abnormalities are minimal and inconsistent (1,2,7). Furthermore, tubular functional integrity is maintained during the renal failure as manifested by an unimpaired sodium reabsorptive capacity and concentrating ability. Finally, more direct evidence is derived from the demonstration that kidneys transplanted from patients with HRS are capable of resuming normal function in the recipient (9).

Despite extensive study, the precise pathogenesis of the HRS remains elusive. Since urinary diagnostic indices suggest intact renal tubular function in HRS, vascular rather than tubular events are felt to be important in the pathogenesis of the renal failure. According to this view, severe afferent arteriolar constriction diminishes glomerular plasma flow and glomerular capillary pressure sufficient to lower effective filtration. In this regard, many studies utilizing diverse hemodynamic techniques have all documented a significant reduction in renal perfusion (10-12). Since a similar reduction of renal perfusion is compatible with urine volumes exceeding one liter in many patients with chronic renal failure (13) it is unlikely that a reduction in mean blood flow per se is responsible for the encountered oliguria.

Our laboratory has applied the 133Xe washout technique and selective renal arteriography to the study of the HRS and demonstrated a significant reduction in both mean renal blood flow as well as preferential reduction in cortical perfusion (10). In addition, Epstein and coworkers (10) carried out simultaneous renal arteriography to delineate further the nature of the hemodynamic abnormalities. Selective renal arteriograms disclosed marked beading and tortuosity of the interlobar and proximal arcuate arteries, and an absence of both distinct cortical nephrograms and of vascular filling of the cortical vessels. Postmortem angiography carried out on the kidneys of five patients studied previously during life disclosed a striking normalization of the vascular abnormalities with reversal of all the vascular abnormalities in the kidneys. The peripheral vasculature filled completely and the previously irregular vessels became smooth and regular. These findings provide additional strong evidence for the functional basis of the renal failure, operating through active renal vasoconstriction.