Subacute Hepatic Failure: Definition, Nomenclature and Criteria for Diagnosis

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We have defined subacute hepatic failure as a clinical entity characterized by persistent or progressive jaundice, 4 weeks after the onset of icteric stage of viral hepatitis and associated with the development of moderate or severe ascites, without any pre-existing liver disease. Liver function tests reveal evidence of hepatocellular injury, with hyperbilirubinemia, moderate elevation of transaminases, hypalbuminemia and prolonged prothrombin time. Patients do not have gastroesophageal varices. Liver histology shows moderate or severe degree of acute hepatitis with bridging necrosis. In India, viral hepatitis is the principal cause of SAHF but several other etiologic agents like toxins and drugs can also lead to it. The prognosis of SAHF is very poor with a mortality rate of about 75%.

Tisdale in 1963, drawing attention to the clinical-pathological entity of subacute hepatitis, stated, "Most physicians recognize these two extremes of hepatitis clinicopathological 'spectrum' — acute benign hepatitis and fatal fulminant hepatitis — but many are unfamiliar with another important hepatitis variant, subacute hepatitis". He described the characteristics of his eight patients which included 6 women and 2 men. Six of them were above the age of 60 years. Prolonged jaundice and ascites were prominent physical signs. He supported his observations by quoting similar patients reported from Norway and Denmark under the title malignant hepatitis with predilection for women over 40 years of age. Tisdale gave a detailed description of histology of this disease as subacute hepatic necrosis or subacute yellow atrophy.

Boyer and Klatkin in 1970 described the pathological entity of subacute hepatic necrosis. They analyzed the clinical features, biochemical abnormalities and prognosis of 32 patients who had liver pathology of subacute hepatic necrosis and noted the following important characteristics: (a) most patients were above the age of 40 years without any gender preference; (b) the prodromal phase was insidious and mild but prolonged; and, (c) the depth and duration of jaundice, ascites and edema were prominent.

Peters and his colleagues in 1978 from the United Kingdom described protracted viral hepatitis with impaired regeneration. They stated, "A pattern of prolonged viral hepatitis that differs from persistent hepatitis or chronic active hepatitis occasionally occurs in older patients. It is characterized by a course usually lasting over 6 weeks and often of several months' duration". More than half of the patients with impaired regeneration recovered completely, while the remainder died within one year from the time of onset. None seemed to run a course of 5 to 10 years. These workers believed that impaired regeneration required a different approach to treatment than chronic hepatitis, since the basic defect was in the regeneration of hepatocytes rather than in continuing viral disease.

In 1985, the liver Unit of the King's College of Medicine and Dentistry, London reported 47 patients, registered over a period of 12 years, under the title of late onset hepatic failure (LOH). In this series, the peak incidence of disease was in the 5th and 6th decades of life and the sex ratio was slightly in favor of women (2:3:2). The onset of illness was generally insidious and all patients had jaundice on admission. Ascites was detected in 62% and none had clinical splenomegaly. Comparison with fulminant hepatic failure showed ascites as a more characteristic feature of LOH and encephalopathy (particularly grade IV) as an important finding in FHF. Cerebral edema was noted more frequently in FHF compared to LOH. The mortality of LOH was as high as of FHF (81% and 90.5% respectively). A large proportion of liver biopsies in LOH showed lobular inflammatory infiltrate in addition to bridging and confluent necrosis.

Bennamou in 1986 reported similar patients under the title of subfulminant hepatitis. We published a review on subacute hepatic failure in 1988 and described a series of 148 patients registered during a 6-year period.

It can thus be concluded that SAHF is a clinical entity, distinct from acute and chronic liver failure. Subacute hepatitis is its pathological equivalent. Overlap in the histological features of fulminant, subacute and chronic hepatitis is greater compared to that in clinical conditions of acute, subacute and chronic hepatic failure. Though most specialists today believe that SAHF is a distinct clinicopathological entity but there is no agreed terminology for this condition. Critical studies on the pathogenesis...
of SAHF may help in the development of rational medical management. Indeed, liver transplantation is clearly indicated as a successful treatment for this condition.

References