Encephalopathy in Infantile Hepatic Cirrhosis

George A. Jervis

New York State Research Institute for Mental Retardation and Letchworth Village Developmental Center, Thiells, NY, USA

Summary. The cases are described of two sibs who developed hepatic cirrhosis in early infancy, accompanied by profound mental retardation. Post mortem in one sib there were multiple foci of demyelination with abundant cellular infiltration, scattered throughout the brain. These unusual pathological changes are briefly commented.

Key words: Child — Encephalopathy — Cirrhosis

With the exception of few rare metabolic diseases, little is known of brain pathology in chronic liver diseases of the child. The purpose of this brief communication is to report of the case of two sibs who developed liver cirrhosis very early in life. Both were severely retarded. Examination of the brain of one sib showed peculiar lesions so far unreported in liver diseases of the child.

Clinical Findings

The family of old American stock consisted of highly educated intelligent parents, a normal daughter and two affected sons. No other members of the family were known to have suffered from brain or liver diseases for two generations.

Case 1. A boy was born at term following normal delivery. Early growth was poor and at the 4 month of life he developed generalized seizures. At the 5 month, enlarged liver was noted, blood bilirubin was 25% total with 13% direct, prothrombin 20s and markedly positive urinary bile reaction. Shortly afterward, he was admitted to a medical center. He was deeply jaundiced and appeared seriously ill. Pupillary reaction was poor, optic discs were blurred, and there was bilateral nystagmus. Diagnosis was biliary atresia, but on laparotomy the liver appeared enlarged and of rubbery consistency. Biopsy showed typical biliary cirrhosis. A week following the operation, the infant developed septic peritonitis and died. The brain was not available for study.

Case 2. The younger brother was born after an uneventful gestation. Weight was 6 pounds. At 2 months, mild jaundice was noted. Total bilirubin was 8.7% (direct 3.5%). The jaundice cleared up in about a week but reappeared at 6 months of life. Prothrombin time was increased and flocculation test was positive. At one year of age, there was rotary and vertical nystagmus, papillary edema, and apparent blindness. The child was obviously retarded. Ventriculogram was normal. Liver biopsy showed biliary cirrhosis. During the following years, there were several hospitalizations because of massive intestinal hemorrhages requiring blood transfusions. At 5 years of age, he was admitted to a State institution. He was an emaciated, jaundiced child 42 pounds in weight, 4 feet in height with a head circumference of 21 in. He was bedridden, unable to stand and able to swallow only soft food. He was blind, corneas were clouded, and nystagmus was present. He reacted to strong noises with a rapid contractions of the extremities. There was conspicuous muscular wasting, deep tendon reflexes were sluggish, Babinski was negative. Liver was hard on palpation and appeared somewhat enlarged. Frequent grand mal seizures, poorly controlled by dilantin were noted during the year in the hospital. He died at 6 years of age of acute pneumonia. The autopsy was performed after 24h.

Pathological Findings

Significant pathological findings were in the liver and the brain. The liver weighed 700 g. Grossly, no normal pattern was seen, the whole organ presenting with small cirrhotic nodules. Histologically, the nodules were surrounded by dense collagenous bands (Fig. 1), central veins were absent and some hepatic cells in many nodules were swollen and vacuolated. Spleen was small and fibrotic. Brain weighed 750 g. External configuration was normal. On gross sections, the ventricles were moderately enlarged but no abnormalities could be seen. Histologically, Nissl preparation showed irregularly distributed decrease of neurons in cerebral cortex. Glia nuclei of Alzheimer type II were increased particularly in the deep layer of the cortex. The main pathological finding consisted of scattered foci of tissue degeneration. Some were visible to the naked eye, others much more numerous could be easily detected under low power magnification. The focus consisted of an accumulation of cellular elements either packed around small blood vessel or loosely distributed in the adjacent tissue (Fig. 2). At higher power, the perivascular cells consisted mainly of macrophages and monocytes. The surrounded tissue contained besides macrophages numerous and large glia cells with abundant cytoplasm (Fig. 3) monocytes were scarce. Fragment of myelin and axis cylinders were occasionally present within the focus while degenerated neuron cells were rare. No thrombi could be detected in the lumen of the vessels within the foci. Some degenerated areas were also seen consisting almost exclusively of macrophages (Fig. 4). There was no apparent reaction of microglia. Polimorphonuclear elements and erythrocytes were not seen.
Fig. 1. Hepatic cirrhosis — silver preparation, × 77

Fig. 2. Overview of a typical focus of demyelination and cellular infiltration — Nissl's stain, × 200

Fig. 3. Detail of various types of cells in perivascular infiltration — Nissl's stain, × 530