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# Hepatic Changes Resembling the Indian Childhood Cirrhosis in an IgM anti-CMV Positive Infant

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This is to describe a neonatal hepatitis with pericellular hepatic fibrosis and Mallory bodies in a sero-postitive infant for IgM anti-CMV. A necropsy of the liver revealed severe heaptocellular swelling with many intracytoplasmic hyaline bodies, pronounced fibrosis of a creeping type, bile stasis with ductular proliferation, and the lack of parenchymal regeneration. These microscopical changes of the liver resembled those of Indian Childhood Cirrhosis (ICC). In the present case the patient's serum IgM anti-CMV is the only clue for the etiological diagnosis.

**Key Words:** Cytomegalovirus, Cirrhosis, Indian childhood cirrhosis, Mallory body

## INTRODUCTION

Diseases that can produce intralobular fibrosis in young children include ICC, CMV infection[1], congenital syphilis, Wilson's disease, Byler's disease[2], and some other inborn errors of metabolism such as tyrosinemia[3], and hereditary fructose intolerance[4]. Mallory bodies may be seen in such liver diseases[5~7] as alcoholic liver disease, ICC, Wilson's disease, biliary atresia, alpha-1-antitrypsin deficiency, primary biliary cirrhosis, jejunoileal bypass, obese diabetes and longstanding biliary obstruction, and have been described in chronic active hepatitis, hepatocellular carcinoma, abetalipoproteinemia, etc.

Among these, ICC is at best known to produce pericellular fibrosis and Mallory bodies without regeneration, resulting in progressive hepatic failure[8]. This disease is largely confined to the Indian subcontinent[9~11], and an increase of dietary copper caused by the use of copper and brass utensils has been suggested for the etiologic factor[12~16].

We experienced and report a necroptic liver which showed Mallory bodies and pericellular fibrosis with histological resemblance to ICC.

## CASE REPORT

The patient was a 9 month-old male infant and was admitted for a further evaluation of his known liver disease. He had had jaundice since 20 th day from birth, and a DISIDA scan performed at another hosptial had suggested possible biliary atresia, which had been excluded by the exploratory laparotomy. The histologic diagnosis of a wedge liver biopsy was neonatal hepatitis. At the age of 4 months he was admitted to this hospital due to dyspnea and cough. At that time his serm was positive for IgM anti-CMV at 1:160. The serum HBV markers, anti-HSV and antibody to Rubella were all negative. The patient admitted again with the same problems and was told to have neonatal hepatitis, bronchiolitis, gastroenteritis and a cavernous hemangioma on his forehead.

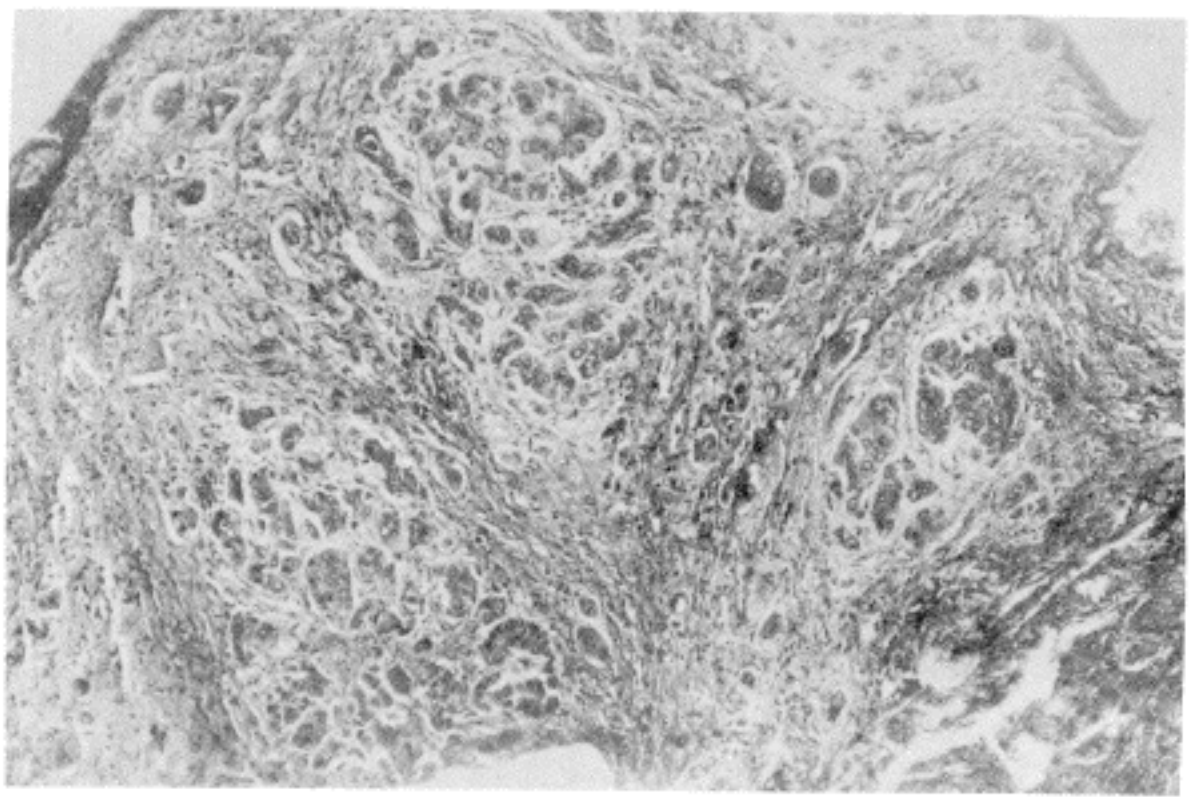

**Fig. 1.** A low power view of the liver necropsy showing extensive fibrosis that forms thick septa and destroys the hepatic cord pattern. Trichrome stain. 100×

The liver and the spleen were palpable by 5 cm and 4 cm below the right and left costal margins respectively. The liver was felt firm and smooth, and had a blunt margin. The chest was symmetrically expanded, but there was subocostal retraction. The breathing sound was coarse with rhonchi and wheezing. The Hb was 9.0 g/dl, Hct 22.6%, WBC 5,600/$mm^3$ and the platelet 77,000/$mm^3$. The prothrombin time was 17.7 sec(43.7%) and the PTT 80 sec. Total protein was 6.7 g/dl, albumin 3.3 g/dl , total bilirubin 21.5 mg/dl, direct bilirubin 9.7 mg/dl, SGOT 265 U and SGPT 72 U. The NH3 was 113 ug/dl. The serum alpha-fetoprotein was more than 12,800 ng/ml. Coombs' tests, both direct and indirect, were also positive and the antiplatelet antibody as well. He became cyanotic and died of pulmonary hemorrhage secondary to hepatic failure.

A necropsy of the liver revealed the lobular architecture almost completely disrupted due to extensive fibrosis that formed thick septa(Fig. 1) as well as insinuated between the liver cells, separating small islands of liver cells floating on a fibrous matrix (Fig. 2-a). The remaining hepatocytes were markedly swollen with giant cell (Fig. 2-b) and acinar transformations. The portal areas and fibrous septa have an increased number of bile ductular structure, and a mild degree of inflammatory hyperplasia. There were no regenerating nodules of liver cells. Cholestatsis was prominent both in parenchymal cells and in bile ducts. Canalicular bile plugs were also pronounced. One peculiar findings was the appearance of Mallory bodies (Fig. 2-c).

There were no clinical and laboratory findings suggestive of alpha-1-antitrypsin deficiency, Wilson's disease or other inborn errors of metabolism, biliary atresia or Byler's disease. The morphologic changes of this infant might be due to CMV infection.

## COMMENT

ICC has been known to affect infants and young children, aged 6 months to 5 years, occurring largely limited to the Indian subcontinent and resulting in progressive hepatocellular failure[8]. But recently several cases showing the features of ICC with hepatic copper overload were reported from 14 countries[17]. Although several etiologic factors, such

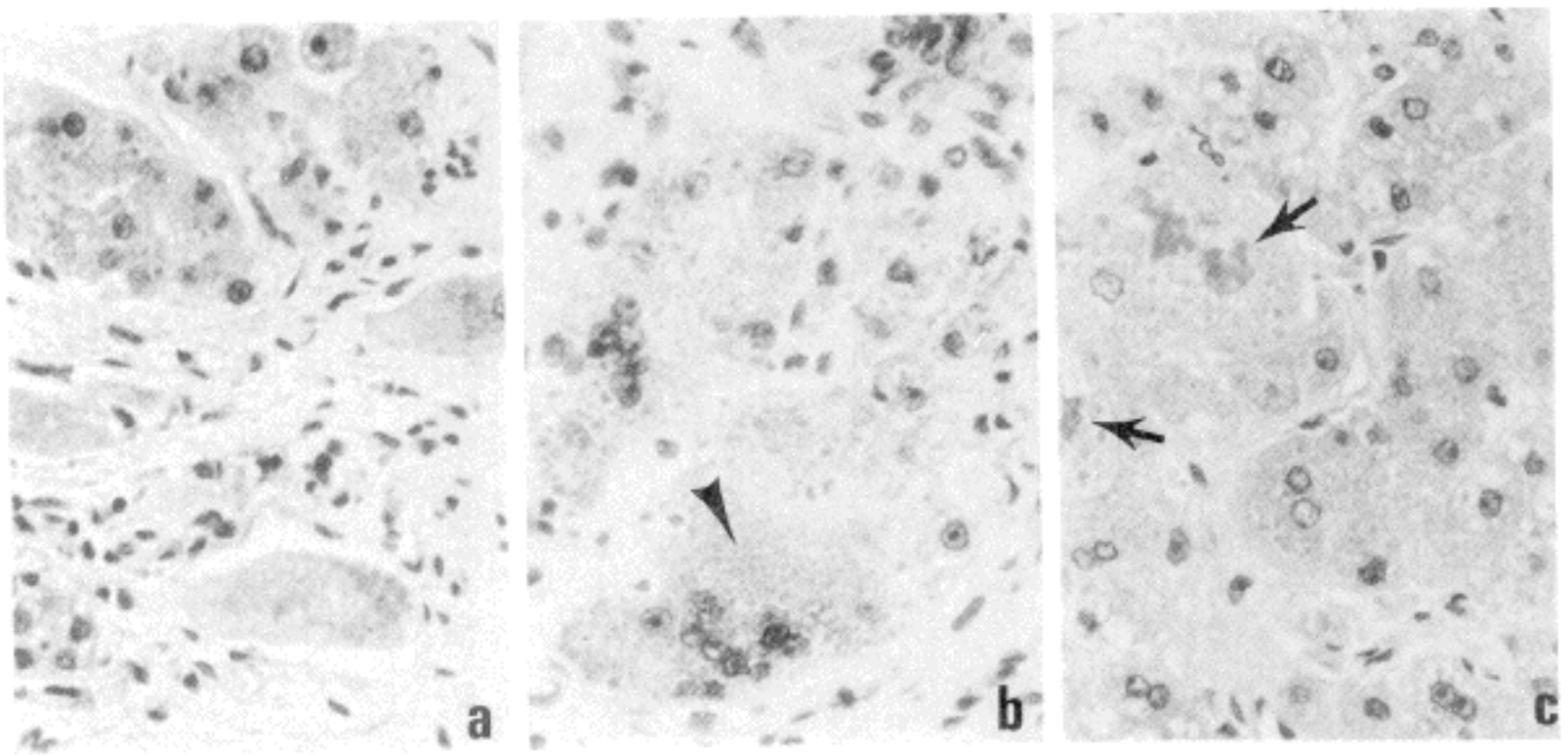


**Fig. 2.** Higher magnification showing (a) perihepatocellular parenchymal fibrosis, (b) giant cell transformation of hepatocytes with intracellular bile stasis (arrow head), and (c) Mallory bodies (arrow). Hematoxylin-eosin stain, 400×

as virus, malnutrition, hepatotoxin, hereditary factor and metabolic defects have been proposed, the exact pathogenesis is yet to be clarified[9]. The possibility of early introduction of artificial food contaminated with copper is being considered as the major cause[12~16].

The hepatic changes seen in the present case fit most of the diagnostic criteria of ICC[17]; widespread fibrosis separating small groups or nodules of liver cells, variable but significant hepatocytic damage, intracytoplasmic hyaline bodies[8,18,19], cholestasis, lobular inflammation, septal or lobular fibrosis, ductular proliferation, minimal or no lipid. Excess of copper and/or copper binding protein, which is one of the characteristics of ICC, was not present in the case under discussion.

Among these, intralobular fibrosis and Mallory hyaline bodies are of interesting. In the present case, however, there are good reasons to exclude all the diseases already listed, which can produce these features, except for the CMV infection.

In children, CMV infection of the liver frequently shows inclusions in the hepatocytes, vascular endothelial cells and bile duct epithelium, where they are surrounded by inflammatory cells. The infected cells degenerate into acidophilic bodies. The portal tracts have polymorphic cellular infillrates[20,21]. In contrast, inclusion bodies are rarely found in adults, whereas sinusoidal lymphocytosis is prominent with focal necrosis, acidophilc bodies and proliferation of kupffer cells, diffuse fatty change of the hepatocytes and glycogen vacuolation are sometimes seen[22].

The definitive diagnosis of CMV hepatitis can be established only by the demonstration of inclusion bearing cells in the liver, isolation of CMV or by the serological evidences[21]. Because the patient's serum was positive for IgM anti-CMV, the ICC like hepatic lesion of this infant seems best to be due to CMV infection.

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## ＝국문초록＝

### 혈청 IgM CMV 항체가 양성인 영아에서 관찰된 유사 Indian Childhood Cirrhosis

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사후 간조직 검사상 간세포 종창, 다핵거대세포 형성, 담즙울체와 같은 신생아 감염의 소견과 함께 Mallory 소체의 출현, 간소엽내의 간세포 주변섬유화 및 간문맥의 진행성 섬유화에 의한 광범위한 간파괴, 간세포 재생의 결여등 Indian Childhood Cirrhosis (ICC)와 유사한 조직상을 보인 1례를 보고하였다.

환자는 생후 9개월된 남아로서 혈청 IgM CMV 항체가 양성이었다. 가족력과 과거력상 진정한 의미의 ICC나 여러가지 유전성 간질환을 의심할 만한 소견이 없는 것으로 보아 CMV 감염이 이 병변의 원인으로 생각되었다.