An Autopsy Case of Juvenile Cirrhosis of the Liver

Takako SASAO, Fumiya UCHINO and Motoko UMEDA*
Department of Pathology;
(Director : Prof. Shuji Hosokawa)
Yamaguchi University School of Medicine, Ube.
**Department of Pediatrics,*
(Director : Prof. Shunzo Konishi)
Yamaguchi University School of Medicine
(Received December 1, 1967)

Cirrhosis of the liver is not a so rare disease in children as has usually been believed, but in our autopsy materials it's rather infrequent. Cirrhosis under the age of 15 years, is considered juvenile cirrhosis.

We recently experienced a case of juvenile cirrhosis, in which ascites and leucocytosis were remarkable clinically.

REPORT OF A CASE

Clinical History :

A 7-year-old boy was admitted to the pediatrics of Yamaguchi University Hospital on May 15, 1967, with the chief complaint of edema. His parents were not in consanguinity and there were no hereditary diseases in their relatives. He had a younger brother, 2-year-old, in good health. He was born in 1960 after normal pregnancy in full term delivery, 3,200 gm in weight and his physical and mental growth was normal. In December, 1966, he had edema of the face and the legs, and hematuria. He was diagnosed as having acute nephritis and treated for about two months.

His present illness began about 3 weeks prior to admission with slight jaundice. Several days before admission, edema and ascites were noticed.

On May 15, 1967, at the time of admission, the patient was a normally developed and moderately nourished boy. Jaundice was not so remarkable. Only the palpebral conjunctiva was slightly icteric. General edema was noticed. The abdomen was distended and there was evidence of ascites. On May 17 he complained of epigastralgia, tenderness, nausea and vomiting. Abdominal distension developed and venous dilatation was noticed. On May 18 he had diarrhea and occult blood was positive. Exploratory abdominal puncture was

---

This case was presented at tenth meeting of Japan-America pathologists' society of Western Japan on 14 October 1967.

done and it showed transudate with numerous pus cells. Day by day, his general condition got worse. He received the puncture several times but ascites increased rapidly and general edema and jaundice became remarkable. Since May 24, bleeding tendency, for example melena and epistaxis, appeared. A few days later, after extraction of a tooth bleeding was continued without cease and his consciousness was disturbed. On the 15th hospital day he began to have dyspnea and expired.

Laboratory examinations are shown in Table 1 and 2. Systemic blood chemistory revealed sever hepatic dysfunction, marked hypoalbuminemia, jaundice and anemia. Biliary obstruction was not suspected. Urinalysis showed slight renal disturbance. Examination of peripheral blood revealed leucocytosis which increased more and more with marked neutrophilia and shift to the left. Paper electrophoresis of serum protein showed marked hypoalbuminemia and increase in gamma-globulin.

Table 1.

LABORATORY EXAMINATION

Systematic Blood Chemistry

Date	May 16	May 24	May 29
Hemoglobin	10.1g/dl	10.3g/dl	6.2g/dl
Serum protein	6.9g/dl	6.0g/dl	5.0g/dl
Albumin	3.2g/dl	1.9g/dl	1.7g/dl
Globulin	3.7g/dl	4.1g/dl	2.3g/dl
A/G Ratio	0.87	0.46	0.52
Icterus index	10<	10<	10<
Total bilirubin	5.9mg/dl	9.1mg/dl	17.5mg/dl
Alk. phosphatase	2.8u	2.8u	2.8u
Cholesterol	68mg/dl	75mg/dl	40mg/dl
Phenol turb. t.	6u	4u	4u
CCFT	1	2	3
GPT	30u	29u	18u
Cholinesterase	0.10 ΔpH	0.12 ΔpH	0.11 ΔpH
NPN	24mg/dl	43mg/dl	38mg/dl
Urea N	11mg/dl	15mg/dl	19mg/dl

Table 2.

LABORATORY EXAMINATION

Urinalysis

Protein (+), Sugar (−), Urobilinogen: normal, Bilirubin (±) Sed. red cell 1-4/HPF, white cell 10-15/HPF, epitherium (+～卅),

Examination of Peripheral Blood

Date	May 15	May 17	May 22	May 25	May 29
RBC	267×10^4	304×10^4	270×10^4	292×10^4	172×10^4
WBC	8,300	11,200	11,800	17,600	45,400
		(90% neutrophilia)		(marked shift to the left)	

Examination of Ascites

Protein: 340mg/dl, Specific gravity: 1,007, Pus cell: numerous.

Paper Electrophoresis of SerumProtein (May 23)

Albumin	27.6%
α_1-globulin	4.8%
α_2-globulin	7.1%
β-globulin	8.4%
γ-globulin	52.0%
Total protein	6.9g/dl
A/G ratio	0.38

Postmortem Examination:

Postmortem examination was performed two hours after the death.

The body was that of a moderate built, moderate nourished boy. The skin was dry and icteric. The palpebral conjunctiva was icteric. There was marked abdominal distention and its wall was covered with the dilated superficial veins. Fluctuation was demonstrated. There was marked pretibial edema. The abdominal cavity contained about 2,000 ml of a straw-colored slightly turbid fluid. Each pleural cavity contained about 100 ml of a straw-colored slightly turbid fluid. The thymus was very atrophic and almost displaced with the adipose tissue.

The liver was small, 390 gm in weight. Its surface was irregularly nodular with small nodules of 1 to 3 mm in diameter. The consistency was elastic firm. The gall-bladder was enlarged and filled with whitish bile (Fig. 1). The cut surfaces were finely nodular and there were relatively spacious areas of interstitium among the nodules.

Other than these nodules there were well defined pea-sized lesions, which were yellowish white (Fig. 2). Many lymph nodes of the hilus hepaticus were swollen. No thrombus was noted in the portal veins. There were no dilated vessels and bile ducts.

Fig. 1. The irregular surface of the liver and the enlarged gall-bladder.

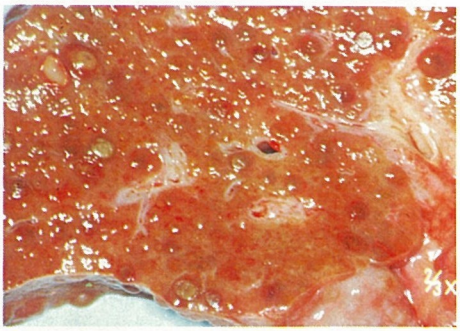

Fig. 2. The cut surface of the liver showing fine nodules and broad interstitium. Yellowish white lesions are abscesses. (at the left)

The spleen weighed 270 gm. The surface was smooth and tense. Section revealed a dark red pulp which was scraped with abundant matter. The follicles were not distinguishable.

Macroscopically, there was not any noticeable change in the heart except for epicardial hemorrhages. The pleura showed disseminated petechial hemorrhages. The both lower lobes were partly atelectatic. Section revealed numerous focal hemorrhages. The hilar lymph nodes were swollen.

Serous membrane of the digestive tract showed petechial hemorrhages. The stomach contained much coffee-ground-like material. The intestine contained black material, too.

The permission of autopsy of the central nervous system was not obtained.

Microscopically, most striking findings were sever destruction of normal liver architecture and enormous proliferation of bile ducts (Fig. 3). Interstitial fibrous bands were broad and many collagenous fibers were proliferated (Fig. 4). In some parts fine collagenous fibers were spreading into the parenchymal areas and separating a small group of liver cells (Fig. 5). Proliferated epithelia of the ducts were surrounded by fine reticular fibers and were presenting canaliculi (Fig. 6). Contracted reticular fibers were preserved in the destructed lobules, but elastic fibers were absorbed and were only seen around the vessels (Fig. 7). In some areas focal necrosis of the liver cells were found and in other areas the whole lobules were necrotic. Some liver cells showed balloonlike swelling, or hyalinization and shrinkage, so-called acidophilic bodies (Fig. 8).

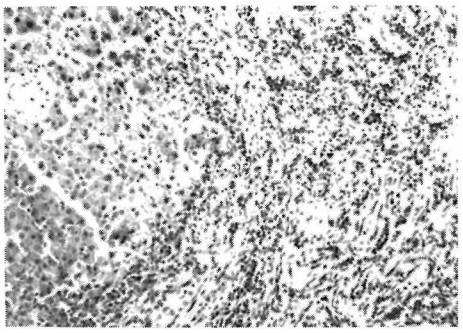

Fig. 3. Sever destruction of normal liver architecture and enormous proliferation of bile ducts. (H.E. × 100)

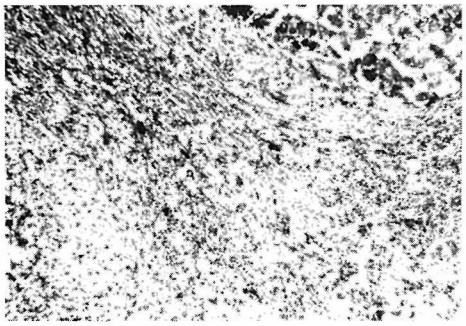

Fig. 4. Proliferated collagenous fibers in the broad interstitium.
(Azan-Mallory Staining × 100)

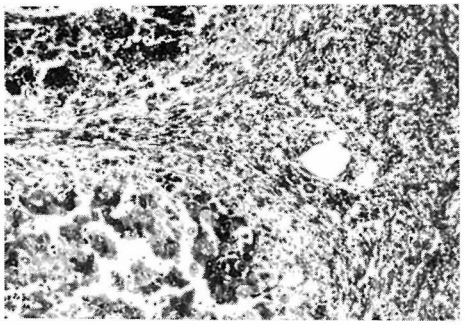

Fig. 5. Fine collagenous fibers spreading into the parenchymal areas.
(Azan-Mallory staining × 100)

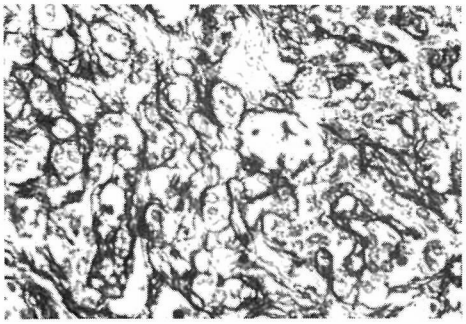

Fig. 6. Reticular fibers surrounding the pro liferated bile ducts.
(silver impregnation technic × 400)

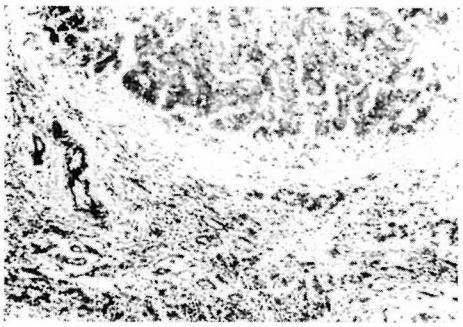

Fig. 7. Elastic fibers are only seen around the vessels at the left.
(Weigert stain. × 100)

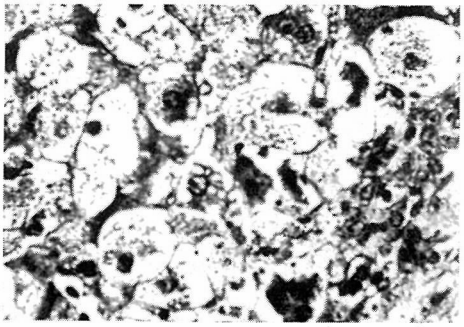

Fig. 8. Ballooning cells and acidophilic bodies.
(H.E. × 400)

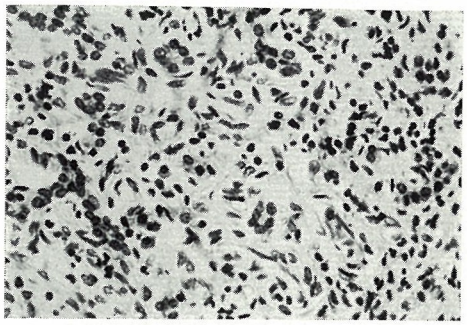

Fig. 9. Cellular infiltration in the interstitium. (H.E. × 400)

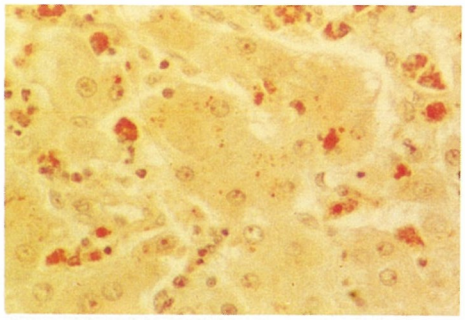

Fig. 10. Copper pigment in the Kupffer cells, liver cells and phagocytes in the fibrous tissues.
(Okamoto & Utamura's staining method. × 400)

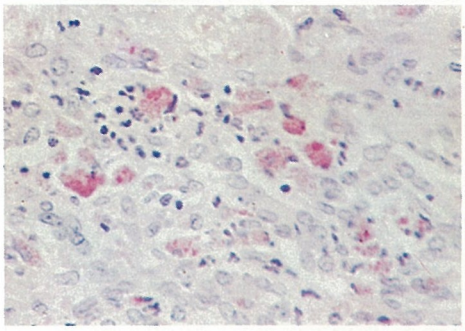

Fig. 11. Acid-fast fuchsin staining positive pigment. (× 400)

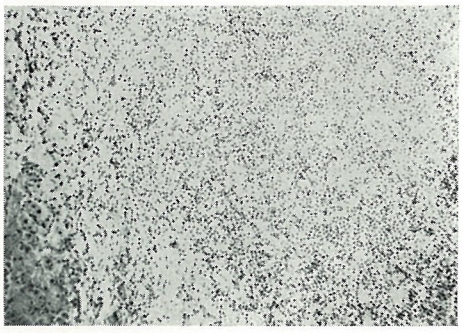

Fig. 12. Abscess of the liver. (H.E. × 100)

Cellular infiltration was found in the broad interstitium. They were lymphocytes, monocytes, plasma cells and neutrophils (Fig. 9). Copper was stained by the method of Okamoto and Utamura. It was found in the Kupffer cells, liver cells and phagocytes in the fibrous tissues (Fig. 10), but iron was not revealed. In paraffin section there was a pigment which was sudanophilic, acidfast fuchsin staining positive (Fig. 11), PAS positive and chrome alum hematoxylin positive. It was found mostly in macrophages in the periphery of the lobule and the interstitium and Kupffer cells. In the liver cells it was found granulally. Fat was revealed in some part of the lobules. Macroscopical, whitish yellow lesions were consisted of small abscess (Fig. 12).

There was a microabscess in the myocardium, too.

The spleen showed congestion and infiltration of numerous neutrophils. Its follicules were almost disappeared. In the lymph nodes the follicles were disa-

ppeared and the reticulum cells were proliferated. Many macrophages showed marked erythrophagia. Bone marrow was hypercellular.

In the kidney mesangial cells were proliferated and some parts of glomerulus adhered to the Bowman's capsule.

Submucosal veins of the esophagus were dilated. The lung showed focal hemorrhages.

Pathological diagnosis was as follows.

1. Postnecrotic liver cirrhosis ;
2. Multiple liver abscesses ;
3. Ascites ;
4. Septic spleen ;
5. Acute lymphadenitis ;
6. Atrophy of the thymus ;
7. Focal hemorrages of the lung ;
8. Petechial hemorrhages of the serous membrane ;
9. Hydro thorax ;
10. Glomerulonephritis.

COMMENT

This is a case of cirrhosis of the liver in 7-year-old boy. As far as we have collected the autopsy cases from "Annual of pathological autopsy cases in Japan" during recent 6 years, there are 176 cases of juvenile cirrhosis in 3,017 cases of cirrhosis of all ages. This number indicates 5.5 % of juvenile cirrhosis of all ages. Keller et al.[1] reported 40 cases of juvenile cirrhosis among 82,866 children admitted to the St. Louis Children's Hospital. Menne and Johnston[2] found 4 in 89 cases of cirrhosis and Karsner[3] found only one in 122 cases of cirrhosis of all ages.

There are many possible causes[4][5][6][7][8][9][10] for the pathogenesis of juvenile cirrhosis, and it is desirable to make an etiological classification but the identification of the etiologic agent in cirrhosis is frequently difficult. The most common cause of liver cirrhosis in children is congenital atresia of the bile duct. During recent years viral hepatitis in childhood has been frequently reported and many authors pointed out that cirrhosis of the liver occured after viral hepatitis in a number of the children. Other than these agents, many etiological agents of juvenile cirrhosis have been listed, for example, congenital metabolic disorders, hemolytic anomaly, cardiac cirrhosis, intoxication and so on.

Concerning our case, the pathological features, as a whole, showed postnecrotic

type of cirrhosis. The destruction of lobule was prominent and a large area was occupied by interstitium in which epitheliar prolifation of bile ducts was prominent. Cellular infiltration of monocytes, lymphocytes, and plasma cells was also observed in the periportal areas. The interstitial connective tissue was consisted of fine collagenous fibers and reticular fibers, but elastic fibers were hardly visible. In some parts collagenous fibers proliferated into the lobule, separating a small group of liver cells. Ballooning cells and acidophilic bodies were seen. Such histologic findings seemed to suggest viral origin.

In our case much copper is observed in the liver. As we could not obtain the permission of autopsy of the brain, we could not exclude Wilson's disease completely. But clinicaly there was no sign which suggested Wilson's disease. The kidney also presents a little copper in the tubular epithelium. But high levels of copper are found only in the liver. According to Butt et al[11], this organ dissimilarity is important in the differentiation of Wilson's disease from other types of cirrhosis.

Other than copper, a sudanophilic, acid-fast fuchsin positive and alum hematoxylin positive pigment was demonstrated. Takada[12] called this pigment as a ceroid-like pigment.

Other than these findings small abscesses were found here and there. By complication of those liver abscesses and septicemia, pre-existing lesion of the liver may be modified variously and histological appearance changed to confusing features.

Other pathological changes such as acute splenitis, microabscess of the myocardium, atrophy of the thymus, acute lymphadenitis are considered to be morphological manifestation of septicemia.

SAMMARY

An autopsy case of juvenile cirrhosis in a 7-year-old boy, who suffered from jaundice, edema and ascites has been reported, and in addition detailed histological and histochemical changes of the liver have been presented.

Postmortem examination disclosed postnecrotic liver cirrhosis with modification of septicemia. Histological findings of the liver was suggestive of viral origin.

REFERENCES

1) P.D. Keller and W.L. Nute: Cirrhosis of the liver in children; a clinical and pathologic study of cases., *J. Ped.*, **34**: 588-619, 1949.
2) F.R. Menne and T.W. Jonson: Cirrhosis of the liver. Its character and incidence in 6,500 autopsies., *Northwest Med.*, **32**: 129-137, 1933., cit. by 3)

3) H.T. Karsner: Morphology and pathogeneses of hepatic cirrhosis., *Am. J. Clin. Path.*, **13**: 569-606, 1943.
4) T. Amano, T. Adachi, Y. Honda and O. Midorikawa: Juvenile hepatosplenomegaly in identical twin brothers., *Acta Path. Jap.*, **16**: 55-68, 1966.
5) J.M. Craig, S.S. Gellis, D.Y. Hsia: Cirrhosis of the liver in infants and children., *A. M. A. Amer. J. Dis. Child.*, **90**: 299-322, 1955.
6) D. Stowens: Diseases of the liver and biliary system., *Pediatric Pathology.*, 591-623, Waverly Press, Inc., Baltimore, Md. 21202 U.S.A. 1959.
7) R. Cameron and P.C. Hou: *Pathological monographs I. Biliary cirrhosis.*, Birmingham, The Kynoch Press, 1962.
8) S. Amano and H. Yamamoto: Infectious hepatitis and cirrhosis as its sequela in Japan... Pathological investigation., *Ann. Report. Inst. Virus Resarch., Kyoto Univ.*, **3**: 185-334, 1960.
9) E.A. Gall: Posthepatitic, postnecrotic and nutritional cirrhosis; A pathologic analysis., *Amer. J. Path.*, **36**: 241-271, 1960.
10) L. Schiff: *Diseases of the liver.*, J. B. Lippincott company, 1956.
11) E.M. Butt, R.E. Nusboum, T.C. Gilmour and S.L. DiDio: Trace metal patterns in disease states. II. Copper storage diseases, with consideration of juvenile cirrhosis, Wilson's diseas, and hepatic copper of the newborn., *Amer. J. Clin. Path.*, **30**: 479-497, 1958.
12) R. Takada: A histochemical study on ceroid pigment., *Tr. Soc. Path. Jap.*, **49**: 1035-1066, 1960, (in Japanese).