RECURRENT INTRAHEPATIC OBSTRUCTIVE JAUNDICE
REPORT OF A CASE *

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In recent years, several new syndromes of jaundice have been recognized, some of which are thought to be due to inborn errors of metabolism. [1,2,3] Furthermore, four cases of benign recurrent jaundice with obstructive features have been reported by Summerskill and Walsh, [4] 1959 and Tygstrup, [5] 1960. In line with this, we are reporting a case of recurrent obstructive jaundice which closely corresponds to these four cases.

Case report: A ten year old girl, suffering from jaundice and itching, was admitted to Hacettepe Children's Hospital on November 30, 1959. She had been in good health until four months prior to admission when she developed pruritis and jaundice accompanied by dark urine, light colored stools and anorexia.

According to her family, the patient had not been in pain or feverish, and the degree of jaundice fluctuated as did the abnormal coloring of the stools. Prior to this jaundice she had always been in good health. The family history was noncontributory but there were cases of jaundice reported among the neighbors.

On admission the patient had no subjective complaints except for a poor appetite and itching. The physical examination revealed no abnormalities except a severe jaundice and an enlarged liver which was palpable 4 cm. below the right costal margin. The edge of the liver was smooth and not tender, the spleen was not felt, stools were acholic and the urine was dark. The patient had no fever.

Laboratory Data: Hemoglobin was 13 Gm. per 100 ml. and the white blood count was 4200 per cubic millimeter with 6 per cent stab, 68 per cent segmented neutrophils and 26 per cent lymphocytes. Urinalysis was normal except for 3 plus to 4 plus bilirubin. Cephalin - cholesterol flocculation, thymol turbidity, alkaline phosphatase, serum cholesterol and serum protein, fasting blood sugar and non - protein nitrogen were all within normal limits. The total serum bilirubin level was 20.3 mg. per 100 ml., 19.4 mg. direct and 0.9 mg. indirect. Initially, urobilin and urobilinogen were not present in the urine and stools were negative for stercobilinogens. The Coombs test was negative and the red cell fragility was within

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normal limits. The examination of the barium filled gastro-intestinal tract showed no abnormality. An exploratory laparotomy was performed during the obstructive stage. The bile tract appeared normal and there was no evidence of extrahepatic obstruction. A surgical liver biopsy performed at this time showed scattered areas of focal necrosis, an appreciable amount of intrahepatic bile stasis, especially in the centrolobular zone, and distended bile canaliculi. In the portal spaces a mild infiltration of mononuclear and polymorphonuclear leukocytes was evident, as well as some proliferation and hyperplasia of Kupffer's cells. There was no detectable pigment in the liver cells (fig. 1).

The patient's jaundice gradually subsided during her hospitalization and there was a concomitant improvement in her general condition. The serum bilirubin decreased to normal, the urine became lighter in color, and the stools became positive for stercobilinogen. She was discharged on January 11, 1960.

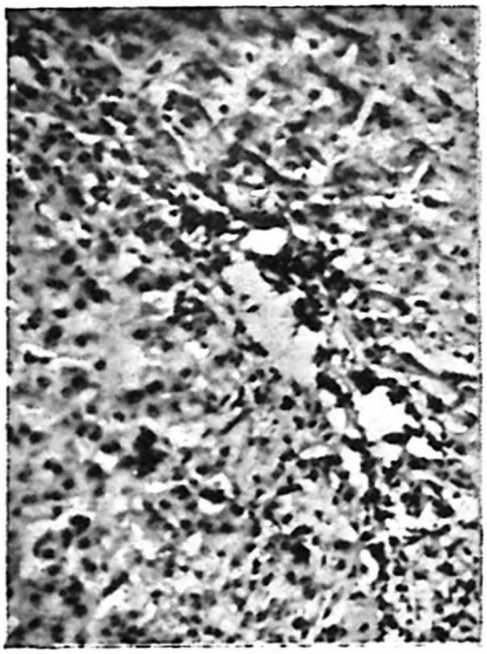

Figure 1.

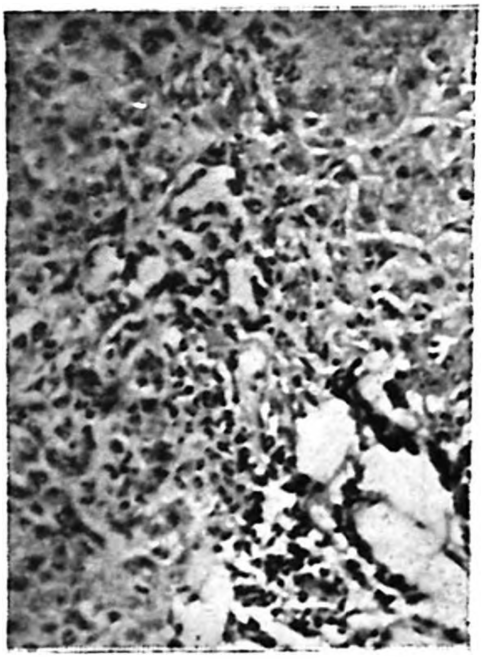

Figure 2.

The Second Admission

In the early days following the patient's discharge, her family reported no jaundice, but on the twenty-sixth day after discharge a recurrence was noted and she was re-admitted on February 9, 1960.

On admission, the patient was tired and had a poor appetite. She had a moderate degree of jaundice and itching. The liver was palpable 3 cm. below the right costal margin, the spleen was not felt. She had dark urine and acholic stools but no fever, no ascites and no edema.

Laboratory data : Hemoglobin was 11.9 Gm. per 100 ml. and the white blood cells were 4320 per cubic millimeter with normal differential. The liver function test results are shown in Table 2. The total serum bilirubin level was 7.8 mg.

per 100 ml., 5.4 mg. direct and 2.4 mg. indirect. Urinalysis was normal except for 1 plus to 2 plus bilirubin. Stool was negative for stercobilinogen. The patient's jaundice gradually subsided and finally entirely disappeared during her hospitalization. The urine became normal in color and the stool positive for stercobilinogen.

On the sixteenth day after admission, while the stool was negative for stercobilinogen, a needle biopsy of the liver was performed and there were no differences between the results of this biopsy and the previous one except for greater round cell infiltration in the portal tracts (fig. 2).

Steroid was used to observe its effect on the blood bilirubin level. 30 mg. of Prednisolone daily, was begun on February 25, 1960. Before treatment, the total serum bilirubin level was 7.8 mg. per 100 ml., with 5.4 mg. per 100 ml. direct bilirubin and 2.4 mg. per 100 ml. indirect. After twenty five days of steroid therapy, the total serum bilirubin fell to 1.1 mg. per 100 ml., with 8.4 mg. per 100 ml. direct bilirubin and 0.7 mg. per 100 ml. indirect. After the blood bilirubin level became normal the dose of steroid was decreased to 5 mg. daily and then the drug was stopped. The serum bilirubin showed a tendency to rise again while the patient was on the 5 mg. of Prednisolone.

After 53 days in the hospital, her parents insisted on taking the patient home. Unfortunately, we were unable to see her again.

Discussion

The presence of bilirubin in the urine and increased direct bilirubin level differentiated this case from those described by Crigler, Najjar and Gilbert. Similarly, increased direct reacting serum bilirubin, normal erythrocyte fragility test and negative Coombs test excluded a hemolytic process. Extrahepatic biliary tract obstruction was excluded by exploratory laparotomy. The absence of lipofuscin in the parenchymal cells of the liver differentiated the case from constitutional hyperbilirubinemia as described by Dubin and Johnson.

From the pathological and clinical findings it must be concluded that this case of jaundice was due to intrahepatic cholestasis. Intrahepatic cholestasis with biliary tract obstruction may be drug-induced or may represent a possible variant of virus hepatitis. [6,7,8,9] The production of cholestatic jaundice by the administration of drugs has been noted frequently in recent years. The drugs implicated include Thiouracil, Methimazole, Cinchophen, Sulfadiazine, Paraaminosalicylic acid, Chlorpromazine, Methyltestosterone and Chloropropamide. [10,11,12,13,14] But there is no history of drug consumption with our case. Probably cholestatic jaundice in this case is produced

TABLE 1

BIOCHEMICAL FINDINGS ON FIRST ADMISSION

DATE	SERUM								BLOOD			
	SERUM BILIRUBIN mg/100 ml.			ALKALINE PHOSPHATASE BODANSKY UNITS	CHOLESTEROL mg/100 ml.	PROTEIN Gm./100 ml.			FASTING BLOOD SUGAR	THYMOL TURBIDITY	CEPHALIN FLOCCULATION	STEROID ADMINISTRATION BY MOUTH mg. PER DAY
	DIRECT	INDIRECT	TOTAL			ALBUMIN	GLOBULIN	TOTAL				
Dec. 1, 1959	19.4	11.8	31.2	9.5	173	4.8	2.8	7.6	63	4	+	—
Dec. 10, 1959	11.2	6.6	17.8	4.0	—	—	—	—	—	—	+	—
Dec. 14, 1959	10.3	6.3	16.6	—	178	3.3	2.4	5.7	—	3	+	—
Dec. 23. 1959	4.8	2.5	7.3	5.3	168	3.9	3.1	7.0	—	—	—	—
Jan. 6, 1960	1.6	0.8	2 4	—	—	—	—	—	—	—	—	—
Jan. 11, 1960	0.9	0.5	1.4	—	—	—	—	—	—	—	—	—

TABLE 2

BIOCHEMICAL FINDINGS ON SECOND ADMISSION

DATE	SERUM								BLOOD			
Feb. 9, 1960	2.1	0.7	2.8	5.3	162	5.0	3.3	8.3	—	2.5	—	—
Feb. 15, 1960	4.5	2.1	6 6	—	—	—	—	—	—	—	—	—
Feb. 19, 1960	5.3	2.5	7.8	15.8	—	—	—	—	—	—	—	—
Feb. 25, 1960	5.4	2.4	7.8	13.9	—	—	—	—	—	—	—	30 mg. Prednisolone
Mar. 2, 1960	4.4	2.4	6.8	8.4	220	—	—	—	—	—	—	20 mg. « «
Mar. 16, 1960	—	—	—	—	—	—	—	—	—	—	—	20 mg. «
Mar. 22, 1960	0.4	0.7	1 1	—	—	—	—	—	—	—	—	10 mg. « «
Mar. 24, 1960	—	—	—	—	—	—	—	—	—	—	—	5 mg. « «
Mar. 28, 1960	0 7	0.9	1.6	—	—	—	—	—	—	—	—	5 mg. « «

by a virus hepatitis. The incidence of jaundice among her neighbors further supports this diagnosis. Precipitating factors for the recurrence of jaundice are not known. It is possible that the etiologic agent is a virus, probably a variant of the infectious hepatitis virus.

Patterson et al., 1954, found a choleretic action of steroids in normal subjects and in one patient with virus hepatitis. However Shay and Sun, 1957, were not able to demonstrate a choleretic action of hydro - cortisone. In our case, during the steroid treatment, jaundice disappeared and at the same time the stools changed from acholic to normal color. It can be suggested that there was a choleretic action of the steroid in this case. It is however, impossible to decide whether the jaundice disappeared because of the choleretic action of the steroid or because of spontaneous amelioration.

Summary

A ten year old girl with recurrent intrahepatic obstructive jaundice is reported. A variant of the infectious hepatitis virus is believed to be responsible for the recurrent course.

We acknowledge with gratitude the interpretations made of our liver biopsy slides by Dr. I. N. Dubin, Dr. W. H. J. Summerskill and Dr. A. Günalp.

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