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Case Reports

A Case of Asymptomatic Hyperbilirubinemia

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CASE REPORT

Five year old (M.Z.) presented to us with the complaint of persistent jaundice for the last one year.

The child was well till the age of four years when the parents noticed that the child had mild jaundice. He was then subjected to various investigations and treatments but no definitive diagnosis had been established. He feels well, has no symptoms and is normal in growth and development. His birth history is insignificant and he has not suffered from jaundice prior to this episode. He has two siblings who are healthy. His parents are first cousins but family history is negative for any similar complaint or chronic liver disease.

On physical examination his weight and height were on the twenty fifth percentile and the only positive finding beside mild icterus was a 1.5 cm palpable liver with upper border in the fifth intercostal space. It was soft, smooth, nontender and non-pulsatile.

Laboratory investigations

His CBC, liver function tests including aminotransferases, total proteins and albumin, cholesterol and glucose were normal, with the exception of total bilirubin of 1.7 (direct 1 mg/dl). His urine examination showed traces of urobilinogen and serum hepatitis B surface antigen was negative. Liver scan showed partial excretion of radionucleoid dye.

With provisional diagnosis of Benign Familial cholestasis, he underwent a percutaneous liver biopsy. Gross appearance of liver tissue was grayish brown. Light microscopy showed cores of liver tissue with a maintained lobular architecture. The portal tracts were normocellular with no significant bile duct proliferation. The limiting plates were intact. There was coarse dark brown pigment in the hepatocytes around the central veins. No other significant feature was seen. The appearance were of a case of Dubin Johnson syndrome.

DISCUSSION

Dubin Johnson Syndrome

This disorder was first described in 1954, almost simultaneously by Dubin and Johnson, and Speniz and Nelson[1,2]. Although worldwide in distribution, affecting both sexes equally, it has a higher frequency among Iranian Jews. The clinical finding is mild jaundice with occasional other symptoms like malaise, vague myalgia, fatigue and weakness. Presenting at any age, it is most common during adolescence. Growth and development are generally normal and the jaundice shows fluctuation due to intercurrent illnesses or intake of drugs that impair hepatic excretion of anions (e.g. oral contra ceptives)[3]. The hyperbilirubinemia is predominantly conjugated. Values range typically between 2-5 mg/dl although occasionally as high as 20 mg/dl have been reported. All other liver function tests are generally normal as are various hematological studies. The diagnosis is made primarily by liver biopsy, though the excretion of minor bile acids like ursodeoxycholic acid is reduced[4]. Imaging studies like oral cholecystography even when supplemented with contrast media fails to visualize the gallbladder but intravenous administration of iodipamide may help in visualization of gall bladder at 4-6 hours[5,6]. Grossly, the liver is pigmented to the point of appearing black in colour. Light microscopy reveals no scarring, hepatocellular necrosis or distortion of Zonal architecture. Instead, the characteristic feature is accumulation of a coarsely granular pigment, most pronounced in the centrilobular zones[7].

The appearance of pigment on electron microscopy suggests that it is lysosomal. Its nature has been the subject of some debate, some authors considering it a lipofuscin and others, melanin derivatives[8]. The differential diagnosis includes benign familial cholestasis (Hepatic storage syndrome) and Rotor's syndrome. The clinical features of these conditions are shown in Table 1. No specific treatment is required but assurance about the benign nature of this disorder is essential. Life expectancy is unaffected in these patients.

Table 1: Principal characteristics of Dubin-Johnson, Rotor's, and hepatic storage syndromes.

	Dubin-Johnson Syndrome	Rotor's Syndrome	Hepatic Storage syndrome
Original description	1954	1948	1971
Appearance of liver	Grossly black	Normal	Normal
Histology of liver	Dark pigment Predominantly in centrilobular areas otherwise normal	Normal no increase in pigmentation	Normal no increase in pigmentation
Serum bilirubin	Increased: usually between 2 and 5 mg/dl: occasionally as high as 25 mg/dl: predominantly direct-reacting (=60% of total)	Increased: usually between 2 and 5 mg/dl: occasionally as high as 25 mg/dl: predominant direct-reacting (=60% of total)	Increased: usually reported between 3 and 7 mg/dl: predominantly direct reacting.
Routine liver function	Normal except for bilirubin	Normal except for bilirubin	Normal except for bilirubin
Oral cholecystogram	Usually does not visualize the gallbladder	Usually visualizes the the gallbladder	Visualizes be delayed up to 20 hours
Serum bile acid	Normal (usually)	Normal	Normal
45 minutes plasma BSP retention	Normal or moderately (20%) increased (usually < 20%) secondary rise at 90-120 min.	Increased (>25%) owing to slow initial disappearance; no secondary increase	Increased (only reported value 36%): no secondary rise
BSP transport maximum (normal 82.15/SD/gm min)	Markedly reduced (0.9.0.4 mg/min)	Minimally to moderately reduced; one series reported 4.4 x 18 mg/min	Normal or slightly reduced (5.7-7 mg/min)
BSP storage capacity (Normal 61-14 mg/mg/dl)	Normal	Reduced; values in one series were 7.7 +3.4 mg/mg/dl	Reduced; reported values 17-23 mg/mg/dl
Urinary coproporphyrin excretion	Normal or slightly increased total > 80% as coproporphyrin-1	Markedly increased total: increased proportion of coproporphyrin-1 but < 80%	No data reported
Presumed defect	Impaired biliary excretion of conjugated organic anions	Impaired biliary excretion: ? Impaired storage capacity	? Impaired storage capacity
Age when hyperbilirubinemia first recognized	Variable (birth to age 70): usually by early adulthood (pregnancy, "pill")	Variable: usually in childhood	Little Data
Symptoms	Non-specific or absent	Non-specific or absent	Non-specific or absent
Physical findings	Jaundice, occasional hepatomegaly	jaundice	jaundice
Treatment	Non: avoid estrogens	None	None
Prognosis	Good	Good	Good
Incidence	Rare, but up to 1:130 in Iranian Jews	Rare	Rare
Inheritance	Autosomal recessive in most kindreds	Autosomal recessive	Unknown

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