CHRONIC IDIOPATHIC NONHEMOLYTIC JAUNDICE (DUBIN-JOHNSON SYNDROME)

Report of a Case

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CHRONIC idiopathic nonhemolytic jaundice was independently described by Dubin and Johnson[1] and by Sprinz and Nelson[2] in 1954. Dubin[3] extensively reviewed the clinical features of the 50 cases that had been reported up to 1958. The commonest clinical findings are jaundice, abdominal pain, fatigue, dark urine, and slight hepatomegaly. The jaundice is due to the presence of both free and conjugated bilirubin in the blood. The characteristic pathologic finding is the presence of an intracellular lipochrome pigment in an otherwise normal-appearing liver. The patient described in this report has many of the features of this unusual syndrome.

Report of a Case

A 35-year-old housewife was in good health until November, 1960. At that time a severely sore throat, extreme fatigue, bloating, recurrent vomiting, and several episodes of moderately severe pain in the right upper quadrant occurred. On roentgen study at another hospital, the gallbladder was poorly visualized.

The symptoms of fatigue, bloating, and pain in the right upper quadrant continued. In February, 1961, three months after the initial symptoms occurred, a mild jaundice was noted for the first time. She was hospitalized for study. Hepatic function tests showed the total serum bilirubin to be 1.65 mg. per 100 ml., and the direct reacting bilirubin to be 1.15 mg. per 100 ml. The sulfobromophthalein test showed 37 per cent retention in 45 minutes. The serum alkaline phosphatase content, serum glutamic transaminase level, serum protein electrophoretic pattern, serum cholesterol content, and serum cholesterol esters were normal. On hepatic biopsy the gross specimen was black, and the histologic diagnosis was Dubin-Johnson syndrome.

Because of persistent symptoms the patient was referred to the Cleveland Clinic for consultation in May, 1961, six months after the initial onset of symptoms. No other member of the patient's immediate family had had jaundice. The mother, father, and two brothers were in good health. The patient had undergone appendectomy at 16 years of age, oophorectomy at 26 years of age, and hysterectomy for endometriosis at 32 years of age. The findings on physical examination were normal.

The laboratory findings included a blood hemoglobin content of 13.6 gm. per 100 ml., and a hematocrit reading of 40 per cent. The white blood cell count, differential count, and reticulocyte count were normal. Hepatic function studies showed the total serum bilirubin to be 1.6 mg., and the direct reacting bilirubin to be 0.4 mg. per 100 ml. The sulfobromophthalein test

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showed 8 per cent retention. Serum alkaline phosphatase content, serum transaminase level, cephalin flocculation test, and protein electrophoretic pattern were normal. A roentgenogram of the chest showed no abnormality; a cholecystogram revealed a poorly visualized gallbladder but no stones.

A biopsy specimen of the liver showed normal hepatic architecture, but the parenchymal cells contained large amounts of a coarsely granular, slightly greenish-yellow pigment. There was no pattern to the pigmentation, and the Kupffer cells were free of pigment. Bile stasis was absent. Special stains of sections for iron and acid-fastness were negative. The findings were considered to be consistent with a diagnosis of Dubin-Johnson syndrome.

The patient's symptoms gradually disappeared and, except for occasional pain in the right upper quadrant and fatigue, she has felt well. In February, 1961, her physician reported normal findings on an intravenous cholangiogram.

Discussion

The Dubin-Johnson syndrome often seems to have a familial distribution. It may occur in either sex and has a wide ethnic distribution. While the age at which onset can occur varies considerably, the majority of patients have noted jaundice before becoming 20 years of age. The degree of jaundice as well as the associated symptoms may fluctuate, and exacerbations are often precipitated by infections, surgery, or pregnancy.

The majority of the patients have abdominal pain, often in the region of the liver. Other symptoms include weakness, nausea or vomiting, anorexia, and diarrhea. In addition to jaundice, many patients have enlargement of the liver, and in some the liver may be tender.

Serum bilirubin levels range from 2.4 to 19 mg. per 100 ml. The direct reacting bilirubin accounts for about 60 per cent of the total bilirubin. Hematologic studies show no evidence of increased destruction of red blood cells. Mild elevations of serum alkaline phosphatase levels, and intermittently positive flocculation tests occur. Retention of sulfobromophthalein frequently occurs,[4] and on oral cholecystography there usually is poor visualization of the gallbladder.

Histologic examination of the liver reveals an intracellular, coarsely granular, lipochrome pigment having a centrolobular distribution. The origin and the composition of this pigment are not known. In some cases a melanin-like pigment accumulates.[5] The exact metabolic defect in the hepatic cells in this syndrome is not known, but apparently it is in the excretory mechanism of the cells. Electron microscopy has shown that the abnormal pigment is located in a cytoplasmic particle known as a lysosome, which is thought to function in the excretion of conjugated bilirubin.[6]

Arias[7] recently reported a family, three members of whom had nonhemolytic jaundice with conjugated bilirubin in the serum. In two of the three members an abnormal pigment was present in the hepatic cells. The hyperbilirubinemia does not depend, therefore, on the presence of the pigment. His study also raises the question of the relationship of this syndrome to the Rotor syndrome, which is also

a familial hyperbilirubinemia of conjugated bilirubin but without pigment in the hepatic cells.

Progressive hepatic disease does not occur in patients having the Dubin-Johnson syndrome; however, recurrence of symptoms with temporary disability is usual. There is at present no specific treatment of this disorder.

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