Cholescintigraphy in the Diagnosis of Rotor Syndrome

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In three patients with chronic conjugated hyperbilirubinemia who carried the diagnosis of Rotor syndrome, ^{99m}Tc-HIDA cholescintigraphy was performed. In these patients, the liver was either not visualized or it was seen very faintly with slow liver uptake, persistent visualization of the cardiac blood pool and prominent kidney excretion. The present observation emphasizes the contribution of cholescintigraphy in the diagnosis of Rotor syndrome.

Key Words: Rotor syndrome; technetium-99m-HIDA cholescintigraphy; hyperbilirubinemia; Dubin-Johnson syndrome

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Chronic nonhemolytic conjugated hyperbilirubinemia characterizes both Rotor and Dubin-Johnson syndromes (*1*). Differentiation between these two hereditary disorders is based mainly on histologic findings seen in liver biopsy specimens (*2*). Plasma clearance of Bromosulfophthalein (BSP) and other anionic dyes along with urinary coproporphyrin isomer excretion have long been considered as diagnostic procedures (*3*).

In this report we present our experience with ^{99m}Tc-HIDA cholescintigraphy in three patients with chronic conjugated hyperbilirubinemia who carried the diagnosis of Rotor syndrome.

CASE REPORTS

Patient One

This patient was a 14-yr-old male who had jaundice since birth. The patient was the only child in the family. There was neither parental consanguinity nor family history of jaundice or liver disease. No past history of hepatitis or blood transfusion could be elicited. There were no significant findings on physical examination except for icteric sclerae and soft, painless hepatomegaly 2 cm below the right costal margin. On investigation, total serum bilirubin concentration was 83.79 μmole/liter, with a conjugated fraction of 80.37 μmole/liter. Other liver function tests and blood chemistries were normal except for glucose-6-phosphate dehydrogenase (G6PD) deficiency. The liver biopsy was normal without pigmented cells. Ultrasound examination revealed normal liver and gallbladder.

Cholescintigraphy was performed using ^{99m}Tc-HIDA. The patient was given 5 mCi (185 MBq) and serial images were obtained. The liver, gallbladder and biliary tree were not visualized even after 2 hr and no radioactivity was excreted into the intestine. Persistent visualization of the cardiac blood pool and prominent kidney excretion was noticed (Fig. 1).

Patient Two

A 6-yr-old male was hospitalized because of jaundice noticed the fifth day of life. He was the only child of healthy unrelated parents. Family history was not contributory for jaundice or liver disease. There was no history of hepatitis or blood transfusion. Physical examination was unremarkable except for obvious icteric sclerae. Total bilirubin was 71.82 μmole/liter with a conjugated component of 59.85 μmole/liter. The hemoglobin electrophoretic pattern showed elevation of HbA_2 (5.9%) and HbF (6.4%). Other blood chemistries were normal. Liver biopsy was denied by the family. Ultrasound examination of liver and gallbladder was normal.

A hepatobiliary scan was performed using ^{99m}Tc-HIDA. The patient was injected with 5 mCi (185 MBq) and serial images were obtained for 24 hr. The liver was not visualized during the entire examination. The radiotracer was retained for a long period of time in the circulation and persistent visualization of the kidneys was noticed (Fig. 2).

Patient Three

A 2-yr-old male was admitted with persistent jaundice that first appeared on the third day of life. His 6-mo-old sister was healthy without jaundice. Family history was not contributory. The physical examination was benign. Admission total biliburin value was 42.75 μmole/liter with a conjugated component of 39.33 μmole/liter. Hemoglobin electrophoresis showed that he was a carrier of β-thalassemia trait. The patient had also G6PD deficiency. Liver function tests were normal. Liver biopsy was denied by the family. Ultrasound examination of liver and gallbladder was normal.

A hepatobiliary scan was performed using ^{99m}Tc-HIDA. A dose of 5 mCi (185 MBq) was injected and serial images were obtained. A very faint hepatic accumulation of radiotracer was noticed after 3 hr with persistent visualization of the cardiac blood pool (Fig. 3).

DISCUSSION

Conjugated hyperbilirubinemia may be attributed to a number of infections, metabolic disorders, anatomic defects, chemical liver injury from a wide variety of drugs (i.e., androgenic and estrogenic steroids, erythromycins,

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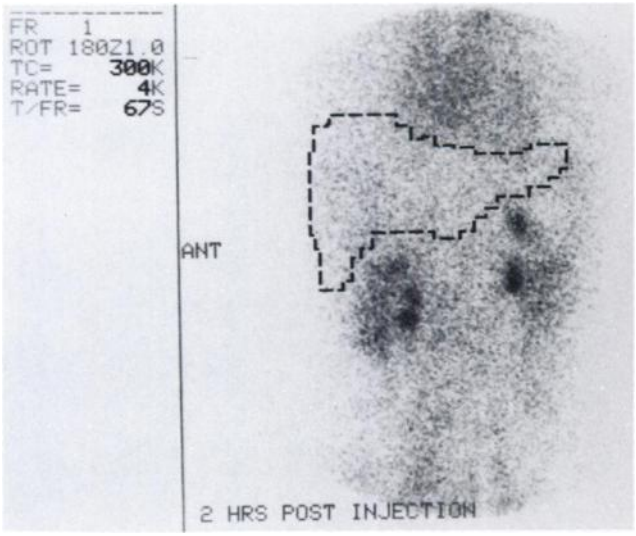

FIGURE 1. Technetium-99m-HIDA cholescintigram. The liver is not visualized and no radioactivity is excreted in the intestine after 2 hr.

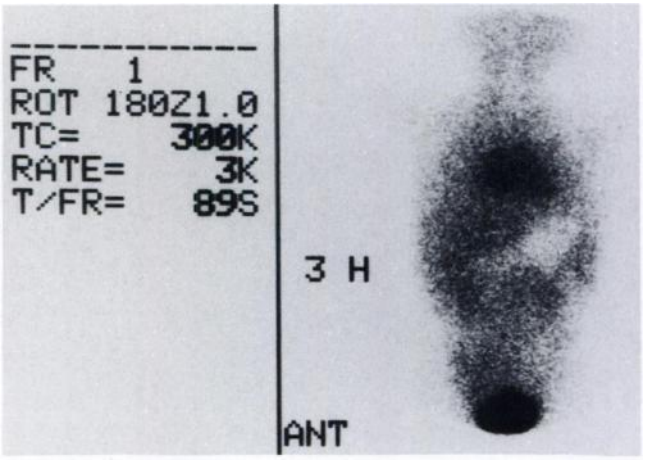

FIGURE 3. Technetium-99m-HIDA cholescintigram. A very faint hepatic accumulation of radiotracer is noticed after 3 hr. The hepatobiliary system is not visualized.

phenothiazines) or may be inherited (*4*). There are two distinct familial pathophysiologic entities, namely the Dubin-Johnson and Rotor syndromes, characterized by chronic, benign, nonhemolytic jaundice due to raised, predominantly direct bilirubin (*1*). Differentiation between the two is made on the basis of liver biopsy, plasma clearance patterns of BSP and determination of coproporphyrin in urine (*3,5*). The former is not an easily accepted procedure especially in cases where no therapeutic gain can be offered to the patient. The latter is no longer advised because of reports of fatal anaphylactoid reactions with BSP (*6*). As far as urinary coproporphyrin is concerned, it is known that measurement of isomer I and III can safely differentiate these two syndromes (*5*). These determinations were not done in our patients due to the unavailability of relevant analytical procedures in our hospital.

Previous reports have stressed the patterns of somewhat variable cholescintigraphic findings by using radioactive dyes such as ^{131}I-Rose bengal, ^{131}I-BSP, ^{99m}Tc-mebrofenin as well as ^{99m}Tc-IDA derivatives in diagnosing Rotor syn-

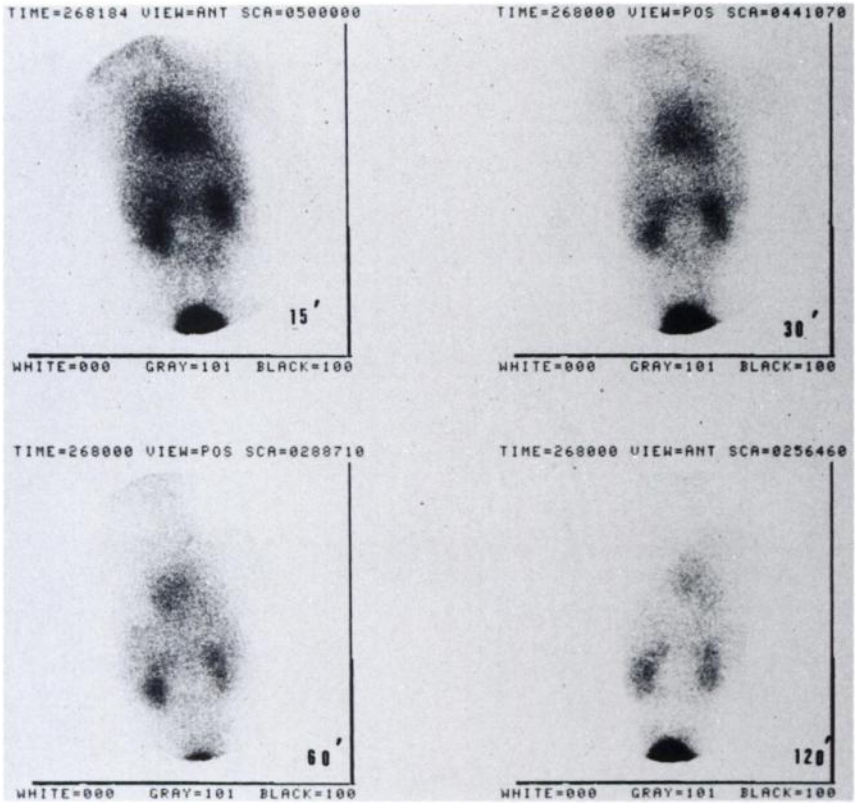

FIGURE 2. Technetium-99m-HIDA cholescintigram. The liver is not visualized and selective renal excretion of the radiotracer is demonstrated.

drome and differentiating this disorder from Dubin-Johnson syndrome and hepatocellular disease (*7–11*). In patients with Dubin-Johnson syndrome, a combination of prolonged and intense visualization of the liver with delayed visualization of gallbladder can be seen. By contrast, in Rotor syndrome scintigraphic findings are markedly different with absent or very faint uptake and prolonged visualization of the cardiac blood pool.

In the first patient, normal histology and isotopic findings identical to that reported by other investigators, can be regarded as compatible with the diagnosis of Rotor syndrome. In this syndrome, abnormal transfer of BSP into the liver associated with abnormalities in storage and conjugation of the dye have been found (*3*). Thus, the absent or very poor uptake of ^{99m}Tc-HIDA seems to be anticipated.

Although a liver biopsy was not done in the remaining two patients, the cholescintigraphic findings were identical to the first and the tentative diagnosis of Rotor syndrome was made. This is supported by the similar clinical presentation and laboratory findings of the three patients while the isotopic pattern is totally different from that seen in patients with Dubin-Johnson syndrome.

In our patients, the ^{99m}Tc-HIDA cholescintigraphic pattern resembles that seen in patients with hepatocellular disease and markedly elevated serum bilirubin. Thus, from the practical point of view, in patients with conjugated hyperbilirubinemia of unknown origin, nonvisualization of the liver with ^{99m}Tc-HIDA may not necessarily be attributed to advanced hepatocellular damage in as much as the same pattern can be seen in a benign entity as the Rotor syndrome.

In conclusion, cholescintigraphy is a simple and informative procedure for the diagnosis of Rotor syndrome and has a place in pediatric hepatology.

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