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The diagnostic value of hepatobiliary scintigraphy in Rotor syndrome in a 3-year-old boy: is it enough?

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Abstract

Rotor syndrome (RS) is a benign, inherited, commonly misdiagnosed cause of conjugated hyperbilirubinemia, whose identification prevents unnecessary invasive investigations. We present the case of a 3-year-old male with phenotypic and laboratory findings of RS, but negative genetic test, whose diagnosis was confirmed by hepatobiliary scintigraphy.

Keywords: Rotor syndrome; hepatobiliary scintigraphy; cholescintigraphy.

Introduction

Rotor syndrome (RS) is a benign, inherited, commonly misdiagnosed cause of conjugated hyperbilirubinemia (*1*) whose identification prevents unnecessary invasive investigations. It is characterized by mild conjugated hyperbilirubinemia (2-5 mg/dl), icteric sclera usually presents shortly after birth and elevated urinary coproporphyrin excretion (*2*). Genetic diagnosis reveals a homozygous inactivation of SLCO1B1 and SLCO1B3 genes (*3*). We present the case of a 3-year-old male with phenotypic and laboratory findings of RS, but negative genetic test, whose diagnosis was confirmed by hepatobiliary cholescintigraphy (HBS).

Case report

A 3-year-old male presented with persistent jaundice since birth. The physical examination was unremarkable, except for mild icterus of sclerae. Serum total biliburin was elevated (2.59 mg/dl) with a conjuctated fraction of 2.41 mg/dl. Liver function tests, abdomen ultrasound, serology for viral and autoimmune hepatitis, and tests for genetic disorders, such as cystic fibrosis and Wilson disease, were normal. Additional investigation revealed elevated coproporphyrin I (97nmol/l, normal range <40 nmol/l) and III (109nmol/l, normal range< 75nmol/l). Eventually, the patient underwent HBS after intravenous injection of 45MBq of Tc-99m Br-IDA, according to the European pediatric card dose (version 5.7.2016). During dynamic acquisition of data, the perfusion phase (2sec/frames for 60seconds) was normal, while the following data (1min/frames for 60minutes) were significantly abnormal. No succession of the normal scintigraphic phases (hepatic, biliary, and intestinal) was noticed, as Tc-99m Br-IDA liver uptake was too slow **(FIGURE 1A)**.

The biliary duct system and gallbladder were unvisualized, while a faint visualization of the liver and small bowel was more evident at the delayed static images **(FIGURE 1B: anterior/posterior, FIGURE 1C: anterior)**. In contrast, an extremely prolonged blood pool phase (visualization of the heart and spleen) and a prominent renal excretion, mimicking liver failure, were noticed.

A molecular genetic analysis with next-generation sequencing was performed, but no sequence of SLCO1B1 and SLCO1B3 genes involving in RS was detected. During a follow-up period of 2 years, the patient has a favorable clinical course without any complication.

Discussion

HBS is an inexpensive and straightforward method and represents the imaging test of choice for RS diagnosis, allowing accurate differential diagnosis (3). Even without considering clinic-laboratory findings, this too faint hepatic visualization, although suggestive of hepatocellular disease, is unlikely consistent with cirrhosis or hepatitis. The abnormal, instead of normal, hepatic perfusion phase (increased and/or anticipated) due to liver arterialization, is more likely in these disorders. Dubin-Johnson syndrome, a similar syndrome of conjugated hyperbilirubinemia, presents, on the contrary, HBS findings of intrahepatic cholestasis (no biliary phase associated with prolonged, rapid and intensive, instead of slow and negligible, liver radiotracer uptake) (*3,4*).

Concerning the genetic diagnosis of RS, SLCO1B1 and SLCO1B3 genes are essential, as they provide instructions for making proteins, called organic anion transporting polypeptide 1B1 (OATP1B1) and organic anion transporting polypeptide 1B3

(OATP1B3), that are expressed in the sinusoidal membrane of hepatocytes and ensure the reabsorption of conjugated bilirubin from the blood into the liver (*3*). In RS, the homozygous inactivation of both genes, results in nonfunctional or absent proteins and increased bilirubinemia and porphyrinuria (*3,5*).

Our case, owing to clinical, laboratory and HBS findings, was considered to be affected by RS, most likely representing the first case without sequences from the two known genes associated with RS.

Conclusion

In the rare case of a child with typical RS clinical, laboratory features, the diagnosis of RS might be confirmed only by HBS typical findings and may not require the conduction of genetic test, which is an expensive, time consuming and as we can conclude, not always cost-effective diagnostic tool.

Conflict of Interest: None to declare.

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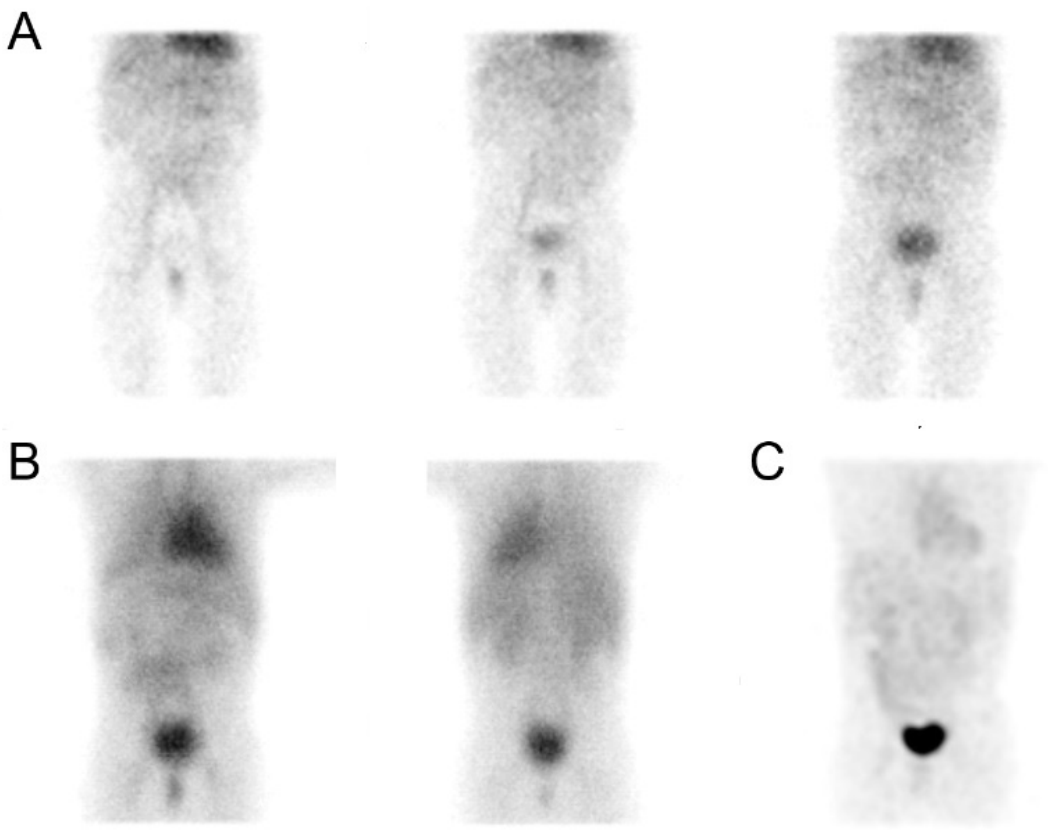

FIGURE 1. Abnormal Tc-99m-Brida hepatobiliary scintigraphy consistent with Rotor syndrome in a 3-year-old male. (A) Left to right: 10^{th}, 30^{th}, and 50^{th} minute/frame images of dynamic acquisition (B) 1.5h-delayed static images (anterior/posterior) and (C) 3h-delayed maximal projection intensity 3D-reconstruction image.