Rotor syndrome

Synonyms: Rotor, Manahan and Florentin syndrome; Rotor's type of bilirubinaemia

What is rotor syndrome?[1]

Rotor syndrome was first described by Rotor et al in 1948 and was initially considered a variant of Dubin-Johnson syndrome. Subsequently, a number of functional studies confirmed that patients with Rotor syndrome do not have defective biliary excretion, but rather a defect in hepatic uptake and storage.

Animal experiments and studies of patients with Rotor syndrome suggest that there are homozygous mutations of both SLCO1B1/OATP1B1 and SLCO1B3/OATP1B3 resulting in simultaneous absence of OATP1B1 and OATP1B3 transporters. SLCO1B1 and SLCO1B3 lie very close together on chromosome 12.

Pathogenesis

It can be distinguished from Dubin-Johnson syndrome because in this syndrome there is an *absence of hepatic pigmentation*. There are also differences in urinary coproporphyrin excretion, hepatic clearance of bromosulphophthalein and oral cholecystography.

There is an impairment of excretion of organic anions from hepatocytes into the canalicular lumen. This causes defective excretion of conjugated bilirubin, its reabsorption into the blood and excretion in the urine.

How common is rotor syndrome? (Epidemiology)

It occurs sporadically in families and is thought to be inherited in an autosomal recessive fashion.[2] There are no available population-based figures for its prevalence or incidence:

- It appears to be most common in the Philippines, where it was originally described by Arturo Belleza Rotor and co-workers in 1948.
- It is exceedingly rare in the UK and worldwide.

Symptoms of rotor syndrome (presentation) [1]

Clinically, the disorder is indistinguishable from Dubin-Johnson syndrome, and presents with predominantly a mixed conjugated and unconjugated hyperbilirubinemia in otherwise asymptomatic individuals.

It can present in the neonatal period or in childhood. Serum total bilirubin levels are usually between 2 and 5 mg/dL, but can be higher.

Any symptoms, if present, may include:

- Chronic jaundice without evidence of haemolysis.
- Attacks of intermittent epigastric discomfort and abdominal pain may occur but are rare.
- There may be episodic fever.

Differential diagnosis

- Dubin-Johnson syndrome.
- Viral hepatitis.
- Drug-induced cholestasis (including anaesthetic reactions).
- Autoimmune hepatitis.
- Wilson's disease.
- Haemochromatosis.
- Alpha-1-antitrypsin deficiency.
- Benign recurrent cholestasis.
- Any cause of obstruction of the small or large bile ducts in children.
- Sarcoidosis.
- Amyloidosis.

Diagnosing rotor syndrome (investigations) [1]

Diagnosis is important to differentiate from other causes of hepatobiliary disorders.

Serum and urinary bilirubin are elevated and largely in conjugated (direct) form. LFTs, ultrasound and oral cholecystogram are otherwise normal.

Urine tests are diagnostic and can differentiate Rotor syndrome from Dubin-Johnson syndrome. In Rotor syndrome, total coproporphyrin excretion in urine is elevated 2–5 fold, with 65% constituting coproporphyrin I.

Further diagnostic or invasive testing is usually not indicated. If performed, a HIDA scan will reveal slow liver uptake and prominent kidney excretion, and histology will show normal liver tissue with absent pigment.

Management of rotor syndrome

Rotor syndrome is benign and does not require any therapy. [1]

Other hepatic disease can damage the liver preferentially in patients with the condition, so it is best to avoid alcohol, hepatotoxic drugs, exposure to viral hepatitis, etc.

Complications of rotor syndrome

Can occasionally progress to liver failure if there is another cause of hepatic compromise.

Prognosis

Usually good with a benign course, unless there is coexistent liver disease.

Further reading

- Morais M, Couvert P, Jeru I, et al; Rotor Syndrome Presenting as Dubin-Johnson Syndrome. Case Rep Gastroenterol. 2022 Aug 16;16(2):452-455. doi: 10.1159/000525517. eCollection 2022 May-Aug.

- Morais MB, Machado MV; Benign inheritable disorders of bilirubin metabolism manifested by conjugated hyperbilirubinemia-A narrative review. United European Gastroenterol J. 2022 Sep;10(7):745-753. doi: 10.1002/ueg2.12279. Epub 2022 Jul 20.

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