

## TEACHING FILES (GRAND ROUNDS)

# RECURRENT HYPERBILIRUBINEMIA IN AN INFANT

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### KEYWORDS

Crigler-Najjar syndrome, phototherapy, unconjugated jaundice

### ARTICLE HISTORY

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### Clinical Problem:

A 7-month-old boy was referred for recurrent indirect hyperbilirubinemia since day 6 of life. The child had received phototherapy twice for same in neonatal period. He was also on phenobarbitone. Whenever, the phenobarbitone was stopped, jaundice used to recur. His milestones were normal. On examination, he was jaundice free and systemic examination was normal. Investigations including G6PD and pyruvate kinase activity, thyroid function tests and hemoglobin electrophoresis were normal.

*What is the diagnosis and management of this patient?*

### Discussion:

The diagnostic evaluation should establish whether the hyperbilirubinemia is unconjugated, conjugated or mixed. If it is unconjugated like in our patient, one should look for anemia and if present, evaluate for hemolysis, and then for specific hemolytic disorders. If there is no anemia, the patient should be evaluated for the possibility of underlying liver disease or inherited disorders of impaired bilirubin conjugation. Normal liver function tests will rule out underlying liver disease and points towards inherited disorders. Recurrent indirect hyperbilirubinemias in an infant can be caused by 2 autosomal recessive disorders- Gilbert syndrome and Crigler-Najjar syndrome. Both of these are 2 ends of the same spectrum with Gilbert syndrome being on the milder side.<sup>1</sup> Gilbert syndrome is a relatively common, benign condition. It occurs due to mildly decreased UDP-glucuronosyltransferase conjugation and impaired bilirubin uptake. It is commonly asymptomatic or presents as mild jaundice, usually vague abdominal pain or distension.<sup>2</sup> There is unconjugated bilirubinemia without overt hemolysis. Crigler-Najjar syndrome has 2 subtypes. Type 1 has absent UDP-glucuronosyltransferase. It presents early in life with unconjugated hyperbilirubinemia and kernicterus, but some patients may not have neurologic

signs until later in life. Type II is similar but less severe and responds to phenobarbitone, which increases liver enzyme synthesis.<sup>3</sup> Since our patient responded to phenobarbitone, the clinical diagnosis most likely in our patient is Crigler-Najjar syndrome type 2. Since patients with Crigler-Najjar syndrome type II are much less likely to develop neurologic consequences than those with type I disease,<sup>3</sup> specific treatment for the hyperbilirubinemia may be unnecessary. However, it may be desirable to treat patients in whom jaundice has impaired quality of life. This can be accomplished by the administration of phenobarbitone, which reduces serum bilirubin levels by at least 25 percent. A response should be expected within two to three weeks.<sup>3</sup> A similar benefit can be expected with clofibrate, which is associated with fewer side effects.<sup>4</sup> If the patient conceives, there is a high risk of increase in bilirubin levels. The unconjugated bilirubin crosses placental barrier and may result in neurological damage in newborn. Phenobarbitone can be used even during pregnancy while clofibrate is contraindicated during pregnancy.<sup>5</sup> The disease runs a benign course and prognosis is good, with normal life span reported even with high bilirubinemia.<sup>6</sup> It does not cause cognitive or motor impairment during childhood. Prenatal diagnosis and liver transplantation currently have no role in the clinical management.<sup>7</sup>

### Compliance with ethical standards

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**Conflict of Interest:** None

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