Why Are My Eyes Yellow?

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Walter, a 55-year-old gentleman, is concerned about his recent asymptomatic yellowish sclera. He had a few similar episodes as a teenager; otherwise, he is healthy.

Medical history

- Hypertension; no other significant issues
- Two adult children
- Non-smoker
- Social drinker (occasional red wine or beer)
- Older brother passed away due to heart attack in early forties
- Medications: Micardis 80 mg q.d. and Crestor 10 mg q.d.

Physical examination

- BP: 128/79 mmHg
- Pulse: 72 bpm
- Respiratory rate: 18 breaths per minute
- Weight: 90 kg
- Height: 185 cm
- Chest is clear
- Heart sounds are normal, no murmurs
- Peripheral pulses are palpable
- No edema
- Abdomen is soft; no mass and no organomegaly
- Neurological examination within normal limit

Clinical Investigation

- CBC count (including reticulocyte count and blood smear): normal
- Hemoglobin: 149g/L
- White blood cells: 5.0 x 10^9/L

- Sugar: 5.8 mmol/L
- Bilirubin total: 41.0 µmol/L (normal: 2.0 to 18 µmol/L; 0.1 to 1mg/dL)
  Indirect: 34.0 µmol/L; direct 7.0 µmol/L (normal: 0 to 7 µmol/L; 0 to 0.2 mg/dL)
- Lipase, amylase: normal
- Uric acid: 343 µmol/L (normal)
- Hepatitis B virus surface antigen: negative
  Hepatitis C virus antibody: negative
  Hepatitis A virus antibody: positive
- CT of abdomen and abdominal ultrasound: No visible evidence of bilary duct obstruction
- No visible abnormalities of the pancreas
- Remainder of liver function is normal

What is your diagnosis?

a. Chronic hepatitis
b. Cholecystitis with jaundice
c. Gilbert's syndrome
d. Liver cirrhosis

Answer: Gilbert's syndrome

About Gilbert's syndrome

Augustine Gilbert and Pierre Lereboullet first described Gilbert's syndrome, the most common inherited cause of unconjugated hyperbilirubinemia, in 1901. This autosomal recessive condition is characterized by intermittent jaundice, in the absence of hemolysis or underlying liver disease. Gilbert's syndrome is usually diagnosed around puberty, possibly because endogenous steroid hormones produced at that time inhibit bilirubin glucuronidation. Initial diagnosis in older patients is usually made when unconjugated hyperbilirubinemia is noted on routine blood test results, or unmasked by an intercurrent illness or stress. At least 30% of patients are asymptomatic, although nonspecific symptoms, such as abdominal cramps, fatigue, and malaise, are common. Abdominal symptoms in these patients are poorly defined. The hyperbilirubinemia is mild, and by definition, less than 6 mg/dL; however, most patients exhibit levels of less than 3 mg/dL. Bilirubin levels may occasionally be normal in as many as one-third of patients. Gilbert's syndrome has long been recognized as being due to underactivity of the conjugating enzyme system, bilirubin-uridine diphosphate glucuronyl transferase (bilirubin-UGT). Bilirubin-UGT is responsible for conjugating bilirubin into bilirubin monoglucuronides and diglucuronides, and is located primarily in the endoplasmic reticulum of hepatocytes. Population studies show that Gilbert's syndrome occurs predominately in men.

Laboratory Tests

CBC count (including reticulocyte count and blood smear): This is a useful screening test to exclude hemolysis. Rarely, red blood cell abnormalities resembling variegate porphyria have been described in persons with Gilbert's syndrome, possibly due to the increased hepatocellular bilirubin concentration.

Lactate dehydrogenase: Levels are elevated in persons with hemolysis, but are normal in those with Gilbert's syndrome.

Liver function tests: With the exception of unconjugated hyperbilirubinemia, standard liver function test results are normal. However, a familial increase in serum alkaline phosphatase levels has been reported in persons with Gilbert's syndrome. Imaging studies are not required to confirm a diagnosis, as the liver is histologically normal, except for occasional accumulation of a lipofuscin-like pigment around the terminal hepatic venules.

Patients with Gilbert's syndrome should be clearly informed of its benign nature, and that hyperbilirubinemia is not associated with increased morbidity; it has an excellent prognosis and is associated with normal life expectancy. Not only is Gilbert's syndrome not harmful, but it may actually prolong life by preventing heart attacks. The bad LDL cholesterol in your bloodstream must be converted to oxidized LDL before it can form plaques in arteries; bilirubin helps to prevent formation of oxidized LDL cholesterol, and therefore helps prevent heart attacks. Dx

Resource
1. Mukherjee S. 2009 Nov. 19. Gilbert Syndrome [Internet]. Available at: <http://emedicine.medscape.com/article/176822-overview>

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