CASE-2: Gilbert syndrome diagnostics

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Case History

An 18-year-old female presented to General Medicine OPD for evaluation of jaundice. The patient had a history of intermittent jaundice for the last one year. At the time of presentation,there was no history of fever, anorexia, weight loss, dark urine, clay-coloured stool, pruritus, pain abdomen, abdominal distension or pedal swelling. She did not have a history of any chronicdisease or blood transfusion and her family history was not significant for any chronic disease.On physical examination, mild pallor and mild icterus were noticed. There was neither any lymphadenopathy nor hepatosplenomegaly. Cardiovascular and central nervous system examination was normal.

The results of the investigations conducted are summarized in Table 1.

Investigation	Result	Reference Interval
Haemoglobin	11.5	12.0–15.0 g/dl
Total Leucocyte Count	7,210	4,000–10,000/μl
Platelet count	3,76,000	1,50,000–4,00,000/μl
Red blood cell count	5.5	4.5–5.5 million/μl
Packed cell volume	37	38–48 %
Mean cell volume	68	83–101 fl
Mean cell haemoglobin	21	27–32 pg
Mean corpuscular haemoglobin concentration	31	30–35 g/dl
Red cell distribution width	20.3	10.0–16.0 %
Reticulocyte count	2.6	1.0–2.7 %
Total Bilirubin	4.7	0.3–1.2 mg/dL
Direct Bilirubin	0.1	0.0–0.3 mg/dL
Indirect Bilirubin	4.6	0.3–0.9 mg/dL
Aspartate transaminase	15	0–35 U/L
Alanine transaminase	14	0–45 U/L

Alkaline phosphatase	73	45–117 U/L
Total protein	6.8	6.0–8.0 g/dL
Albumin	4.9	3.2–4.5 g/dL
Globulin	1.9	2.5–3.5 g/dL
Albumin/Globulin ratio	2.6	1.5–2.5
Lactate dehydrogenase	154	<247 U/L
Iron	89	60–180 μg/dL
Total iron binding capacity	282	244–450 μg/dL
Ferritin	38	10–291ng/ml
Transferrin saturation	32	12.8–36.4 %
HBsAg	Non-reactive	--
Anti-HCV	Non-reactive	--
HAV-IgM Ab	Non-reactive	--
Anti-HEV-IgM	Non-reactive	--
G6PD screening	Normal	--
Haptoglobin	44	36–195 mg/dl
Direct Coombs' test	Negative	--
Peripheral blood smear examination	Predominantly microcytic hypochromic RBCs,anisocytosis, poikilocytosis, few pencil cells and target cells werenoted	--

The laboratory investigations of this patient showed that the patient had mild microcytic hypochromic anaemia. However, since the iron studies were found to be normal, the physician decided to order an Hb HPLC study. The biochemist discussed the Hb HPLC findings (Figure 1)with the treating physician and screening of both parents was considered for confirmation of the findings. The patient's father turned out to be a carrier of thalassaemia and the mother of Hb D-Punjab.Assessment of liver function showed mild unconjugated hyperbilirubinaemia withnormal serum proteins and liver enzymes. The workup for haemolysis was negative. Thus, a genetic analysis of the UGT1A1 polymorphism was conducted, revealing the patient's UGT1A1*28/*28 genotype, which is linked to a significant decrease in UGT enzyme activity.

Questions

1. What are the abnormal findings in Hb HPLC results in this patient?
2. What is the cause of hyperbilirubinemia in this patient?
3. What guidance ought to be provided to this patient?

Discussion

Question 1

Hb HPLC study revealed the presence of HbD, high HbF and normal HbA2 in this patient. HPLC findings are suggestive of compound heterozygous HbD-Punjab and beta thalassemia trait with a false normal HbA2. The screening of parents for

Question 2

The absence of evident hemolysis and underlying hepatic pathology indicates the possible presence of Gilbert syndrome. Genetic assessment of the UGT1A1 polymorphism confirms thatthe patient has the UGT1A1*28/*28 genotype that is associated with severely reduced UGT enzyme activity. This genetic profile strongly suggests that the primary factor contributing to unconjugated hyperbilirubinemia is most likely the reduced conjugation of bilirubin resulting from diminished activity of the UGT enzyme in this patient. Notably, a homozygous HbD state typically only results in sub-clinical jaundice, making Gilbert syndrome a major contributor to the observed hyperbilirubinemia.

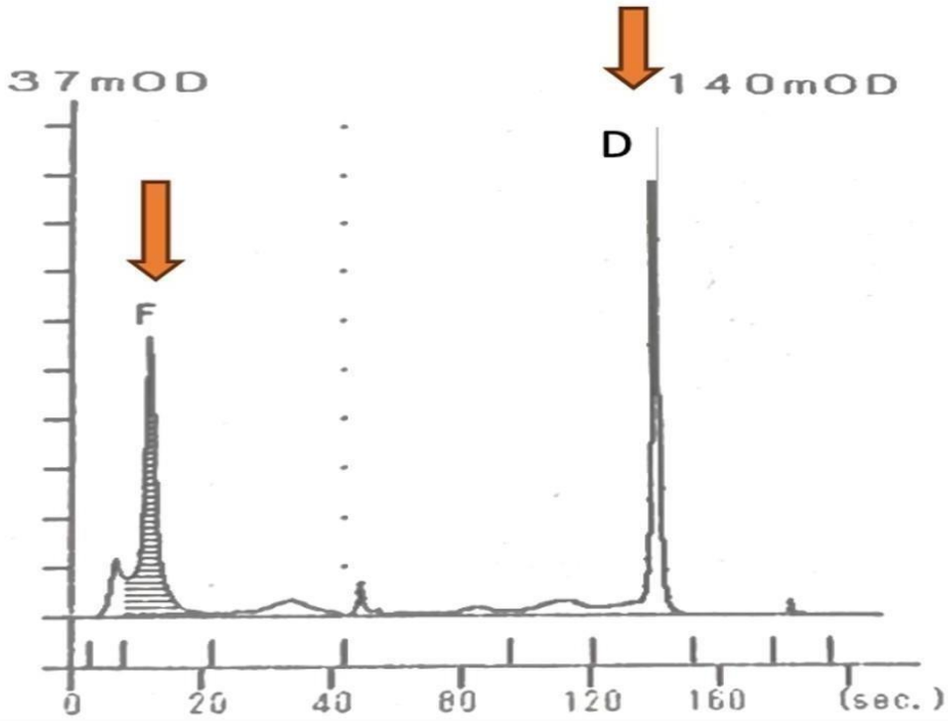
Question 3

The patient needs to be counseled and reassured regarding the benign course of the disease. She should be sensitized about various precipitating factors like fever, physical exertion, prolonged fasting, etc. that may increase her bilirubin levels. The patient should receive guidance to refrain from undergoing unnecessary laboratory investigations to avoid thepotential discomfort or inconvenience associated with repeated blood draws.

References

1. Torres L de S, Okumura JV, Silva DGH da, Bonini-Domingos CR. Hemoglobin D-Punjab: Origin, distribution and laboratory diagnosis. Rev Bras HematolHemoter. 2015;37(2):120–6.
2. Basmanj MT, Karimipoor M, Amirian A, Jafarinejad M, Katouzian L, Valaei A, et al. Co-inheritance of hemoglobin D and β-thalassemia traits in three Iranian families: Clinical relevance. Arch Iran Med. 2011;14(1):61–3.
3. Galanello R, Origa R. Beta-thalassemia. Orphanet J Rare Dis. 2010;5(1):1–15.
4. Vítek L, Tiribelli C. Gilbert´s syndrome revisited. J Hepatol. 2023;79(4):1049–55.
5. Petrenko AA, Pivnik A V, Kim PP, Demidova EY, Surin VL, Abdullaev AO, et al. Coinheritanceof HbD-Punjab/β+-thalassemia (IVSI+5 G-C) in a patient with Gilbert's syndrome. Ter Arkh. 2018;90(7):105–9.

Fig. 1 HPLC chromatogram of blood sample



Peak		Time (at second)	Peak Area Value	Percentage
P1		6	459	1.2
P2	F	12	2098	5.7
P3		33	555	1.5
P4		49	248	0.7
P5	A2	111	1264	3.4
P6	D	141	31766	85.9
P7		166	173	0.5
P8		182	426	1.2
Total Area Value			36989	