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Case Report

A Patient with Recurrent Jaundice Diagnosed to be A Case of Mixed Etiology of Autoimmune and Genetic Disease: A Case Report

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Abstract:

An Adolescent 18 year old male patient had H/O recurrent jaundice. Patient was asymptomatic without any comorbities. Later he was found to be a case of autoimmune hepatitis and Gibert's syndrome. Autoimmune profile was positive, other causes of indirect hyperbilirubinemia were excluded and Gilbert's syndrome was diagnosed.

Keywords: Autoimmune hepatitis, Gilbert's syndrome.

Introduction

Autoimmune liver disease (AILD) is a group of hepatobiliary diseases and of autoimmune abnormalities, according to the characteristics of clinical manifestations, biochemical, imaging and pathology. There are several types which include autoimmune hepatitis, Primary biliary cirrhosis, Primary sclerosing cholangitis and overlap syndrome (includes both AIH and PBC/PSC). Autoimmune hepatitis is a chronic inflammatory liver disease, characterised by immune mediated hepatocellular injury. This condition is more prevalent in Female sex.[1,2] AIH can present as overlap syndromes (OS) also. These OS are suspected in patients with having additional cholestatic symptoms, abnormal cholangiograms or a positive antimitochondrial antibody (AMA) serology [3]. On further genetic study he was diagnosed with Gilbert's syndrome.

Case Report

A young male patient, 18 years old, was admitted for the complaint of recurrent jaundice for the last 5 years. He had h/o previous admissions at several hospitals and was treated on the basis of OPD also.

Patient had c/o Fever since one month, yellowish discolouration of eyes since 20 days this time and severe itching was present with marks of itch on body parts, and constipation on and off. He had no c/o nausea, vomiting and pain abdomen.

Stool colour was normal. On abdominal examination, mild hepatomegaly was present. There was no ascites, no splenomegaly. Other organs were normal. Other systems examination was normal. No h/o pedal edema or generalised antisera, There was no shortness of breath, loss of appetite, loss of weight or steatorrhea, loose motion, altered sensorium.

There was no H/o diabetes, hypertension, drug intake or any addiction to alcohol.

He was alert, conscious, oriented at the time of admission. BP 122/78 mmHg, Pulse rate 88/min, regular Spo2 99%. Chest examination and cardiovascular system was normal, RBS 188 mg/dl and Temperature 99.9 F.

Following Lab investigations done

- Typhoid IgG and IgM negative (kit used- Enteroscreen-WB, Zephyr Biomedicals)
- HBsAg -ve
- Anti HCV -ve
- Anti HAV -ve, (test was done on VIDAS automated immunoassay analyzer)
- Anti HEV -ve, (Kit used – Wantai HEV IgM ELISA)
- Slit lamp examination was negative for KF ring or SLE.
- Serum Ceruloplasmin 48 mg/dl (Normal - Method Immunonephelometry)
- Serum Gamma Glutamyl Transferase 23 U/L (Normal – Method IFCC without pyridoxal phosphate)
- Serum Ferritin 240 ng/ml (Machine used Beckman Coulter – AU480)

Outside USG whole abdomen- Liver was 14 cm, normal shape and echotexture, no evidence of intrahepatic biliary dilatation. CBD collapsed GB normal, Portal vein normal in caliber. Spleen is mildly enlarged~ 13 cm.

- HB 12 gm/dl
- TLC $8.42\times10^{3/}\mu l$
- Plt count $337\times10^{3/}\mu l$
- MCV 97.20fl
- (Machines used – Sysmex XN-1000,SysmexXNL 550/Alinti HQ)

LFT- serum Bilirubin 12.65 mg/dl (direct 6.51) SGOT/AST 50.80 U/L, SGPT/ALT 27.53 U/L Serum Alk. Phosphatase 308.40U/L (Machines used- BECKMAN COULTER- AU480).

- Serum calcium(ionic) 1.13mmol/l (
- Serum creatinine 0.91 mg/dl
- Serum potassium 4.87 mmol/L
- Serum sodium 140 mmol.L
- PT/INR 16.40/1.28 sec
- Total IgG levels (<1600mg/dl) – 3000 mg/dl (day2), 855 mg/dl (day 21)

Table 1:

	Day 1	Day 4	Day8	Day 10	Day14	Day 18	Day21	Day23	Day24
S.Bil(mg/dl)Total Direct Method DIAZO (surfactant)	14.65 6.51	12.30 6.20	11.83 5.6	10.70 5.0	8.8 4.2	7.6 4.0	6.0 3.2	4.23 2.1	3.1 1.0
SGOT/AST DIAZO	50.80	42.66	40.0	48.8	50.0	45.30	35.90	46.20	52.80
SGPT/ALT Method(IFCC without pyridoxal phosphatase)	27.53	30.20	42.90	35.60	52.80	48.50	46.90	43.40	38.76
Serum Alk. Phosphatase (IFCC without pyridoxal phosphate)	308	302	285	240	214	156	130	124	146

CECT ABDOMEN report revealed enlarged liver size 160mm, left lobe of liver is extending to covering the spleen is sub diaphragmatic region- beavers tail. Portal vein is prominent ~ 15mm.GB partially distended, CBD, Pancreas, Kidney, Prostate normal. Spleen is enlarged ~130 mm. Few splenunculi, largest ~7.5 8.6 mm in perisplenic region.

Table 2: Autoimmune Profile (IFA)

Test Name	Result	Dilution Factor
Antinuclear antibody (ANA)	negative	1:100
Antimitochondrial Antibody (AMA)	Negative	1:100
Anti-smooth Muscle Antibody (ASMA)	Positive	1:100
Anti LKM-1	Negative	1:100
Anti F- actin	Positive	1:100

Machines used- ION PGM Life Technologies, Routine urine – normal

Liver biopsy has revealed interface hepatitis, piecemeal necrosis. Inflammation in the portal area, cells is primarily lymphocytes and plasma cells.

MRCP report

Liver enlarged (~180mm) and spleen (~145mm). Rest reports normal.

Hemoglobinopathies not detected and coomb's test negative excluding hemolytic anemia.

Genotyping was done which showed Family 1 member A Complex Locus (UGT1A1) gene polymorphism.

Discussion

AIH is classified into three (subtypes I, II and III) based on distinctive serologic profiles [4].

Type I is the most common type [5]. Antibodies to ANA, SMA, LKM type I and anti-SLA are diagnostic serologic markers with low sensitivity but high specificity.

Diagnosis of AIH is according to Simplified Diagnostic Criteria (SDC) which was validated by the International Hepatitis Group (IAIHG) in 2008[9]. When the score is 6, it is probable while a score of 7 is diagnostic for AIH. The levels of AST, ALT and gamma globulin in the blood show the severity of disease.

When there is mixed hyperbilirubinemia other causes must be excluded. Coomb's test can be positive and negative. When overt hemolytic causes are ruled out, Familial unconjugated hyperbilirubinemia like Gilbert and Criggler-Najjar syndromes should be suspected.

Gilbert's syndrome is a genetically acquired autosomal recessive disorder. This is diagnosed by reduced UGT1A1 enzyme activity when there is additional thymine-adenine(TA) repeats present in the TATAA element in the promoter region of the UGT1A1 gene[6] this does not requires therapy as only 10% of general population is affected and do not require therapy [6,7].

GS remains undetected throughout life until it is triggered by sepsis, medications, or stress [6,8]. In our case, GS may have been triggered by the underlying autoimmune hepatitis flare or vice versa. More studies are needed to establish the exact relationship. In this case GS does not require therapy. Patient improved spontaneously without adding steroids. Ursodeoxycholic acid was given and the patient responded. Autoimmune hepatitis is more prevalent in females than males. Here in this case patient was Male and possibility of autoimmune hepatitis with Gilbert's syndrome was diagnosed. Both associations are not common in population or this is undermined. Further awareness and feasibility of testing and early reporting is required.

Patient was asked to follow up regularly.

Conclusion

Jaundice in AIH is mainly hepatocellular type but if there is cholestatic pattern type any co-existence of PSC or PBC must be excluded.

Overlap or genetic type must be considered in unconjugated or mixed type of hyperbilirubinemia and additional hemolytic causes or inherited syndromes such as Gilbert's syndrome should be taken into consideration.

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