Dubin-Johnson syndrome presenting after acute viral hepatitis

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ABSTRACT

Rising in blood bilirubin is a common manifestation in internal medicine that can have various causes. Hyperbilirubinemia can manifest either conjugated or unconjugated. Conjugated or direct hyperbilirubinemia usually being caused by hepatocellular disease or cholestatic liver disease. Merely conjugated hyperbilirubinemia is the main manifestation of two congenital syndroms including dubin-johnson and rotor, but can be seen in some patients with recurrent benign intrahepatic cholestasis. In this article beside the introduction of patient with dubin-johnson syndrome that is a benign and rare condition, we will imply clinical and laboratory features.

Keywords: Dubin-Johnson syndrome, Conjugated hyperbilirubinemia, Viral hepatitis.

CASE REPORT

Introduction

The Dubin-Johnson syndrome (DJS) is characterized by a conjugated hyperbilirubinemia. The inheritance is autosomal recessive. The highest prevalence is seen in Sephardic Jews from Iran and Iraq that is 1:3000 who also often have an associated coagulation factor VII deficiency (1-4). Dubin Johnson syndrome manifests with an intermittent jaundice in the first two decades of life. pregnancy or the intake of oral contraceptive may provoke manifestation of the disease. Except for the jaundice most patients have no other complaints. The prognosis and development of DJS is benign (5).

Case Report

The patient is a 22-year old male that came to the office 3 year ago for the first time with fever, jaundice, fatigue and dark urine. He had no complaint of pruritus, abdominal pain and GI-bleeding. He had no history of alcohol intake or any drug use (herbal or chemical). Family history for liver disease is negative. In that period of time Liver Function Test were impaired and all serological studies was normal but HAVab IgM was positive, the patient was being treated with the suspicion of acute viral hepatitis A (table 1).

In the recent past 3 years total bilirubin has been fluctuates between 8.9- 13.5 mg/dL and the direct part between 7.4-9.5 mg/dL. Despite the regression of symptoms and reduction of liver enzymes to the normal levels, the jaundice remained persistent (table 1). Abdominal sonography in 3 years ago revealed nothing significant but mild hepatomegaly with heterogenous echo.

Recently, liver biopsy was done and containing a specimen consisting of two pieces of small creamy needle-shaped dark brown tissue totally measuring 3 cm in length and 0.1 cm in diameter.
Table 1. Paraclinical Evaluations from first presentation until present

|                      | During first attack | In past 3 years after first attack | Current |
|----------------------|---------------------|------------------------------------|---------|
| AST (IU/L)           | 125                 | 33                                 | 19      |
| ALT (IU/L)           | 271                 | 31                                 | 23      |
| ALP (IU/L)           | 221                 | 240                                | 184     |
| INR                  | 1.4                 | 1.2                                | 1.1     |
| Alb (gr/dl)          | 3.3                 | 3.8                                | 3.6     |
| α-1 AntiTrypsin      | Normal              | Normal                             | Normal  |
| Anti LKM Ab          | Negative            | Negative                           | Negative|
| ANA,ASMA             | Negative            | Negative                           | Negative|
| HBS Ag, HBC Ab (IgM/IgG) | Negative          | Negative                           | Negative|
| HCV, HIV             | Negative            | Negative                           | Negative|
| HAV (total)          | Positive            | Positive                           | Positive|
| HAV Ab (IgM)         | Positive            | Positive                           | Negative|
| HAV Ab (IgG)         | Negative            | Negative                           | Positive|
| Ceruloplasmin        | Normal              | Normal                             | Normal  |
| TSH                  | Normal              | Normal                             | Normal  |
| S.P. electrophoresis | Normal              | Normal                             | Normal  |
| Anti EMA (IgG, IgM)  | Negative            | Negative                           | Negative|
| P-ANCA               | Negative            | Negative                           | Negative|
| Total Bilirubin (mg/dl) | 11.9              | 13.5                               | 8.9     |
| Direct Bilirubin (mg/dl) | 9.3                  | 9.5                                | 7.4     |

AST= aspartate aminotransferase; ALT= Alanine transaminase; ALP= Alkaline phosphatase; INR= International normalized ratio; Alb= Albumin; LKM Ab= liver kidney microsome antibody; ASMA= Anti-Smooth Muscle Antibody; ANA= Antinuclear Antibody; Ab= Antibody; Ag= Antigen; Ig= Immunoglobulin; HBS= hepatitis B surface; HBC= Hepatitis B Core; HCV= Hepatitis Virus Type C; HIV= Human immunodeficiency virus; HAV= Hepatitis A virus; TSH= thyroid stimulating hormone; S.P= Serum Protein; EMA= Endomysial Antibody; P-ANCA= Perinuclear Anti-Neutrophil Cytoplasmic Antibody

Sections show intact lobular and vascular architecture. Individual hepatocytes contain abundant coarse brown pigment granules especially in perivenular areas. Portal tracts show mild lymphocytic infiltration. Masson trichrome shows no significant fibrosis and other special stains were negative. These features were compatible with clinical diagnosis of DJS (Figure 1).

He had one episode of upper GI bleeding that Esophagogastroduodenoscopy revealed grade B esophagitis and small duodenal ulcer. In urine Coproporphyrin study 88% of urinary Coproporphyrin was type I.
Discussion

DJS is listed as a rare disease by the office of rare disease (ORD) of the national institutes of Health (NIH) (6, 7). In this situation we see no clinical and laboratory findings except prolonged jaundice. The diagnosis is based on clinical and laboratory findings especially liver biopsy. Despite the normal liver enzymes, only the bilirubin is higher than normal level that is mainly conjugated part. In liver biopsy we can see pigmented brownish granules (8, 9).

Diagnosis can be confirmed by the measurement of urine Coproporphyrin. The total Coproporphyrin in urine is normal, but 85-90% of urinary Coproporphyrin is type I, whereas in normal persons 75% of urinary Coproporphyrin is type III (7, 9, 10). In our patient the jaundice was being provoked after a viral hepatitis and despite comprehensive work up, only direct hyperbilirubinemia was seen. The prognosis of DJS is favorable with a normal life expectancy. A therapy is neither available nor required (11).

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