Case Report

Late onset Wilson Disease with normal neuro-psychiatric status: A case report

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ABSTRACT

Introduction: Late onset Wilson disease (WD) is a rare form of WD. WD has variability of clinical presentations from acute liver failure to chronic liver disease (CLD). The hepatic and neurological variants of WD have wider variations.

Case presentation: A 55-year-old female, known case of CLD, presenting with generalized body swelling and abdominal pain, was diagnosed with late onset WD with normal neuro-psychiatric status. She was treated with zinc and considered for liver transplantation.

Clinical discussion: Late onset WD is itself a rare form of WD. Within it, neurological manifestations are common in late onset WD, which was quite opposite as compared to our case. Similarly, diagnostic delay has been a concern in late onset WD with CLD as with our case.

Conclusions: In spite of being uncommon in later age, WD and its different variations like with normal neuro-psychiatric status should be considered as an etiology in cases of unexplained liver diseases.

1. Introduction

Wilson disease (WD), an autosomal recessive variant, is a multi-system disorder affecting liver primarily. It affects brain and osseomuscular system progressively [1]. It is classically described as “progressive lenticular degeneration” by Dr. Samuel Alexander Kinnier Wilson [2,3]. Although WD is commonly seen in children and younger adult population, there are many reported cases of WD diagnosed at older age [1,4]. Usually, the hepatic presentation of WD is common in children and younger population. And as the age increases, the neurological presentation of WD is common (4). The cases of late onset neurological variant-WD without Kayser-Fleischer (KF) ring have been reported in literature [5,6]. But cases of late onset WD with normal neuro-psychiatric status have been scarce in medical literature. Hence, this is a case of late onset WD in a 55-year-old female with normal neurological status.

2. Case presentation

A 55-year-old Hindu female presented to the emergency department of our center with generalized body swelling and abdominal pain. The pain was burning type mostly located towards epigastric region. It was not associated with nausea, vomiting, waterbrash and diarrhea. She was a diagnosed case of chronic liver disease (CLD) for four years whose etiology was unknown till then. She gave negative history for alcohol consumption and use of liver toxic drugs. There was no family history of liver disease. There was jaundice present in whole body, pallor and bilateral pitting pedal edema on general examination. Her vitals were stable at admission. On per abdominal examination, the abdomen was distended with flanks full. There was generalized tenderness and shifting dullness was present. There were no signs of hepatic encephalopathy (HE). The higher mental function and rest of central nervous system examinations were normal.

The baseline investigations are shown in Table 1.

As from clinical examination and investigations, she presented as CLD with decompensating features like ascites, jaundice and coagulopathy. The ascitic fluid analysis showed total count of 100 cells/cubic mm and discrete leukocyte count of 80% lymphocytes and 20% neutrophils. The patient was not in spontaneous bacterial peritonitis (SBP). Similarly, ultrasound of abdomen and pelvis revealed, coarse echotexture of liver
parenchyma with irregular outline suggestive of CLD and moderate ascites. The previously done esophagogastrroduodenoscopy showed small esophageal varices. These investigations were done to confirm the liver pathology and to evaluate the etiologies for chronic liver disease as esophageal varices. These investigations were done to confirm the liver pathology and to evaluate the etiologies for chronic liver disease as –

- Etiological workup.
- Table 2

presentations. Over the years from its first description (1912), the spectrum of alanine transferase (ALT) or aspartate transferase (AST), non-alcoholic liver disease (compensated or decompensated), asymptomatic elevation of alanine transferase (ALT) or aspartate transferase (AST), non-alcoholic fatty liver disease, acute hepatitis and hepatocellular carcinoma. Similarly, neurological presentations are dystonia, tremor, dysarthria, ataxia, parkinsonism, chorea and peripheral neuropathy. Several other involvements include psychiatric, ocular, cardiac, endocrinologic, hematologic, renal, musculoskeletal and cutaneous features of WD has been ever changing. The newer concepts and understanding about the disease are still evolving. As WD has been described as a rare disease, the prevalence of disease was found to be between 1.2/100,000 and 2.0/100,000 in European countries (7). And the average prevalence worldwide was estimated to be around 30 per million population [8]. It has been exceeded by recent genetic studies as 142 per million population [9]. The majority of patients fall between age 5 and 35 but the variations can be seen from as early as 9 months of age to ninth decade [9,10].

The mean age with hepatic and neurological presentations in WD has been described to be 11 years and about 15–21 years respectively [7]. The neurologic variant frequency increases with age. But variations are found among these findings too which pose challenge in diagnosis of WD at earlier stage. Wilson disease is an inborn error in copper metabolism due to the mutation in ATP7B gene, located on chromosome 13. The diagnostic criteria for WD has been suggested by few guidelines like American Association for the Study of Liver Diseases (AASLD) using clinical and biochemical algorithm and European Association for the Study of the Liver (EASL) using Leipzig scoring system [11–13]. The algorithms for diagnosis of WD by AASLD and Leipzig scoring system are shown in Fig. 3 and Table 3 respectively.

On the basis of AASLD, the diagnosis was established as WD in our case as it met all the three criteria for its diagnosis in unexplained liver disease [8]. The three criteria are presence of KF ring, serum CPN <20 mg/dl and 24-h urine copper >40 mcg. Similarly, based on EASL guideline using Leipzig scoring, she was diagnosed as WD as the diagnosis would be established when the score come to be 4 or more [12]. The score was 5 which included presence of KF ring, serum CPN level 0.1–0.2 g/L and 24-h urinary copper > 2 × upper limit of normal (ULN).

The hepatic manifestations in WD include acute liver failure, chronic liver disease (compensated or decompensated), asymptomatic elevation of alanine transferase (ALT) or aspartate transferase (AST), non-alcoholic fatty liver disease, acute hepatitis and hepatocellular carcinoma. Similarly, neurological presentations are dystonia, tremor, dysarthria, ataxia, parkinsonism, chorea and peripheral neuropathy. Several other involvements include psychiatric, ocular, cardiac, endocrinologic, hematologic, renal, musculoskeletal and cutaneous features

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### Table 1

Baseline investigations (TIBC: Total Iron Binding Capacity; CRP-C: C-Reactive Protein-C).

| Laboratory tests            | Result   | Unit  | Reference range |
|-----------------------------|----------|-------|-----------------|
| Total Leukocytes Count      | 3.7      | 10³/µL| 4-11            |
| Neutrophil                  | 55%      |       | 40-80           |
| Lymphocyte                  | 37%      |       | 20-40           |
| Hemoglobin                  | 10.3 (L) | g/dL  | 13-17           |
| Platelet Count              | 90 (L)   | 10³/µL| 150-450         |
| Red Blood Cell (RBC) Count  | 3.36     | 10⁶/µL| 4.5-5.5         |
| Urea                        | 29       | mg/dL | 17-43           |
| Creatinine                  | 0.9      | mg/dL | 0.7-1.3         |
| Sodium                      | 141      | mEq/L | 135-145         |
| Potassium                   | 3.7      | mEq/L | 3.5-5.5         |
| Bilirubin Total             | 2.3 (H)  | mg/dL | 0.1-1.2         |
| Bilirubin Direct            | 1.2 (H)  | mg/dL | 0.0-0.2         |
| Amylase                     | 52       | U/L   | 40-140          |
| Alkaline Phosphatase (ALP)  | 85       | U/L   | 53-128          |
| Alanine Transferase (ALT)   | 32       | U/L   | 0-35            |
| Aspartate Transferase (AST) | 65 (H)   | U/L   | 0-35            |
| Random Blood Glucose        | 108.8    | mg/dL | 70-140          |
| Prothrombin time (PT)       | 19.3 (H) | seconds | 11-13.5     |
| International Normalized Ratio (INR) | 1.4 (H) |         | 0.8-1.1        |
| Troponin I                  | Negative |       |                 |
| Urine Routine Examination   | Normal   |       |                 |
| Lactate Dehydrogenase (LDH) | 204      | U/L   | 140-280         |
| Total Cholesterol           | 157      | mg/dL | <200            |
| Triglyceride                | 98       | mg/dL | 70-150          |
| Serum Iron                  | 117.47   | µg/dL | 50-100          |
| Ferritin                    | 687.2    | µg/L  | 20-250          |
| CRP-C                       | Negative |       |                 |
| TIBC                        | 139      | µg/dL | 228-428         |

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### Table 2

Etiological workup.

| Serology                           | Non-reactive for HIV, HbAg and HCV |
|------------------------------------|-----------------------------------|
| Alcohol history                    | Negative                           |
| Lipid profile and blood sugar      | Within Normal Limits               |
| Serum Ceruloplasmin (CPN)          | 10.80 mg/dL (Normal range: 20-60) |
| 24 h urinary copper                | 43.64 µg/day (Normal range: 2-50) |
|                                   | 229.60 µg/L (Normal range: 2-80)  |
| Ophthalmology consultation         | Kayser-Fleischer (KF) seen in both eye |
As neurological features increase with age and late onset WD is rare [8,14], our case was diagnosed as late-onset WD with normal neuropsychiatric status. Similarly, there was delay of 4 years in diagnosis of WD with hepatic presentations from the time of onset of early hepatic symptoms. There were no any neuropsychiatric features as described above. This was a typical finding in accordance with the literature showing longer delay from onset of symptoms until definite diagnosis of WD with neuropsychiatric symptoms than that of WD with hepatic symptoms [15,16].

Although our patient had CLD with decompensating features while the diagnosis of WD was made, it was not severe enough to consider for immediate liver transplantation as described in literature [9]. She was treated on Zinc at first as she was stable on general examination. The consideration for liver transplantation was put on hold until the response of Zinc therapy. As described in literature, the prognosis is variable for decompensated CLD in WD [9]. It was our limitation that we could not assess the prognosis because of inadequate follow up.

There were certain limitations in our article like inability to perform liver biopsy and gene sequencing due to unavailability of facility in our center. We could not do follow up with the patient to assess the long-term course of symptoms, progress of the therapy and prognosis of the disease. In addition, we also could not perform screening of family members for WD due to unavailability of the facility.

4. Conclusions

The discussion and amendments in the spectrum of WD are never ending topics. In the amidst of 21st century the variations in WD are being reported and published in a significant amount. We have reported such a variation of WD in our case report as late-onset WD diagnosed as decompensated CLD with normal neuropsychiatric status. It was an incidental finding during the etiology workup for unexplained liver disease. Though neuropsychiatric features are common with increasing age in WD, it will be wise to consider it even if the central nervous system (CNS) examination is normal, as it was in our case. This case report adds onto the current understanding of WD and its variability which may be useful to all the clinicians around the world in recognizing WD in a more diverse way.

Ethical approval

This is a case report, therefore, it did not require ethical approval from ethics committee.

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Table 3
Scoring system developed at the 8th International Meeting on Wilson’s disease, Leipzig 2001.

| Typical clinical symptoms and signs | Other tests |
|-------------------------------------|-------------|
| **KF rings**                        | Liver copper (in the absence of cholestasis) |
| Present 2                           | =>5x ULN (=>4 umol/g) 2 |
| Absent 0                            | 0.8-4 umol/g 1 |
|                                    | Normal (0.8 umol/g) –1 |
|                                    | Rhodamine-Positive granules 1 |
| **Neurological Symptoms**           | Urinary copper (in the absence of acute hepatitis) |
| Severe 2                            | →1x ULN 1 |
| Mild 1                              | →2x ULN 2 |
| Absent 0                            | Normal, but >5x ULN after → penicillamine 2 |
| **Serum Ceruloplasmin**             | Mutation analysis |
| Normal (>0.2 g/L)                   | On both chromosomes detected 4 |
| 0.1–0.2 g/L                         | On 1 chromosome detected 1 |
| < 0.1 g/L                           | No mutations detected 0 |
| **Coombs-negative hemolytic anemia**|                  |
| Present 1                           |                  |
| Absent 0                            |                  |
| **Total score**                     | **Evaluation**  |
| 1) 4 or more Diagnosed established  |                  |
| 2) 3 Diagnosed possible, more tests needed |                  |
| 3) 2 or less Diagnosis very unlikely |                  |

Legend: Reproduced from Ferenci P, Czlonkowska A, Stremmel W, Houwen R, Rosenberg W, Schilsy M et al. EASL Clinical Practice Guidelines: Wilson’s disease. Journal of Hepatology. 2012; 56(3):671–85. https://doi.org/10.1016/j.jhep.2011.11.007 with permission from Elsevier.

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