

Wilson's Disease with Superimposed Autoimmune Features: A Case Report

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ABSTRACT

The association of Wilson's disease (WD) with autoimmune hepatitis (AIH) has rarely been documented. The difficulties in differential diagnosis of WD and AIH have seen specially in the paediatric population. Children with WD specially in younger ones, may have clinical features indistinguishable from autoimmune hepatitis. We report a case of 8-year old girl child who presented with jaundice, anaemia, leg oedema and arthritis. Ultimately the patient was diagnosed as a case of WD with AIH after meticulous investigation. Treatment was started with prednisolone, D-penicillamine and subsequently prednisolone was tapered with addition of azathioprine. D-penicillamine was stopped, with clinical and biochemical improvement and zinc was added to continue life-long. Follow up after 8 months of initial treatment she was non anaemic and non-icteric. Her leg oedema and arthritis also subsided. Liver biochemistry returned to normal level. It is important therefore to recommend strongly a thorough screening for AIH in patients with initial diagnosis of WD and also screening for WD for patients presenting with AIH. So a combined therapy may be of early benefit.

Key words: Autoimmune hepatitis, Wilson's disease, Prednisolone, Penicillamine.

INTRODUCTION

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism with a prevalence of approximately 1:3000. Mutations of the copper transforming ATPase, ATP7B can lead to decreased biliary copper excretion and accumulation of copper predominantly in the liver and extra hepatic organs such as brain and the cornea.¹ The disease typically begins with an asymptomatic period of subclinical hepatitis and progress to liver cirrhosis and neuropsychiatric symptoms. A small proportion of patient may present with acute liver failure (ALF), without pre-existing clinical signs of liver diseases.^{2,3} Autoimmune hepatitis (AIH) is a chronic necro-inflammatory liver diseases characterized histologically by a dense

mononuclear cell infiltrate in the portal tract and serologically the presence of non-organ and liver specific auto antibodies and increased level of Immunoglobulin G (IgG) in the absence of known etiology.^{4,5} Autoimmune hepatitis may be overlapped by other liver diseases with proven or possible autoimmune background, such as primary biliary cirrhosis or primary sclerosing cholangitis.^{6,7}

Co-existence of WD with AIH may present sometime with a diagnostic problem. Patients with WD may show features of AIH. In this paper we present a patient with evidence of WD along with several generally accepted features of autoimmune hepatitis, i.e., co-existence of WD and AIH. Though WD in children is not an

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uncommon diagnosis, yet we are not very much familiar about co-existence of WD with AIH. So this case report may give better information and permit a more focused investigation which will allow the cases to be diagnosed with greater frequency and accuracy.

CASE REPORT

A 9-year-old girl was referred to the Department of Paediatric Gastroenterology and Nutrition of Bangabandhu Sheikh Mujib Medical University (BSMMU) with history of jaundice for 5 months, leg oedema for 2 months, pain in the knees and ankles for 1 month. She came from a non-consanguineous family, her parents and other siblings were in good health. There was no history of recent use of offending drugs, blood transfusion or any surgery. Physical examination revealed that the girl was moderately icteric and pale. She had bipedal oedema but no ascites and organomegaly. K-F ring (Kayser–Fleischer Rings) was present in both eyes (Fig 1).



Fig. 1: The child with Wilson's disease and Autoimmune Hepatitis

Neurological examination showed no abnormalities. Laboratory investigation showed serum alanine aminotransferase (ALT) to be 86 U/L, total bilirubin 3.2 mg/dl, serum albumin 2 gm/dl, increased prothrombin time. INR (International Normalized Ratio) was 2.84 (Normal-0.8-1.2). Her serum ceruloplasmin level was 20 mg/dl (Normal 20-60 mg/dl), urinary excretion of copper at baseline was 140 µg/24 hrs (Normal <100 µg/24 hours), which after penicillamine challenge was 1250 µg/24 hours (>1200 suggestive of Wilson Disease). Viral markers for hepatitis B & C (HBV, HCV) were

negative. Serum IgG was 19 g/L (Normal 6-16 g/L), antinuclear antibody was positive 1:400 (1:40 dilution cut-off for positive), anti-smooth muscle antibody (SMA) was negative, anti-liver kidney microsomal enzyme-1 (LKM-1) was positive, low level of complement-3 (C3) 0.5 g/L (Normal-0.75-1.75 g/L) and complement-4 (C4) 0.14g/l (Normal-0.14-0.54 g/L). Liver biopsy was not done due to patient's unwillingness. The patient was treated with prednisolone and d-penicillamine initially. Subsequently prednisolone was given in a tapered-dose with addition of azathioprine. D-penicillamine stopped with clinical and biochemical improvement and zinc was advised to continue lifelong. In the last follow up after 8 months of initial treatment she was not anaemic and jaundiced with oedema and arthritis subsided. All the biochemical parameters returned to normal limit (Hb, 11.50 gm/dl, ALT-29 U/l, INR- 1.26, urinary copper 285 µg/24 hrs, IgG 8.8 g/l).

DISCUSSION

The diagnosis of Wilson's disease may be a clinical challenge. Normal ceruloplasmin levels in patients with all types of presentation of WD and the absence of Kayser-Fleischer rings are findings which lead to a missed diagnosis of WD. Nevertheless, the simultaneous presence of three characteristic features of WD: low serum ceruloplasmin, increased 24 h urinary copper, and specifically the grossly increased hepatic copper permit a diagnosis of WD without doubt. The association of Wilson's disease with autoimmune hepatitis has rarely been documented.^{8,9} The difficulties in differential diagnosis of WD and AIH have been seen specially in the pediatric population.^{10,11} Patients with WD specially in younger ones may have clinical features and histologic findings on liver biopsy indistinguishable from autoimmune hepatitis.^{12,13,14} In some patients concomitant WD and autoimmune hepatitis cannot be excluded.¹⁵ The presence of low titre auto antibodies presumed to be secondary to exposure of antigen by hepatocyte necrosis may cause confusion.¹⁵ In WD certain features of autoimmunity are usually absent and plasma immunoglobulin are usually

not raised. Wilson disease may quite commonly present as chronic active hepatitis, a histological picture also found in autoimmune, drug induced or viral hepatitis. Scott et al¹² described in a study of 17 patients with WD who presented as chronic active hepatitis. In all these patients, tests for SMA (Smooth Muscle Antibody) ANA (Antinuclear Antibody) and hepatitis B surface antigen were negative.¹² In another study, Schilsky et al¹³ described 20 patients with WD who presented with chronic active hepatitis, but in that series the presence of autoantibodies, which are crucial for diagnosis of AIH, was not confirmed.¹³

In this case report we described one patient with WD with several superimposed features suggesting that the disease had an autoimmune background. An initial diagnosis of autoimmune hepatitis deserves treatment with steroid & azathioprine. If response to steroid is poor, a thorough screening for WD is necessary. Failure to diagnose WD in such cases may lead to hepatic failure eventually and the necessity of liver transplantation.

CONCLUSION

It is important to recommend strongly a thorough screening for autoimmune hepatitis in patients with initial diagnosis of Wilson's disease and also screening for WD for patients presenting with AIH so that a combined therapy with prednisolone and D-penicillamine may be of early benefit.

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