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Case Report

Wilson's disease presenting with transient pancytopenia – An uncommon presentation of rare disease

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ABSTRACT

Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism, characterised by an excess accumulation of free copper in the liver, brain, and eyes. Patients with WD commonly present with hepatic or neurological symptoms, whereas pancytopenia is an unusual initial presentation of this disease. We are presenting the case of an 8-year-old boy with WD who presented with pancytopenia.

Keywords: Wilson's disease, Autosomal recessive, Pancytopenia, Kayser–Fleischer rings

INTRODUCTION

Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism, characterised by excess accumulation of free copper in the liver, brain, eyes, and other tissues. Its diagnosis is based on typical clinical features such as Kayser–Fleischer (KF) rings, neurological symptoms and/or low serum ceruloplasmin levels.[1] Patients with WD commonly present with hepatic or neurological symptoms, and early detection and management have favourable results.[2] Pancytopenia is an unusual initial presentation of this disease, and when present, it diverts the usual diagnostic algorithm, thus delaying the treatment.[3] Here, we describe an 8-year-old boy with WD who initially presented with pancytopenia.

CASE REPORT

An 8 years and 1-month-old boy presented with fever for 4 days. His history revealed that when the boy was 6 years old, he developed fever followed by jaundice for 10 days. During that time, platelet count had dropped to 73,000/μL of blood. The doctors had advised a bone marrow study, but the parents had refused. Three months back, the child developed fever again and the platelet count at that time was 82,000/μL of blood. There was a history of transfusion (one unit packed red cell and one unit platelet) almost a year back. On clinical examination, the boy was conscious and oriented. He had bilateral cataracts and small hypopigmented spots over his upper chest and back suggestive of tinea versicolor. He had short stubby fingers and firm swelling of the right testis. The liver was palpable and 3.5 cm below the right costal margin in the mid-clavicular line with the liver span being 9.5 cm. The spleen was also palpable and 2 cm below the left costal margin. A complete haemogram showed mild anaemia (haemoglobin – 9 g/dL), leukopenia (total leukcocyte count – 3240/μL of blood), and thrombocytopenia (platelet count – 100,000/μL of blood). The absolute

neutrophil count was 1070/μL of blood. Peripheral smear was reported as pancytopenia. Red blood cell indices and serum iron panel were normal (Serum ferritin – 102 μg/L, serum iron – 52 μg/dL, total iron binding capacity – 320 μg/dL, transferrin saturation – 32%, mean corpuscular volume – 82.7 fl, mean corpuscular hemoglobin concentration – 34.7 g/dL, mean corpuscular haemoglobin – 28.7 pg and red cell distribution width – 15%). Prothrombin time was normal (21.8 s), whereas activated partial thromboplastin time was prolonged (66.6 s). Liver function test revealed normal bilirubin and mild elevation of alanine aminotransferase (40 U/L) and aspartate aminotransferase (58 U/L) with a marked increase in alkaline phosphatase (529 U/L). Total serum protein and albumin were reduced. Ultrasound of the abdomen revealed altered liver echotexture with a 10.6 cm liver span and mild splenomegaly with no ascites. Upper gastrointestinal (GI) endoscopy revealed no varies. Slit-lamp examination revealed bilateral sunflower cataract with KF ring. Serology for human immunodeficiency virus, hepatitis B and C was negative. Serum ceruloplasmin was low, <9.7 mg/dL (normal 18–50 mg/dL) and 24 h urinary copper level was 114.09 mcg/dL (normal 20–50 μg/24 h). Factor VIII and IX assay was normal. Bone marrow aspiration was also normal. Genetic testing detected pathogenic variants in the ATP7B gene (c.2131G>T in Exon 8 with homozygosity) confirming the diagnosis of WD. Thrombocytopenia and leukopenia normalised as the fever settled. However, our diagnosis of WD was delayed due to the atypical presenting feature of pancytopenia.

DISCUSSION

WD (Syn: Hepatolenticular degeneration) is an inherited autosomal recessive disorder characterised by a defect in cellular copper transport, with an approximate prevalence of 1 in 30,000 live births. It results from a mutation in the ATP7B gene located on chromosome 13.[4] Patients with WD commonly present with hepatic or neurological manifestations. Diagnosis is based on considering the clinical and biochemical parameters. KF rings are identified in 50–60% of patients with hepatic involvement.[1] No extra tests are needed for the diagnosis of WD if KF rings are present and serum ceruloplasmin levels are low. In 85% of patients, serum ceruloplasmin levels are below the normal range. However, in the absence of KF rings, a low ceruloplasmin level is not diagnostic for WD, as it may be below the normal range in severely malnourished individuals and carriers of the WD gene. The utility of urinary copper is limited in clinical practice.[1]

Pancytopenia is the simultaneous occurrence of anaemia, leukopenia, and thrombocytopenia. Anaemia, infections and bleeding are the cardinal features of pancytopenia. There are many causes for pancytopenia, such as megaloblastic anaemia, hypersplenism, malaria, leukaemia, aplastic anaemia and autoimmune disorders, and rare causes including WD, Kala-azar, HIV, and alcoholism.[5]

Treatment with penicillamine, a copper chelator resulting in copper deficiency, has been documented to result in cytopenias.[6] However, our case presented with pancytopenia as the initial symptom, which is rare in WD. The pancytopenia was transient in our case, ruling out the possibility of hypersplenism being the sole contributor. The pancytopenia could possibly be due to a viral infection along with associated transient hypersplenism. The child presented with pancytopenia whenever he had a fever, which led to misguidance in arriving at a diagnosis.'

CONCLUSION

This unusual presentation may misguide the clinician and delay the treatment, worsening the condition. Thus, we are presenting this case so that we can shed some light on this rare presentation of WD, which is known to occur rarely. The patient we are presenting had past episodes of fever, followed by jaundice and pancytopenia. The cause of pancytopenia could be a viral fever causing transient bone marrow suppression. This presentation could have been the reason for missing the workup for WD in the first instance, thus resulting in a delay in diagnosis and treatment. WD should be suspected in cases of unexplained pancytopenia, which could be a rare initial presentation.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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