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Case Report
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A Pediatric Case of Wilson's Disease Presenting with Arthralgia

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Abstract

Wilson's Disease (WD) is a rare inherited disorder characterized by impaired hepatic copper metabolism, resulting in copper accumulation and multi-systemic manifestations, but arthritis as an initial manifestation is rare. We report a pediatric case of WD visiting the hospital for arthralgia, and the patient reported gradual improvement with proper therapy.

Abbreviations

WD: Wilson's Disease; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; TBA: Total Bile Acid; TB: Total Bilirubin; MRI: Magnetic Resonance Imaging

Introduction

Wilson's Disease (WD) is an autosomal recessive disorder caused by mutations in the *ATP7B* gene, leading to impaired hepatic copper transport and subsequent copper deposition in various tissues. The initial clinical presentation is commonly characterized by hepatic, neurologic, or psychiatric/behavioral disturbances [1]. In addition, there can be involvement of the eyes, kidneys, heart, bones and joints, blood, endocrine system, and sleep patterns [2]. However, arthralgia as the initial manifestation of WD, is frequently inadequately acknowledged. In this report, we present a pediatric case of WD with osteoarticular symptoms, with the aim of raising awareness among pediatric physicians regarding the early identification of atypical WD symptoms.

Case Presentation

A male child, aged ten years old, was hospitalized due to a recurring joint pain in the lower limbs for a period of five months. Specifically, the child suffered from pain in the right knee joint without a definite cause. The pain was not severe, bearable, and would subside naturally after approximately one minute. Additionally, there was mild swelling in the affected joints, followed by the gradual onset of pain in the left knee and right ankle joint. The child also experienced slight difficulty in walking, indicating some instability. He did not visit hospital before, and has no significant past medical history or family history.

The patient experienced overall tenderness in the abdominal region. The liver was palpable, nearly three centimeters below the rib costal margin in the midclavicular, displaying a firm consistency, and the spleen was not palpable. The right ankle joint displayed localized swelling, with slightly elevated skin temperature and tenderness. The remaining examinations were no special.

The laboratory detections indicated abnormal liver function: Alanine Aminotransferase (ALT) 59 U/L (normal range <49 U/L), Aspartate Aminotransferase (AST) 110 U/L (normal range <40 U/L), Total Bile Acid (TBA) 43.5 umol/L (normal range 0-10 umol/L), Total Bilirubin (TB) 33.0 umol/L (normal range 5-23 umol/L), direct bilirubin 12.3 umol/L (normal range <8 umol/L), indirect bilirubin 20.7 umol/L (normal range <20.7 umol/L). The ceruloplasmin level measured 42 mg/L (normal range 190-670 mg/L), and serum copper concentration was 346.7 μg/L (normal range 800-1900 μg/L). The 24-h urinary copper excretion amounted to 166.4 μg/24h (normal range 15-30 μg/24h). Coagulation assessment revealed an extended prothrombin time of 16.2 sec (normal range 8.1-14.4 seconds), alongside a fibrinogen concentration of 183 mg/dL (normal range 200-400 mg/dL). No other significant abnormalities were detected. Autoantibody analysis demonstrated a positive presence of anti-nuclear antibody displaying a speckled pattern at a dilution of 1:100. However, no other irregularities were identified. Various assessments yielded normal outcomes, including complete blood count, C-reactive protein, procalcitonin, erythrocyte sedimentation rate, urinalysis,

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lipid profile, fasting blood glucose, renal function, electrolytes, rheumatoid factor assays, serological fluid immunology and cellular immunology evaluations, HLA-B27 analysis, and autoimmune liver disease antibody screening. Investigations for antibodies against hepatitis A and hepatitis E, cytomegalovirus DNA, Gamma Interferon Release Assay and bone marrow smear examinations all generated negative findings. Enhanced Magnetic Resonance Imaging (MRI) of the upper abdomen demonstrated abnormal liver morphology and signal, accompanied by splenomegaly and slight portal vein thickening, suggestive of potential liver cirrhosis with regenerative nodules. Bilaterally normal sacroiliac joints were observed in the enhanced MRI of the joints. However, mild soft tissue swelling and a minor joint effusion were noted in the right ankle. Furthermore, abnormal signal intensity was detected in the distal metaphysis and epiphysis of the right tibia, fibula, and navicular bone within the right foot. Both chest computed tomography and enhanced MRI of the head yielded unremarkable findings. Ophthalmic examination indicated the presence of yellow-brown pigment deposition at the corneal margin in both eyes.

WD was considered as a diagnosis. The pediatric patient underwent a low-copper diet and received treatment involving penicillamine and zinc preparations to diminish copper absorption. Following one week of treatment, the patient reported alleviated joint pain, although residual tenderness persisted in the right ankle joint. Upon discharge, the patient continued the oral administration of penicillamine and zinc preparations. One month later, the patient no longer experienced pain or joint tenderness. Liver function tests displayed improved outcomes, with ALT at 64 U/L, AST at 78 U/L, TBA at 21.6 umol/L, and normal TB and coagulation function. The patient underwent lifelong copper-chelation therapy and was consistently monitored through regular outpatient visits.

Discussion

WD is a rare genetic disorder characterized by impaired copper metabolism, presenting with a wide range of clinical symptoms. Hepatic symptoms represent the most prevalent initial indications [3-5], encompassing hepatomegaly, isolated splenomegaly, elevated serum aminotransferase levels, jaundice, acute hepatitis, cirrhosis, and even acute liver failure [4,5]. Neurological symptoms and brain damages in WD are the primary extrahepatic manifestations of copper toxicity, including tremor, dystonia and impairment of cognition and attention, as well as imbalance and incoordination. Other atypical symptoms predominantly involve kidneys, eyes, heart, bones, and other organs [2].

The diversity of clinical manifestations of WD often makes it difficult to differentiate WD from other diseases. The main challenge is the early recognition of atypical or rare symptoms in WD [6]. Reports indicated that the average time to diagnose WD remained prolonged, exceeding two years from symptom onset [3,7,8]. Articular manifestations had been observed as atypical and initial symptoms in WD patients, potentially leading to adverse outcomes due to misdiagnosis [9-12]. It was reported that a young male patient with WD initially presented at a hospital primarily due to a forearm bone fracture [12]. Another patient, aged 30, experienced gradually progressive pain in both small and large joints for fourteen years before receiving a WD diagnosis [9]. Additionally, a seven-year-old girl suffered from lower limb pain, deformity, and subsequently underwent corrective surgery, followed by a leg fracture. WD was diagnosed four years later in this patient when neurological symptoms emerged [10]. It is crucial to differentiate WD from arthritis in patients. Delayed diagnosis, treatment, or inconsistent management of WD may result in irreversible brain damage or even death. The patient in this case visited the hospital for arthralgia in lower limbs, and subsequent evaluations revealed hepatomegaly and liver disfunctions. After screening with ceruloplasmin, serum copper, urinary copper, and Kayser-Fleischer Ring, the diagnosis of WD was confirmed. Early and lifelong treatment is the principle of WD management. Following the administration of a low-copper diet, chelating agents like penicillamine, and zinc salts therapy, the patient experienced alleviation of joint pain and exhibited partial restoration of liver function. Early diagnosis and treatment prevented the development of joint deformities or bone fractures.

Conclusion

Wilson's disease should be considered in the differential diagnosis of patients presenting with arthritis, especially in the presence of abnormal liver function tests. Timely diagnosis and appropriate treatment can result in favorable outcomes and prevent long-term complications associated with copper deposition.

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