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OLGU SUNUMU / CASE REPORT

Wilson's Disease Presenting With Pancytopenia

Pansitopeni ile Başvuran Bir Wilson Hastalığı Olgusu

Can Acıpayam[1], Ali Altunay[2], Nilüfer İlhan[3], Nesrin Atçı[4]

[1]Kahramanmaraş Sütçü İmam Üniversitesi, Tıp Fakültesi, Pediatrik Hematoloji ve Onkoloji Ana Bilim Dalı, Kahramanmaraş.
[2]Mustafa Kemal Üniversitesi, Tayfur Ata Sökmen Tıp Fakültesi, Pediatri Ana Bilim Dalı, Hatay.
[3]Mustafa Kemal Üniversitesi, Tayfur Ata Sökmen Tıp Fakültesi, Göz Hastalıkları Ana Bilim Dalı, Hatay.
[4]Mustafa Kemal Üniversitesi, Tayfur Ata Sökmen Tıp Fakültesi, Radyoloji Ana Bilim Dalı, Hatay.

ABSTRACT

Wilson's disease is an autosomal recessive disorder of copper metabolism characterized by excessive amount of copper in liver, brain, eye and other body tissues. Diagnosis is based on the presence of Kayser-Fleischer rings, typical neurological symptoms, and/or a low serum ceruloplasmin concentration. The main clinical symptoms are usually due to hepatic and/or neurologic involvement. Pancytopenia is a rare initial symptom of Wilson Disease. An 11-year-old female presented with pancytopenia. This raised suspicion of Wilson's disease, which was confirmed by Kayser-Fleischer rings, a low ceruloplasmin level and raised 24-hour urine copper level. Thus a pancytopenia may be the initial manifestation of Wilson's disease in some patients of Wilson's disease.

Key Words: Wilson's disease, pancytopenia, Kayser-Fleischer rings

ÖZET

Wilson hastalığı karaciğer, beyin, göz ve diğer vücut dokularında aşırı miktarda bakır birikimi ile karakterize bakır metabolizmasının otozomal resesif geçişli bir hastalığıdır. Tanı, Kayser-Fleischer halkası, tipik nörolojik semptomlar ve/veya düşük serum seruloplazmin konsantrasyonu varlığına dayanmaktadır. Başlıca klinik belirtiler; karaciğer ve/veya nörolojik tutulum ile ilişkilidir. Pansitopeni, Wilson Hastalığının nadir bir başlangıç belirtisidir. Vakamız, pansitopeni ile prezente olmuş 11 yaş kız hastadır. Wilson hastalığından şüphe duyulan bu hastamızda, Kayser-Fleischer halkaları, düşük seruloplazmin düzeyi ve yüksek 24 saatlik idrar bakır düzeyi varlığı ile tanı kesinleşmiştir. Bizim vakamızda olduğu gibi pansitopeni wilson hastalarında hastalığın ilk belirtisi olabilmektedir.

Anahtar Kelimeler: Wilson hastalığı, pansitopeni, Kayser-Fleischer halkası

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İletişim: Can Acıpayam, Kahramanmaraş Sütcü İmam Üni. Tıp Fak., Pediatrik Hematolojisi ve Onkolojisi AD **E-posta:** cacipayam@hotmail.com

INTRODUCTION

Wilson disease (WD) is an autosomal recessive disorder of copper metabolism that results in accumulation of copper in the liver, brain, cornea, kidney, and other tissues (1). WD is seen approximately 1 in 30,000-50,000 worldwide. Mutations in the WD gene, especially *ATP7B* mutation cause failure of copper excretion from hepatocyte into bile and a defective synthesis of ceruloplasmin. Ceruloplasmin is a serum glycoprotein which carries the most of copper in the blood and the patients with WD have low levels of ceruloplasmin (2).

Accumulation of copper in the body ultimately leads to liver disease, neurologic symptoms, and Kayser-Fleischer (KF) corneal rings which have been described as "classical symptom triad" of WD. Early diagnosis and appropriate management can treat WD. If left untreated, WD can progress to fatal hepatic failure or severe neurologic deterioration and death. Clinical phenotypes include hepatic, hemolytic, neurologic and psychiatric diseases (3-5).

Patients with WD usually present with liver disease or neurologic symptoms, but the initial clinical manifestation may be pancytopenia (6,

7). Pancytopenia is an unusual clinical symptom of WD. We present a case who developed pancytopenia as the initial manifestation of WD.

CASE PRESENTATION

An 11-year old female, was applied to hospital with complaints of headache and vomiting for 10 days. She had no fever. Her mother, father, brothers and sister had no remarkable medical history. The parents were first-degree relatives (cousins). On examination, her vital signs were normal, except pallor. She had a body weight of 32 kg and moderate anemia. Abdominal examination showed enlarged liver, which was non-tender and 2 cm below the right costal margin in the midclavicular line. Spleen was non-palpable.

The blood count showed a white cell count 2,800/mm^3, absolute neutrophil count 1,440/mm^3, hemoglobin 9.9 g/dL, and platelet count 67,000/mm^3. The differential leukocyte count was neutrophil 70%, lymphocyte 30%. Blood chemistry revealed total serum protein 6.2 g/dL, albumin 3 g/dL, aspartate aminotransferase (AST) 63 IU/L, alanine aminotransferase (ALT) 61 IU/L , blood urea nitrogen 7.8 mg/dL, serum creatinine 0.6 mg/dL, total bilirubin 0.62 mg/dL and direct bilirubin 0.31 mg/dL. The serum concentrations of electrolytes were normal. The prothrombin time was 15.6 seconds and the partial thromboplastin time 37.9 seconds. Viral markers were all negative. Bone marrow aspiration examination was normal. Abdominal ultrasonography showed a heterogeneous echogenic liver. The liver parenchyma was in coarse granular structure**.** Her brain computed tomography was normal. The detailed medical history of patient's family was taken again due to lack of positive findings in examinations to investigate the etiology of pancytopenia. The history revealed that there were family members with WD (two sons of father's uncle aged 35 and 36-years-old).The ophthalmological evaluation showed the presence of the KF ring (Fig. 1). Serum ceruloplasmin level was 9.87 mg/dL (normal range 20.9-48.4 mg/dL). The 24 hour urine copper level was 220 µg/L (normal <20 µg/L). Laboratory data supported the diagnosis of WD.

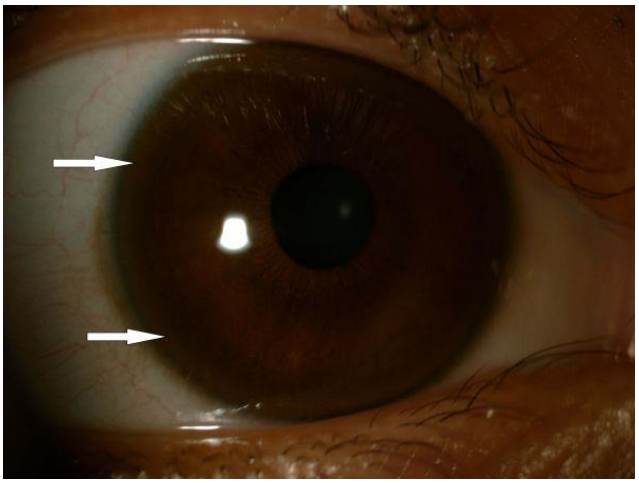

Figure 1. Image of the patient's cornea showing Kayser-Fleischer ring (arrows).

DISCUSSION

Patients with WD usually present with liver disease or neurologic symptoms. However hematologic symptoms may be seen as the first sign of the disease. Although hematologic symptoms are unusual, pancytopenia has rarely been reported as an initial clinical manifestation (6-9).

The diagnosis of WD is based on a combination of several clinical and biochemical parameters. KF rings are identified in 50 to 100% of patients, depending on the presenting symptoms (9). KF

ring is a useful indicator of severe copper overload. KF rings are present in 95% of patients with neurological symptoms, in 50–60% of patients without neurological symptoms and in only 10% of asymptomatic siblings (10). No additional tests are required for diagnosis if KF rings are present and/or serum ceruloplasmin levels are low. Serum ceruloplasmin levels below the normal range are found in more than 85% of patients (9). On the other hand, a low ceruloplasmin level itself is not diagnostic for WD in the absence of KF rings. Ceruloplasmin level may be low in serious malnourished patients and in heterozygous carriers of the WD gene. Urinary copper excretion is increased in patients with WD, however, its usefulness is limited in the clinical practice (9, 10).

In our case, the etiology of pancytopenia was not determined so the patient's detailed medical history was taken again. Eventually there were WD patients of her family members. Ophthalmological examination was performed immediately and KF rings were detected. Then laboratory tests revealed slight elevated serum levels of alanine aminotransferase, and aspartate aminotransferase, as well as low serum levels of ceruloplasmin. Also urinary copper excretion was elevated.

In conclusions, in patients with unexplained pancytopenia of childhood, WD should be considered. Thus, evaluation of the cases presented with pancytopenia for WD may prevent the delay in diagnosis and unnecessary laboratory investigations.

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