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Case Report

Rare Presentation of Wilson Disease in an 11-year-old Sudanese Girl

Mumen Abdalazim Dafallah[1], Elsanosi Habour[2], Esraa Ahmed Ragab[1], Zahraa Mamoun Shouk[1], Fawzeia Hamad[2], Musaab Ahmed[3], and Mohamed H. Ahmed[4]

[1]Faculty of Medicine, University of Gezira, Sudan
[2]Wad Medani Pediatric Teaching Hospital, Wad Medani, Sudan
[3]Center of Medical and Bio-allied Health Sciences Research, College of Medicine, Ajman University, Ajman, United Arab Emirates
[4]Department of Medicine and HIV Metabolic Clinic, Milton Keynes University Hospital NHS Foundation Trust, Eaglestone, Milton Keynes, Buckinghamshire, UK

ORCID:
Mumen Abdalazim Dafallah: http://orcid.org/0000-0002-4300-9481
Elsanosi Habour: http://orcid.org/0000-0003-1179-6705
Esraa Ahmed Ragab: http://orcid.org/0000-0003-3048-5216
Zahraa Mamoun Shouk: http://orcid.org/0000-0001-9037-9103
Fawzeia Hamad: http://orcid.org/0000-0003-4856-4238

Corresponding Author:
Mumen Abdalazim Dafallah;
Faculty of Medicine,
University of Gezira, Sudan
email: Mumenab-dalazim36@gmail.com

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Abstract

Background: Wilson disease is an inherited disorder in which excessive amount of copper accumulates in various tissues of the body. Clinical features related to copper deposition in the liver may appear in the first and second decades followed by neurologic and psychiatric thereafter; however, many patients have a combination of these symptoms.

Case: We report a case of 11 year-old girl, admitted to Wad Medani Pediatric Teaching Hospital with generalized body swellings for four days. Initial investigations showed proteinuria and hypoalbuminemia, thought to be due to nephrotic syndrome. Days later, patient developed jaundice and neuropsychiatric manifestations. A slit lamb examination confirmed the presence of Kayser–Fleischer ring (KF ring) and she scored high in the scoring system for the diagnosis of Wilson disease. D-penicillamine treatment therapy was started and unfortunately the patient's clinical condition deteriorated gradually, and eventually went into deep coma and died. Wilson disease mainly affects the liver, but the initial presentation was completely compatible with nephrotic syndrome.

Conclusion: Diagnosis of Wilson disease should be suspected in a child presenting with generalized body swellings even in the absence of clinical evidence of hepatic and/or neuropsychiatric involvements.

Keywords: Wilson disease, nephrotic syndrome, case report, pediatrics, Sudan

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1. Introduction

Wilson disease is an inherited disorder in which excessive amount of copper accumulates in various tissues of the body [1]. Liver and the basal ganglia of the brain are the primary affected organs [2]. Kayser-Fleischer ring (KF) is the hallmark of Wilson disease [3]. The disease affects 1 in every 30,000 individuals worldwide and it can affect people at any age [1]. Although the presentation of the disease can vary widely, clinical manifestation due to disturbance of liver function, neuropsychiatric manifestations, and KF ring are the key features of Wilson disease [3]. Low serum ceruloplasmin in combination with KF rings is sufficient to make the diagnosis; however the scoring system proposed by the Working Party at the 8th International Meeting on Wilson's Disease, Leipzig 2001 has a good diagnostic accuracy [3]. To the best of our knowledge, Wilson disease has not been reported in Sudanese children. In this case report, we report a case of Wilson disease in a child presented with generalized body swellings.

2. Case Presentation

We report a case of 11year-old girl with no prior medical history, admitted to Wad Medani Pediatric Teaching Hospital, with generalized body swelling for four days.The swellings started in the face and gradually progressed and became generalized. Two days later, the patient developed jaundice with dark urine and no change in the stool color or itching. The patient was a fifth class-primary school student with good academic performance. Parents are first-degree cousins. No family history of similar condition and no other siblings have similar condition.

Clinical examination showed that the patient was conscious, oriented to time, place, and person.Blood pressure was 125/85 mmHg, Pulse 90 bpm, and Respiratory rate 26 c/pm. Despite the clinical evidence of ascites, the spleen and liver were not palpable (liver span = 10 cm). The speech was normal, recent and remote memories were intact, and no abnormal behavior. In addition, cranial nerves, sensory systems, reflexes, and sphincters were intact. Upper and lower limbs bilaterally showed normal power, reflexes, and tone. Examinations of other systems were unremarkable.

Urine analysis showed albuminuria(+++), albumin creatine ratio of 2mg/mmol(normal range < 3), uncountable RBCs, and no RBCs cast or granular casts in urine.International normalization ration = 1.1 (normal range is ≤ 1.1). Table 1 presents the result of liver function tests. Renal function tests and electrolytes were within normal range. Serological tests for hepatitis B and C viruses and human immunodeficiency virus were negative.Random

blood glucose was 66 mg/dl and complete blood count showed neutrophil leukocytosis.Importantly, abdominal ultrasound confirmed the presence of moderate to-massive ascites with enlarged liver with coarse texture and irregular border (cirrhotic changes), thick-edematous gall bladder, and normal biliary system (Figure **1**).

Considering the generalized oedema, hypoalbuminemia, and proteinuria, the patient was diagnosed initially with nephrotic syndrome and put on prednisolone tablets 5mg at a dose of 1mg/kg/day (3 tablets every 8 hr), frusemide tablets 40mg twice daily, and penicillin 2 million units every 6 hr. In addition, amlodipine tablets5 mg once daily was administered to control her high blood pressure. After a few days, the patient showed a considerable clinical improvement in terms of reduction in body swelling, improvement in jaundice, and started to have a clear urine. However, amlodipine was increased to 5 mg twice a day due to persistent high blood pressure. Unfortunately, two days later following the improvement in her clinical symptoms, she suddenly developed hand tremors,clumsiness, speech became slurred and dysarthric with drooling of saliva, shuffling gait with tendency to fall, and abnormal behavior (unintentional and purposeless jumping) was noted. She complained of vague right hypochondriac pain. Blood pressure was found to be 140/88 mmHg, brain CT was normal (Figure **2**) .Importantly, slit lamb examination by an ophthalmologist showed the presence of KF ring as shown in Figure **3**. Due to the unavailability of these investigations in our hospital, we were unable to perform the 24-hr urine copper and serum ceruloplasmin levels. However, the scoring systems developed at the 8th International Meeting on Wilson Disease in Leipzig, 2001 may assist in establishing the diagnosis of Wilson disease; a score of 4 is diagnostic of Wilson disease (Table 2). Serum ceruloplasmin, coombs-negative hemolytic anemia, KF rings, and neurological symptoms must be applied to establish the scoring system. Wilson disease scoring system provides a good diagnostic accuracy. Our patient got a score of 4 (KFring = 2 points and severe neurological symptoms = 2 points) and the diagnosis of Wilson's disease was highly likely. Immediately, D-penicillamine tablets 250 mg twice daily was started and zinc acetate syrup was later added as maintenance therapy.

Days later, the patient's clinical condition deteriorated gradually, and she became comatose with Glasgow Coma Scale score of 3. The patient was then put in regimen of hepatic encephalopathy including dextrose 5% 500ml every 8 hr, cefotaxime injection at a dose of 20ml/kg/day (900ml every 6hr), metronidazole injection 500ml every 8 hr and lactulose syrup 5ml twice daily. Unfortunately, she could not recover and died two days later.

Diagnostic challenges: 24-hr urine copper and serum ceruloplasmin levels were not done due to the un-availability of these investigations in our hospital. The scoring system developed at the 8th International Meeting on Wilson Disease in Leipzig 2001 was possible alternative.

3. Discussion

Wilson disease is an autosomal recessive disorder due to inborn error of metabolism of copper [3]. High rate of consanguinity increases the chance of passing the genes to future generation. Although the disease is common in children, the diagnosis is always difficult [4]. In developing countries, the prevalence has been estimated to be between 6 and 21% of children with chronic liver disease [5].The insidious process of the disease and complex clinical presentation in association with lack of diagnostic facility may leave clinician with only possible alternative diagnostic tool which is the use of Wilson scoring system. The mean age of diagnosis of Wilson disease in Japan was found to be around 12 years [6]. In this case report, the patient's age was 11 years. In addition, our patient presented with generalized body swellings, hypoalbuminemia, proteinuria, and a possible diagnosis of nephrotic syndrome. Several case reports showed that the initial presentations of Wilson disease can be similar to nephrotic syndrome [7, 8]. *Esezoboret al.* reported a diagnosis of Wilson disease in an eight year-old boy from Nigeria, with an initial presentation of nephrotic syndrome that deteriorated gradually and developed into jaundice, severe coagulopathy, and prominent extrapyramidal features consisting of rigidity, tremors, shuffling gait, slurred speech, and emotional liability [8]. It was also suggested that any form of liver disease might be present in patients with Wilson disease and the presentation varies from a symptomatic to fulminant hepatic cirrhosis and hepatic encephalopathy [3]. Our patient developed jaundice, malaise, and abdominal pain during the course of the disease which raised the suspicion for liver failure. Liver failure in Wilson disease carries high mortality rate if left untreated [3] (Table3).

Patients with Wilson disease may first present with neuropsychiatric manifestations. Tremors, muscle rigidity, dysphagia, dysarthria, ataxia, drooling of saliva, mood liability, and inappropriate behavior are common [1, 9, 10]. Our patient developed neuropsychiatric manifestations very rapidly and subsequently became disabled and bedridden. In Figure **4** we have shown the sequence of events in days in relation to the clinical presentation and how her condition deteriorated gradually.

The diagnosis was made by using the scoring systems developed at the 8th International Meeting on Wilson Disease. This scoring system has a good diagnostic accuracy and a high sensitivity and specificity (a score of 4 established the diagnosis).Serumceruloplasmin (the major carrier of copper in the blood), total serum copper (which includes copper incorporated in ceruloplasmin), neurological symptoms, and KF rings are the main components of the scoring system [3]. A score of 4 can make the diagnosis of Wilson's disease.

The commonest ophthalmological finding in patients with Wilson's disease is KF ring. It is due to deposition of excess copper on the inner surface of the cornea in the Descemet membrane. It mainly affects patients with neurological involvement in Wilson's disease and is typically not found in every Wilson's disease patient. It's color is usually golden-brown and does not cause any symptoms. Silt lamb examination is mandatory to confirm its presence. KF ring disappears with treatment over three to five years in the majority of cases [11–13].

Pharmacological management including D-penicillamine, trientine, tetrathiomolybdate, and zink are the main stays of treatment [3, 14]. D-penicillamine, the commonly used drug, increases the urinary excretion of copper. The maintenance dose in pediatric is 20 mg/kg/day given in two or three divided doses [15]. Zink salts are usually added to reduce copper absorption and is administered in a dose of 150 mg /day in three doses, 30 min before meals [3, 13]. Despite all these therapies, liver transplantation is the treatment of choice for acute liver failure or decompensated liver cirrhosis due to Wilson's disease [16].

4. Conclusion

The diagnosis of Wilson's disease needs a high rate of clinical suspicion. We conclude that generalized body swellings might be the first presenting manifestation of the disease even in the absence of clinical evidence of hepatic or neuropsychiatric involvements.

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Ethical Considerations

Written informed consent was obtained from the parents of the patient for participation and publication of this case report and accompanying images. This study was approved by the Research Ethical Committee, University of Gezira Faculty of Medicine, Sudan.

Competing Interests

None.

Availability of Data and Material

Not applicable.

Funding

Nil.

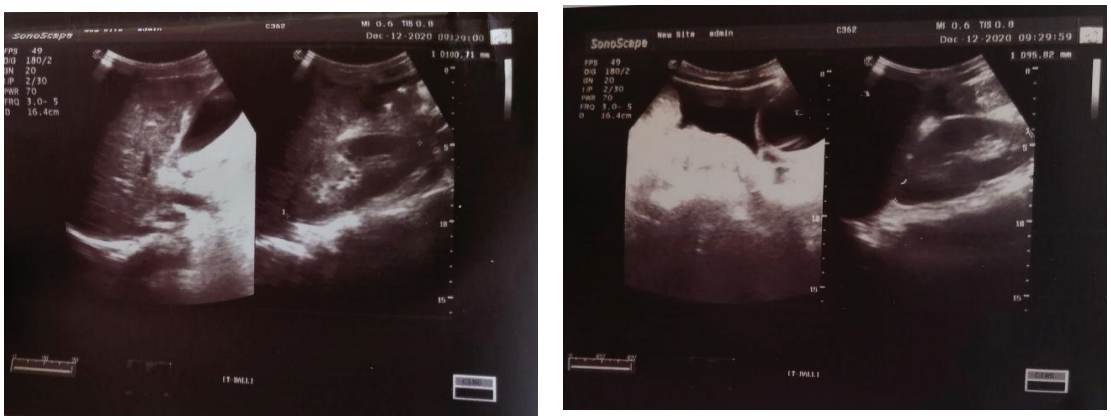

Figure 1: Abdominal ultrasound showing enlarged liver with cirrhotic changes and moderate-to-massive ascites.

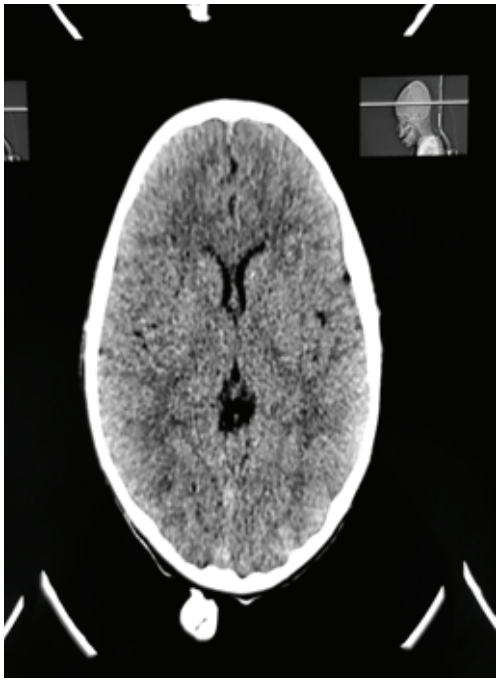

Figure 2: Brain CT scan of the patient showing normal basal ganglia (white arrow).

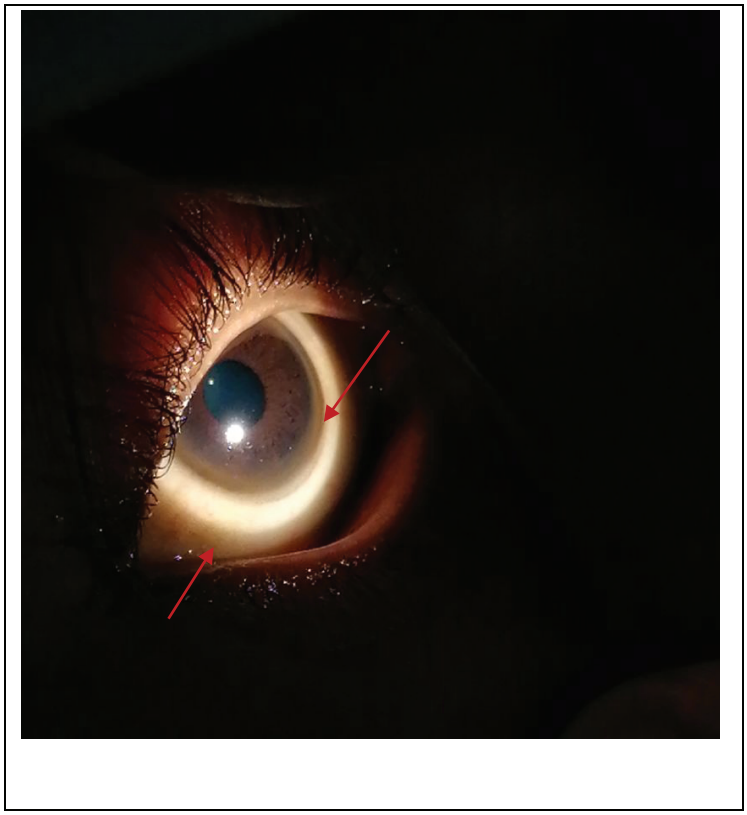

Figure 3: A slit lamb examination showing Kayser–Fleischer ring (red arrow).

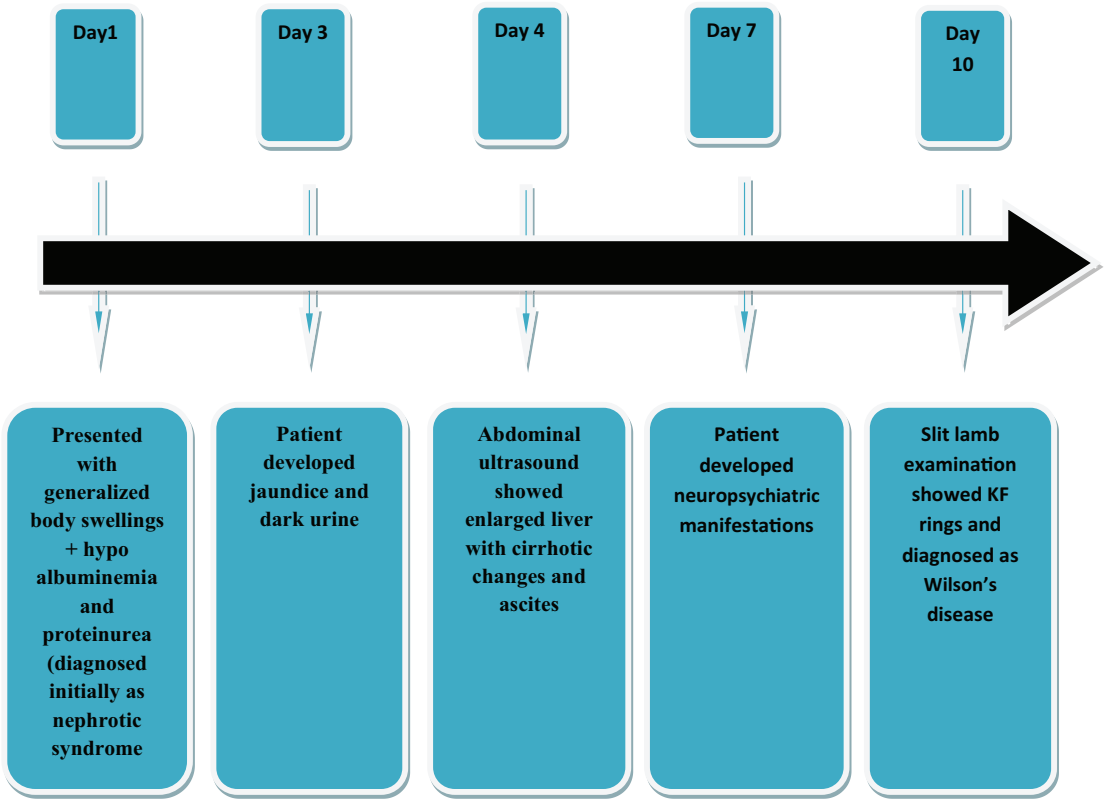

Figure 4: Timeline describing patient's key date in diagnosis.

TABLE 1: Liver function tests.

Test	Day 1	Day 10	Normal values
Serum total protein	5.8	5.0	6.6–8.3 mg/dl
Serum albumin	2.2	1.8	3.5–5.3 mg/dl
Serum globulin	3.6	3.1	2.0–3.5 mg/dl
Serum bilirubin	0.9	0.4	Up to 1.1 mg/dl
Conjugated bilirubin	0.3	0.1	Up to 0.25 mg/dl
Unconjugated bilirubin	0.6	0.3	<0.7 mg/dl
Serum alanine transaminase	55	51	Up to 40 U/L
Serum aspartate transaminase	123	123	Up to 40 U/L
Serum alkaline phosphatase	253	247	Up to 115 U/L

Table 2: Scoring systems developed at the 8th International Meeting on Wilson's disease in Leipzig 2001.

Typical clinical symptoms and signs		
Evaluation	**Score**	**Our patient score**
Kayser–Fleischer ring		
Present	2	2
Absent	0	
Neurological symptoms		
Severe	2	2
Mild	1	
Absent	0	
Serum ceruloplasmin		
Normal (>0.2 g/L)	0	—
0.1–0.2 g/L	1	
<0.1 g/L	2	
Coombs-negative hemolytic		
Anemia		0
Present	1	
Absent	0	
TOTAL SCORE		**4**

Table 3: Prognostic index in Wilson's disease.

Parameter	**1***	**2***	**3***	**4***	**Our patient results**	**Our patient score**
Serum bilirubin (µmol/L)	100–150	151–200	201–300	>300	15.39 µmol/L	_
AST (U/L)	100–150	151–300	301–400	>400	123 U/L	1
INR	1.3–1.6	1.7–1.9	2.0–2.4	>2.4	1.1	–
WBC (10^9/L)	6.8–8.3	8.4–10.3	10.4–15.3	>15.3	15.5 10^9/L	4
Albumin(g/L)	34–44	25–33	21–24	<21	22 g/L	3
TOTAL SCORE						**8**

A score >11 is associated with high probability of death without liver transplantation

TOTAL SCORE	**Diagnosis**
4 or more	Diagnosis established
3	Diagnosis possible, more tests needed
2 or less	Diagnosis very unlikely

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