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Pulmonary Hypertension as an Initial Presentation of Wilson's Disease: A Case Report

Fariba Rezaeetalab (MD)[1], Mahnaz Mozdourian (MD)[*2]

[1]*Lung Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.*
[2]*Department of Internal Medicine Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*

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ABSTRACT

Wilson's disease is a rare genetic disorder, which is associated with clinical manifestations such as liver dysfunction, psychological and neurological issues, and specific laboratory findings demonstrating the increased urinary excretion of copper and copper accumulation in the body. Wilson's disease is occasionally presented by atypical features, which delay the diagnosis of this rare disorder. This study aimed to describe the case of a patient with pulmonary and portal hypertension as a primary manifestation of Wilson's disease. A young male patient was admitted to the emergency department due to the deterioration of respiratory symptoms and overall weakness. The patient had a history of dyspnea and fatigue, which was diagnosed as idiopathic pulmonary hypertension. In the previous admission, the liver function test of the patient was not disrupted, and serum/urinary copper and ceruloplasmin levels were normal. In the current admission, the patient had elevated bilirubin and enzyme levels, as well as abnormal copper and ceruloplasmin levels. Moreover, portal hypertensive gastropathy and Kayser-Fleischer ring were detected in further investigations, confirming the diagnosis of Wilson's disease. To the best of our knowledge, this was the first report on Wilson's disease initially presented with pulmonary and portal hypertension.

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Introduction

Wilson's disease is a rare autosomal recessive disorder, which is caused by abnormal copper metabolism with the approximate prevalence of 1.5 cases per 100,000 (1). Decreased copper excretion and accumulation of copper in the body organs lead to the specific manifestations of the disease, which mostly depend on the involved organs (2). Some of the typical manifestations of Wilson's disease include changes in the personality and liver function, movement disorders in adults, increased 24-hour urinary copper, and decreased ceruloplasmin and serum copper in most of the cases. However, Wilson's disease may not be presented with such typical features and could be misdiagnosed in atypical patients (3).

According to the literature, hepatopulmonary syndrome, polyneuropathy, and nephrotic syndrome are among the rare, initial presentations of Wilson's disease (4-6). Furthermore, reports suggest that some patients may present with isolated features, such as neurological symptoms without hepatic involvement (7). Such uncommon presentations and the rare nature of the disease could lead to delayed diagnosis and prolongation of the interval between the initial presentations of the patient to the disease diagnosis (8). Pulmonary and portal hypertensions are considered to be the

***Corresponding author:** Mahnaz Mozdourian.
Department of Internal Medicine Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
***E-mail:** mozdorianmh@mums.ac.ir*
***Tel:**00989122965603*

most uncommon manifestations of Wilson's disease.

This article aimed to discuss the case of a young male presenting with pulmonary and portal hypertension as the primary manifestations of Wilson's disease.

Case report

A 26-year-old male patient was referred to the emergency department due to sudden dyspnea and fatigue. The patient had been admitted to the cardiology service department due to exertional dyspnea, lower-extremity edema, and fatigue six months before. The previous transthoracic echocardiography results of the patient indicated an ejection-fraction of 50-55%, right ventricular pressure overload, severe right ventricular enlargement, and systolic pulmonary artery pressure of 60 mmHg. The complete blood count only revealed decreased platelet level, and the other biochemical tests (liver and kidney function enzymes, thyroid hormone levels) were not remarkable. In addition, the anti-nuclear antibody, anti-smooth muscle antibodies, liver kidney microsomal antibody, and hepatitis B and C serology were negative. The ultrasonography of the liver and biliary ducts was normal.

Based on the age and gender of the patient, testing for Wilson's disease had been performed in the previous visit, and the urinary copper and serum ceruloplasmin levels were within the normal range. Considering the possible diagnosis of idiopathic pulmonary hypertension, the patient was a candidate for right heart catheterization. However, the patient was not willing to undergo the procedure and was discharged willingly. After discharge from the hospital, the patient experienced gradual fatigue and weakness, which diminished his daily activities. In the current admission, the patient presented with sudden severe dyspnea and pleuritic chest pain.

Upon admission, blood pressure was stable (systolic blood pressure: 140 mmHg, diastolic blood pressure: 90 mmHg), the respiratory rate was estimated at 26 breath per minute (oxygen saturation: 97%), and the pulse rate was 120 beat/minute. Loud P2 cardiac sound was auscultated while the longs were clear on auscultation. However, the physical examination of the other organs was unremarkable. Through the possible impression of pulmonary thromboembolism, computed tomography angiography was performed to report pulmonary hypertension (Figure 1).

The laboratory findings of the patient indicated elevated aspartate transaminase (244; normal range: 5-40) and alanine transaminase (58; normal range: 5-40), as well as increased international normalized ratio (4.2). On the other hand, the endoscopic workup revealed gastroesophageal reflux (LA class B) and diffuse snake-skin appearance with some red signs throughout the stomach (portal hypertensive gastropathy). Through the possible impression of Wilson's disease, urinary copper and serum ceruloplasmin levels were reordered. The new laboratory results revealed increased urinary copper and decreased ceruloplasmin levels. In addition, the brain MRI demonstrated high signal intensity on the T2 and FLAIR images of the left-sided white matter (Figure 2).

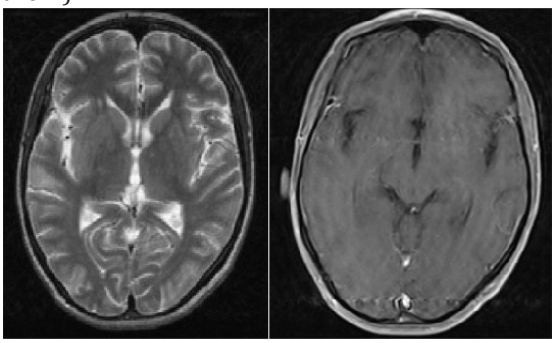

Figure 1. Computed Tomography Angiography Demonstrating Bilateral Pulmonary Hypertension and Pulmonary Effusionn

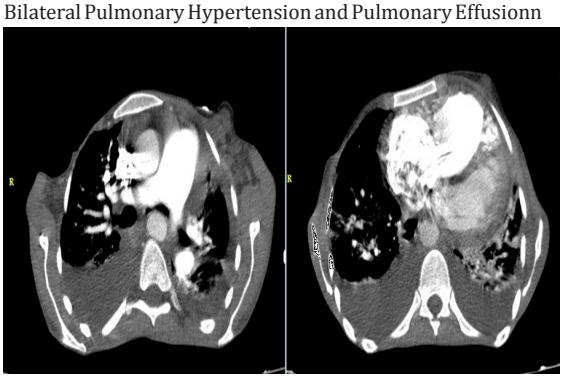

Figure 2. Brain Magnetic Resonance Imaging Demonstrating High Signal Intensity on T2 and FLAIR Images of Left-sided White Matter

The Kayser-Fleischer ring was detected by an ophthalmologist, and the diagnosis of Wilson's disease was confirmed based on the ophthalmic findings, liver dysfunction, and pulmonary artery hypertension, along with the increased urinary copper and serum ceruloplasmin levels. The patient received treatment with triethylenetetramine (250 mg every 8 hours), and all his family members were advised to be evaluated for the serum and ophthalmic findings of Wilson's disease. The patient responded well to the therapy and became symptom-free within six months of follow-up.

Discussion

Data is scarce regarding the natural history of Wilson's disease, and the clinical presentations and age of onset are also diverse (3). This study

aimed to describe a case of Wilson's disease in a young male patient presenting with pulmonary hypertension as the primary manifestation of the disease. The patient was initially managed as a case of idiopathic pulmonary hypertension, and further diagnostic workups revealed the increased exertion of urinary copper and decreased serum ceruloplasmin, as well as the Kayser-Fleischer ring and hepatic dysfunction.

The abnormal accommodation of copper is the main pathophysiological mechanism involved in Wilson's disease. The manifestations of this genetic disorder vary from an asymptomatic patient with abnormal biochemical tests to more severe presentations (e.g., liver failure) (7, 8). The nervous, cardiovascular, hepatic, and pulmonary systems are most frequently involved in Wilson's disease (2, 8). In the current case, the main presentations of Wilson's disease were right ventricular hypertrophy, pressure overload, portopulmonary hypertension, and hepatic dysfunction. Cardiac involvement in Wilson's disease is often mild (9). In this regard, Quick et al. evaluated the autonomic and cardiac function in patients with Wilson's disease, demonstrating that diastolic dysfunction was prevalent in these patients, while pulmonary hypertension was not detectable in any of the cases (10).

To the best of our knowledge, this report is the first case of Wilson's disease presented with portal and pulmonary hypertension. A similar case to our patient has been reported by Giouleme et al. (11), who described the case of a 51-year-old patient with portopulmonary hypertension and sarcoidosis-induced pericarditis. In the mentioned study, the patient was a known case of Wilson's disease, which was diagnosed due to hepatic failure and jaundice and successfully treated with D-penicillamine (11). Moreover, the patient in the mentioned research developed pulmonary hypertension many years later after the diagnosis of Wilson's disease, which was also successfully treated with bosentan and confirmed two years after the development of pulmonary hypertension attesting to sarcoidosis (11). However, the researchers reported that differentiating the main cause of portopulmonary hypertension due to sarcoidosis or Wilson's disease may be difficult (11).

Another study in this regard demonstrated portal hypertension in Wilson's disease as confirmed by hepatopulmonary syndrome in the patients. In addition, Lahiri et al. reported a case of hepatopulmonary syndrome as the primary manifestation of Wilson's disease in a 20-year-old female patient (4). In the mentioned study, some of the most remarkable clinical findings included cyanosis, clubbing, polycythemia, and splenomegaly (4). Similar to our patient, the patient in the study by Lahiri et al. had portal hypertension and esophageal varices on the endoscopic examination. However, our patient had no findings indicating central cyanosis or clubbing. According to the literature, hepatopulmonary syndrome may present in patients with liver dysfunction without portal hypertension or vice versa (4). Moreover, no specific correlations have been reported between hepatopulmonary syndrome and severity of liver dysfunction (4).

Based on the findings in this regard, it is recommended that hepatopulmonary syndrome be considered a differential diagnosis for central cyanosis even in patients without liver dysfunction (4). Moreover, it has been demonstrated that the hepatic manifestations of Wilson's disease may vary widely in different patients, ranging from asymptomatic hepatomegaly to decompensated cirrhosis (3), which highlights the need to consider Wilson's disease as a possible cause of acute hepatitis or even cirrhosis of unknown etiology (3).

Regardless of the rare presentation of Wilson's disease in our patient, the laboratory evaluations may also be negative in some patients. As the negative copper and ceruloplasmin results proved negative twice, we eliminated the possible laboratory errors. It is also notable that the classic triad of Wilson's disease may be incomplete or even absent in up to 3% of the cases (3).

Conclusion

Wilson's disease is a multisystem disease, which may not manifest with typical features limited only to the brain and liver. The present report demonstrated that portopulmonary hypertension may be the initial manifestation of Wilson's disease. Therefore, Wilson's disease should be considered in the workup of such clinical conditions when other possible causes are rolled out and the Wilson's triad is not completely present.

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None.

Conflict of Interest

The authors declare no conflict of interest.

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