

To Cite:

Sagar VVSS, Shukla S, Acharya S, Kumar S, Akhil CVS. Wilson's disease manifesting as Hepatopulmonary syndrome- A rare case report. Medical Science, 2022, 26, ms78e1956.

doi: <https://doi.org/10.54905/disssi/v26i121/ms78e1956>

Author Affiliation:

¹Resident, Department of General Medicine, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: vvssagar@gmail.com

²Professor, Department of Pathology, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: samarth21174@gmail.com

³Professor and Head, Department of General Medicine, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: souryaacharya74@gmail.com

⁴Professor, Department of General Medicine, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: sunilkumarmed@gmail.com

⁵Resident, Department of Pediatrics, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: me.akhilpandu@gmail.com

Corresponding author

Resident, Department of General Medicine, Jawaharlal Nehru Medical College & Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India; Email: vvssagar@gmail.com

Peer-Review History

Received: 04 January 2022

Reviewed & Revised: 05/January/2022 to 17/February/2022

Accepted: 19 February 2022

Published: 24 February 2022

Peer-review Method

External peer-review was done through double-blind method.

URL: <https://www.discoveryjournals.org/medicallscience>



This work is licensed under a Creative Commons Attribution 4.0 International License.



Copyright © 2022 Discovery Scientific Society.

Wilson's disease manifesting as Hepatopulmonary syndrome- A rare case report

Sagar VVSS¹✉, Samarth Shukla², Sourya Acharya³, Sunil Kumar⁴, Chitturi Venkata Sai Akhil⁵

ABSTRACT

Wilson's disease presents with a wide clinical spectrum, most common being hepatic involvement and neuro-psychiatric features. Hepatopulmonary syndrome (HPS) is one of the rare complications of liver failure presenting as breathlessness, platypnea, orthodeoxia and central cyanosis. Wilson's disease rarely presents initially with central cyanosis and clubbing. A case of 16 year old female who presented dyspnoea, platypnea, clubbing and cyanosis focuses on rare presentation of Wilson's disease as hepatopulmonary syndrome.

Keywords: copper, cyanosis, clubbing, platypnoea

1. INTRODUCTION

Liver diseases are less likely considered as the primary cause in case of initial presentation of cyanosis and clubbing. Long standing hepatic failure may lead to hypoxia due to several causes of which hepatopulmonary syndrome is considered responsible in cases of liver failure. It is a triad consists of liver failure, hypoxemia, and intrapulmonary vasodilation. The intrapulmonary vasodilation can be detected by transthoracic contrast echocardiography. Alterations in the pulmonary vascular flow prevails mechanism underneath it. Irrespective of the cause of HPS, most commonly it presents with respiratory symptoms. Hence, consider it as one of the differential diagnosis while investigating a case of cyanosis (Lahiri et al., 2015).

Wilson disease (WD) is an autosomal-recessive disorder due to genetic mutation of ATP7B affecting copper metabolism. It can present in any age group like in children, adolescents and adults with hepatic or neuropsychiatric manifestations (most commonly in adolescents). In this case report, we promulgating a 16 year old female presenting with cyanosis, platypnea, orthodeoxia and clubbing diagnosed as HPS secondary to Wilson disease. Wilson's disease manifesting as hepatopulmonary syndrome was reported in a limited number of studies making it a rare presentation. Manifestation of HPS was reported in Wilson disease in addition to various other liver diseases. But HPS being the initial presentation of Wilson disease rather than hepatic or neuropsychiatric symptoms is rare (Shribman et al., 2019).

2. CASE REPORT

A female aged 16 years presented with complaints of breathlessness at rest (NYHA-Grade IV), yellowish discolouration of eyes and urine, bluish discolouration of tongue, lips and fingers since 6 years and multiple episodes of black stools, abdominal pain, generalised body ache since 10 days. Patient had breathlessness aggravated on standing and relieved on lying down suggestive of platypnoea, and easy fatiguability. The above mentioned symptoms progressed in six years. Patient had no history of improvement in breathlessness, bluish discolouration on squatting, recurrent respiratory infections in childhood, blood in vomitings, bilateral lower limb swelling, abdominal distension, chest pain, palpitations, cough, hemoptysis, pale stools. Patient had no history of diabetes, hypertension, tuberculosis, bronchial asthma, thyroid disorder.

On General examination patient had tachycardia with 110/minute, tachypneic-30/min thoracoabdominal, blood pressure of 100/70 mm of Hg, Jugular venous pressure 8cm of water from sternal angle, pulse oximetry showed 79% saturation in supine position on room air which had reduced to 60% on sitting position suggestive of orthodeoxia. She had central cyanosis as shown in figure 1a and b, clubbing of both upper extremities as shown in figure 2, jaundice noted in sclera of both eyes. No signs of pallor, pedal edema, lymphadenopathy noted. Kayser-Fleischer ring noted on ocular examination as shown in figure 3.



Figure 1(a) Central cyanosis showing bluish discoloration of tongue and 1(b) Lips



Figure 2 showing clubbing in fingers of upper limb



Figure 3 showing Kayser-Fleischer ring on slitlamp examination.

Clinical examination reveals normal findings for cardiac and respiratory systems. Abdomen on examination revealed mild splenomegaly just palpable, mild hepatomegaly present. Central nervous system examination revealed normal. Laboratory investigations revealed polycythemia with haemoglobin 16.8gm/dl, haematocrit 48.7, WBC 4700 cells/cumm, platelets 26,000 cells/cumm, coagulation profile suggestive of prothrombin time 11.9, APTT 34, INR 1.49, urea 15mg/dl(9-20), creatinine 0.4mg/dl (0.4-1.25), serum sodium 140mmol/l(137-145), serum potassium 4.4 mmol/l(3.5-5.1), total bilirubin 4mg/dl(0.2-1.3), conjugated 1.4mg/dl(0-0.3), unconjugated 2.6mg/dl(0-1.1), SGOT 32U/L(17-59), SGPT 24U/L(<50), Serum ferritin 72.5ng/ml(17.9-464), albumin 2gm/dl(3.5-5), Viral markers such as hepatitis B,C were negative. Anti nuclear antibodies was done by indirect immunofluorescence which was negative. Anti smooth muscle antibody titre was negative. Serum IgG 15.2gm/l (7-16). Liver kidney microsomal 1 antibody level was done by ELISA- 4.02 RU/ml which was normal (Negative<20, Positive >20).

Chest x ray showed focal radio opaque lesion in right lung field in mid zone. ECG showed sinus tachycardia. USG abdomen revealed coarse hepatic echotexture with dilated portal vein with splenomegaly with mild to moderate ascites with portal hypertension. Contrast – enhanced echocardiography with IV agitated saline was positive suggests intrapulmonary shunting which confirmed hepato-pulmonary syndrome. Rest all cardiac valves were normal in structure and function with an intact inter atrial and interventricular septae without any hypertrophied left ventricle, dilatation or regional motion wall abnormality at rest or asymmetrical septal hypertrophy. The left ventricular ejection fraction was 65%, LV diastolic function was normal, and no clots, vegetations or pericardial effusion was noted.

On further evaluation; Serum ceruloplasmin was low 0.12gm/l (0.16-0.45), 24 hour urinary copper was elevated 415ug/24 hours (2-80). Chromosomal analysis showed a normal chromosomal complements having a modal number of 46 chromosomes including two X were noted from peripheral blood sample processed. Based on AASLD (American Association for the Study of Liver Diseases) guidelines 2008 this case was diagnosed as Wilson's disease. The initial presentation in this case attributes to HPS due to complication of hepatic failure (Roberts & Schilsky, 2008).

3. DISCUSSION

Wilson disease is an autosomal recessive disorder affecting copper metabolism leading to copper overload ultimately end up with toxicity. The genetic mutation encodes copper transporting ATPase affecting copper excretion through bile leading to oxidative damage to the liver due to accumulation of copper (Aboussouan & Stoller, 2000). Copper absorbed from gut is taken up by hepatic organ and released into the peripheral vasculature bounds to ceruloplasmin. ATP7B helps for transportation in liver cells before binding and biliary excretion of copper whereas mutation or dysfunction in this gene leads to copper accumulation in liver causing oxidative damage and the release of unbound free copper into systemic circulation (Almohana, 2011). Copper which released into systemic circulation can also accumulates in brain causing cellular damage and manifests as tremor, dystonia, dysarthria, drooling and dysphagia. Neurological features such as cerebellum impairment, choreiform movements, exaggeration of reflexes,

convulsions and impaired cognition are additionally seen (Krowka et al., 2000). Ophthalmological feature commonly seen in Wilson's disease is Kayser-Fleischer (KF) ring in which deposition of copper seen in posterior elastic lamina of cornea which can be appreciable as a greenish or golden-brown ring at peripheral cornea. Other organs such as cardiac, renal and skeletal systems are rarely involved (Finelli, 1995).

Wilson's disease common presentation was cirrhosis of liver having features such as pedal oedema, icterus, peritoneal fluid collection and encephalopathy and leads to various complications such as portal hypertension which is significant among them. Subject presenting with dyspnea and central cyanosis in a case of chronic liver failure had various reasons. Major subset has cardiopulmonary diseases without any relation to liver pathology. Another subset has cirrhosis complications and rare underlying etiologies became the culprit. Two rare complications observed as per literature in cirrhosis patients causing pulmonary dysfunction are HPS and portopulmonary hypertension (Schenk et al., 2002).

The probable identified prime cause of hypoxia in HPS is due to intrapulmonary abnormal vasculature. Factors contributing for this cause are raised ET-1 levels, loss of pulmonary vasomotor control due to decreased hepatic venous flow and kupffer cell activation due to translocation of gut bacteria causing sequential rise in NO synthase ultimately leads to vasodilation (Kennedy & Knudson, 1977).

Dyspnoea is the usual symptom in HPS. Platypnea and orthodeoxia are the symptoms explained to be as breathlessness and desaturation while assuming sitting posture are the clinical features which reinforce the diagnosis of HPS. In addition clubbing, cyanosis, cutaneous spider nevi also plays a major part. Spider nevi represents intrapulmonary vascular dilatations in HPS having significant role in strengthening diagnosis (Schilsky, 2005).

In this case, patient presented with cyanosis, polycythemia, orthodeoxia, clubbing, platypnea and hepatosplenomegaly which instigates into assessment for HPS. The uniqueness in this case was initial presentation of patient with hypoxia and ultimately it was diagnosed as liver cirrhosis due to Wilson's disease with a complication of pulmonary vasculature, namely HPS. The fact drawn here is HPS needs to be scrutinized in a patient having hypoxia and central cyanosis even with absence of signs of hepatocellular failure besides accentuating the rare feature of HPS.

4. CONCLUSION

This case describes unusual manifestation of Wilson disease which adds to the wide spectrum. Contemplation of HPS as differential in the patients with initial presentation of central cyanosis confers proper approach. Liver transplantation becomes the possible management for hepatopulmonary syndrome with better outcome of 5 year survival rate. As hypoxemia are progressive, prognosis and outcome proportional to severity of hypoxemia. Post transplant issues in HPS notably are recurrence, infection, post transplant hypoxemia, hypoxemia resolution with progressive pulmonary hypertension; diffusion lung capacity doesn't improve despite improved oxygenation

Acknowledgement

We thank the authors who were all contributed to this case report and patient who gave her consent for publication, ophthalmologist who found KF ring.

Author Contributions

VVSSS & SA- Initiated the idea of publication and contributed for development of manuscript

SA- Diagnosed the condition

SS & SK- Reviewed and edited the manuscript

CVSA- Provided the related information regarding Wilson disease presenting as hepatopulmonary syndrome

Informed consent

Written & Oral informed consent was obtained from patient whom identifying information is included in this manuscript.

Funding

This study has not received any external funding.

Conflict of interests

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Aboussouan LS, Stoller JK. The hepatopulmonary syndrome. Baillieres Best Pract Res ClinGastroenterol 2000; 14(6):1033-1048.
2. Almohana S. Prevalence of clinically significant Hepatopulmonary Syndrome among Patients with Chronic Liver Disease and Portal Hypertension. Al-Kindy Col Med J 2011; 7(1):61-66.
3. Finelli PF. Kayser-Fleischer ring: hepatolenticular degeneration (Wilson's disease). Neurol 1995; 45(7):1261-2. doi: 10.1212/wnl.45.7.1261. PMID: 7617179.
4. Kennedy TC, Knudson RJ. Exercise-aggravated hypoxemia and orthodeoxia in cirrhosis. Chest 1977; 72:305-309.
5. Krowka MJ, Wiseman GA, Burnett OL, Spivey JR, Therneau T, Porayko MK, et al. Hepatopulmonary syndrome: a prospective study of relationships between severity of liver disease, PaO₂ response to 100% oxygen, and brain uptake after (99m)Tc MAA lung scanning. Chest 2000; 118: 615-624.
6. Lahiri D, Agarwal R, Mondal D, Roy MK, Sarkar N, Mukhopadhyay J. Hepatopulmonary Syndrome as the First Manifestation of Wilson Disease. J Case Rep 2015; 5:37-41
7. Roberts EA, Schilsky ML; American Association for Study of Liver Diseases (AASLD). Diagnosis and treatment of Wilson disease: an update. Hepatol 2008; 47(6):2089-111. doi: 10.1002/hep.22261. PMID: 18506894.
8. Schenk P, Fuhrmann V, Madl C, Funk G, Lehr S, Kandel O. Hepatopulmonary syndrome: prevalence and predictive value of various cut offs for arterial oxygenation and their clinical consequences. Gut 2002; 51:853- 859.
9. Schilsky ML. Wilson disease: new insights into pathogenesis, diagnosis, and future therapy. Curr Gastroenterol Rep 2005; 7:26-31.
10. Shribman S, Warner TT, Dooley JS. Clinical presentations of Wilson disease. Ann Transl Med 2019; 7(Suppl 2):S60. doi: 10.21037/atm.2019.04.27