

# Hepatic Hydrothorax- An Unusal Presentation of Wilson's Disease: A Case Report with Review of Relevant Literature

NAZMABEGUM<sup>1</sup>, A.S.M. BAZLUL KARIM<sup>2</sup>, WAHIDUZZAMAN MAZUMDER<sup>3</sup>

## Introduction:

Wilson's disease is a genetic disorder of copper metabolism<sup>1</sup>. The disease was first described in 1912 by "Kinnear Wilson" as "progressive hepatolenticular degeneration" as a familial, lethal neurologic disease accompanied by chronic liver disease leading to cirrhosis<sup>2</sup>. The association of corneal copper deposits with this disorder was later made by Kayser and Fleisher<sup>3</sup>. Wilson's disease (WD) is an inherited autosomal recessive disorder affecting 30 individuals per million of population<sup>4</sup>. In 1993 the gene ATP7B that is abnormal in WD was identified<sup>5</sup>. The ATP7B gene encodes metal transporting protein P type ATPase which plays a crucial role in copper excretion into the bile<sup>6</sup>. The clinical presentation of Wilson's disease is variable. It can present clinically as liver disease (asymptomatic hepatomegaly, isolated splenomegaly, persistently elevated serum aminotransferase activity, acute hepatitis, fulminant hepatic failure, cirrhosis), as a progressive neurologic disorder or as psychiatric illness<sup>7,8</sup>. Apart from neurologic and psychiatric illness, patients with Wilson's disease may present with important extra-hepatic manifestation including renal abnormalities<sup>9</sup> (aminoaciduria, nephrolithiasis), skeletal abnormalities<sup>10</sup> (premature osteoporosis and arthritis), cardiomyopathy<sup>11</sup>, pancreatitis<sup>12</sup>, hypoparathyroidism<sup>13</sup>, infertility and miscarriages<sup>14</sup>. Hepatic hydrothorax is another uncommon manifestation. Hepatic hydrothorax is defined as a significant pleural effusion usually greater than 500 ml, in a cirrhotic patient, without an underlying pulmonary and cardiac disease<sup>15</sup>. It seems to be a relatively uncommon complication of portal hypertension with an estimated prevalence of 5-12% in patients with cirrhosis of the liver<sup>16</sup>. We report an interesting case of Wilson's disease with an uncommon presentation of pleural effusion. Possible mechanism of the process,

diagnostic features and literature review for the same is discussed. So far our knowledge goes till now there is no case reporting of Wilson disease with pleural effusion in our country.

## Case report

Shakil a 10 years old immunized boy of nonconsanguinous parents, hailing from Gajipur was admitted with the complaints of jaundice for 5 months, gradual distension of abdomen for one and half months, fever for 1 month, and respiratory distress for 5 days. He also had history of melaena on two occasions. Fever was low grade and intermittent in nature and was not associated with chills, rigor, cough, dysuria, rash, convulsion, joint pain and also there was no history of contact with tuberculous patients, blood transfusion and parenteral medication. None of his family members suffered from jaundice or liver diseases. Shakil was alert, co-operative, but he was dyspnoeic, mildly icteric and had gynaecomastia. He had hepatomegaly (4 cm) which was firm and nontender, splenomegaly (2.5 cm) and ascites. He also had right sided pleural effusion from 4<sup>th</sup> intercostals space in the midclavicular line. Other systemic examination including cardiovascular and neurological examination revealed no abnormality. Laboratory investigations showed Hb 9.2 gm/dl, total WBC count 12,800/cmm (polymorphs 50%, lymphocytes 42%). Liver function test showed serum ALT 125 UL, bilirubin 2.8mg/dl, prothrombin time 32.1s (Control 11.8 sec, INR 2.8 sec), albumin 26.8gm/L. Ultrasonogram of abdomen revealed hepatosplenomegaly, ascites and right sided pleural effusion. Two column of small sized oesophageal varices were also detected by endoscopy of upper GIT. Viral screening for HBsAg and anti HCV were negative. Slit lamp examination of eye showed Kayser - Fleisher ring (KF ring) in either eye close to the corneal limbus. Twenty four hours urinary copper excretion was increased (300± 0.9mcg/L) and had decreased serum ceruloplasmin (0.03g/L) level. X-ray chest revealed right sided pleural effusion. Necessary investigations were done considering the common

1. Assistant Professor, Department of Paediatrics, OSD, DGHS, Dhaka

2. Professor, Dept of Paediatric Gastroenterology and Nutrition, BSMMU, Dhaka

3. Student, MD (Paediatric Gastroenterology), BSMMU, Dhaka

**Correspondence:** Dr. Nazma Begum

aetiologies of unilateral pleural effusion like pneumonia, pulmonary tuberculosis, lymphoma and autoimmune causes. His tuberculin test was negative, serum LDH was 303 U/L and serum ANA was negative. Biochemical analysis of pleural fluid revealed protein 7gm/L (transudative) and glucose 6.1 mmol/L, cytopathology showed acellular smear with no malignant cell. Considering endemic zone DAT for Kala-azar was done and was found negative. Based on above clinical manifestations and laboratory parameters a diagnosis of Wilson's disease was made. By exclusion of common causes (infection, tuberculosis, malignancy, autoimmune and cardiac causes), pleural effusion was considered as hepatic hydrothorax.

Shakil was managed supportively with salt restricted diet, diuretics, injection vitamin K, fresh frozen plasma, H<sub>2</sub> blocker and lactulose. Therapeutic thoracentesis was also done. Specific management for Wilson's disease was given with oral penicillamine and zinc (25 mg three times daily). His dyspnoea subsided with above mentioned management. At a three-month follow-up, his 24 hours urinary copper excretion reduced to (126± 0.9mcg/L), prothrombin time remained prolonged to 20 sec and X-ray chest showed a partial resolution of pleural effusion. He was advised to continue zinc for the rest of the life.

### Discussion

Wilson's disease has a wide spectrum of clinical presentation. Hepatic hydrothorax is usually right sided (65-87% of reported cases). However it may be left sided or bilateral. In the vast majority of cases, ascites are also present<sup>17</sup>. This 10 years old boy also presented with right sided pleural effusion and ascites. Hypoalbuminemia<sup>15</sup>, increased pressure in azygos vein<sup>18</sup>, fluid leakage via diaphragmatic lymphatic channel<sup>19</sup> were considered as the possible pathogenesis for the development of hepatic hydrothorax. But these mechanisms fail to explain why hepatic hydrothorax is predominantly right sided. In 1955, Emerson described for the first time a diaphragmatic fenestration in a patient with cirrhosis and pleural effusion.<sup>20</sup> Microscopic examination of these defects revealed discontinuities in the collagen bundles that make up the tendinous portion of the diaphragm. Increase in the intra- abdominal pressure, for example, as a result of ascites, coughing, vomiting or straining might lead to small herniation through these gaps into the pleural cavity<sup>20</sup>. These herniations,

also known as pleuroperitoneal blebs, may rupture<sup>20</sup>. The ensuing defects which are typically less than 1 cm in diameter allow free communication between the peritoneal and pleural spaces. This theory is further supported by the fact that air, dyes or radiolabeled substances intra-abdominally injected in patients with hepatic hydrothorax move rapidly into the pleural cavity<sup>21</sup>. Autopsy studies suggest the pleuroperitoneal blebs occur less frequently in the left hemidiaphragm, as it seems to be thicker and more muscular<sup>18</sup>.

The diagnosis of hepatic hydrothorax should be suspected in a patient with established cirrhosis and portal hypertension, unilateral pleural effusion, most commonly right sided<sup>22</sup>. A variety of respiratory symptoms, including dyspnoea, nonproductive cough, chest pain and fatigue due to hypoxemia may also occur.<sup>22</sup> Patients rarely presents with signs and symptoms of respiratory failure due to an acute tension hydrothorax. In a majority of cases pleural effusion may be noted incidentally on a chest radiography performed for other reasons. A diagnostic thoracentesis should be performed in all cases with suspected hepatic hydrothorax.<sup>22</sup>

**Table-I**

*Composition of pleural fluid in patients with uncomplicated hepatic hydrothorax<sup>16</sup>*

Cell count<1000/cmm
Polymorphonuclear leukocyte count<250/cmm
Protein concentration<2.5g/dl
Glucose conc. Similar to that of serum
Pleural fluid/serum protein ratio<0.5
Pleural fluid/serum albumin gradient >1.1
Pleural fluid/serum LDH ratio>0.6
PH >7.4

In patients with cirrhosis and pleural effusion, a thorough investigation for primary cardiopulmonary disorder should be performed. In this index case other relevant investigations considering pleural effusion were done and no convincing feature was found to establish other diagnosis. In a recent study a diagnosis other than hepatic hydrothorax was established in 18% of cirrhotics with pleural effusion<sup>23</sup>.

Spontaneous bacterial empyema (SBEM) represents a distinct complication of hepatic hydrothorax. The pathogenesis of SBEM remains unclear. It might occur

as a result of direct bacterial spread from peritoneal cavity<sup>24</sup>.

**Diagnostic criteria of Spontaneous bacterial empyema (SBEM)<sup>24</sup>:**

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- Serum/pleural albumin gradient >1.1g/dl
  - Polymorphonuclear leukocyte count >500/cmm
  - Absence of pneumonia or a contagious infection process on chest radiography
  - Therapeutic modalities in patients with hepatic hydrothorax<sup>16, 25</sup>
  - Medical management-salt restricted diet, diuretics
  - Therapeutic thoracocentesis
  - Tran-jugular intrahepatic porto-systemic shunt
  - Surgical intervention -Tube thoracostomy- injection of a sclerosing agent
    - Surgical repair of diaphragmatic defects.
    - Peritoneovenous shunting
    - Liver transplantation
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The vast majority of cases patients with hepatic hydrothorax have end stage liver disease.

Management of hepatic hydrothorax is difficult, as diuretics and salt restriction fails to resolve the fluid completely. However, it usually runs a benign course as observed in our case.

**Conclusion:**

This case serves as a reminder that pleural effusion can also be the clinical manifestations of Wilson's disease. The clinician should suspect the diagnosis of hepatic hydrothorax in a patient who presents with right sided pleural effusion with cirrhosis and ascites in the absence of any convincing features of pulmonary and cardiac diseases. Still a search for other causes of transudative pleural effusion must be carried out as potentially reversible conditions may be found.

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