Acute Liver Failure for Liver Transplantation Due to Hepatolenticular Degeneration:a Case Report and Literature Review

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Case report

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Abstract

Background

Wilson disease (WD) is a genetic disease of abnormal copper metabolism, pediatric acute liver failure (PALF) is a life-threatening illness. Wilson's disease with acute liver failure has rapid progress, and high mortality, especially in children.

Case presentation

The patient was a 14-year-old girl who developed vomiting, jaundice within 7 days, leading to the initial suspicion of acute liver failure. Results of further investigation by geen and histological examination were consistent with a diagnosis of Wilson disease. She was treated with plasma exchange and DPMAS. After six days of treatment, coagulation routine and bilirubin improved, and she was gradually conscious. On the 8th day after admission, the condition was deteriorate, she was confusion, and had dyspnea, bleeding. The coagulation routine continued to deteriorate, bilirubin did not decrease significantly. Doppler ultrasound examination showed that the portal vein blood flow direction was away from the liver. Abdominal CT showed gastric varicose veins. She underwent liver transplantation. Thirty-three days later, she recovered. Patients with PALF should be transferred to a center with a transplant unit early. Once conservative treatment fails, LT should be performed.

Conclusion

A review of the literature shows that Wilson disease can occur at any age, including childhood. Wilson's disease with acute liver failure has rapid progress, and high mortality. Early diagnosis and treatment is the key to improving the prognosis.

Background

Pediatric acute liver failure (PALF) is a life-threatening illness. Hepatolenticular degeneration, also known as Wilson disease (WD) is a genetic disease of abnormal copper metabolism, with an incidence of about 1/30,000 and 1/100,000[1]. The manifestations of WD are diverse.. Wilson's disease with acute liver failure has rapid progress, and high mortality. For patients with irreversible PALF, liver transplantation (LT) is the ultimate lifesaving therapy. However, it's difficult to determine the optimal timing of transplantation. Here, we present a case of PALF due to WD. A child with acute liver failure admitted to our hospital was diagnosed as hepatolenticular degeneration and undergoing liver transplantation, we reported the case to improve clinicians' understanding of disease diagnosis.

Case Report

A 14-year female was admitted to the hospital with fever for seven days and jaundice for four days. Seven days before admission, the child developed fever, the maximum body temperature was 38°C,

accompanied by abdominal pain, diarrhea, take one tablet of compound paracetamol (each containing acetaminophen 250 mg, Amantadine hydrochloride 100 mg). Four days ago, she had abdominal distension, jaundice. The laboratory data were as follows: the 1st day of admission: activated partial thromboplastin time (APTT) 67.4 s, prothrombin time (PT) 36.5 s, INR 3.46, prothrombin activity (PTA) 20 %, fibrinogen (FBG) 1.30g/l; aspartate aminotransferase (AST) 161.5 U/L (normal range: 15-40U/L), alanine aminotransferase (ALT) 15.3 U/L (normal range: 9-50U/L), γ-glutamyltransferase (GGT) 135 U/L, total bilirubin (TBIL) 1013.5 umol/L (normal range: 0-26 μmol/L), direct bilirubin (DBIL) 645.5 umol/L (normal range: 0-6.8 μmol/L), indirect bilirubin (IDBIL) 368.0 umol/L (normal range: 5-20 μmol/L);white blood cell 25.05×10^9/L, neutrophil percentage 0.78, lymphocyte percentage 0.11, red blood cell 1.97×10^{12}/L, hemoglobin 74 g/ L, platelet 209×10^9/L;C-reactive protein（CRP） 12.64 mg/L; procalcitonin 9.15 ng/mL; Ascites routine: protein 5.48 g/L, white blood cells 114×10^6/L, red blood cells 100×10^6/L, mononuclear 0.61, troponin 1.29 ng/ml; BNP 2660 pg/ml. The 2nd day of admission: white blood cells 28.06×10^9/L, lymphocyte percentage 0.13, red blood cells 1.47×10^{12}/L, hemoglobin 59 g/L, platelets 163×10^9/L; AST 210.0 U/L, ALT 17.4 U/L, γ-GGT 118.1 U/L, TBIL 1302.8 umol/L, DBIL 779.2 umol/L, IDBIL 523.6 umol/L; APTT 66.8 s, PT 34.1 s, INR 3.34, PTA 20%, FBG 0.83g /l; NSE 88.80 ng/ml, ceruloplasmin 0.121 g/L (0.2-0.5); lactate dehydrogenase (ascites) 58 U/L; adenosine deaminase (ascites) 1.1 U/L; ferritin 5610.3 ug/L, complement C3 0.58 g/L, complement C4 0.06 g/L; urine bilirubin 3+, urine occult blood 3 +, urine protein 2 +, urine Copper 30.18 umol/24 h; blood ammonia 80 umol/L; hemolysis test, erythrocyte sedimentation rate, hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, blood lipids, amylase, lipase, thyroid function, EB,CMV antibody and nucleic acid quantification, respiratory pathogens, ANA series, autoantibody detection and blood culture were normal. Abdominal color Doppler ultrasound: the liver parenchyma had fine and enhanced echos, the portal vein blood flow direction was away from the liver, cholestasis in the gallbladder, fluid in the abdominal cavity, ascite. Lung CT: inflammation of the lungs, pleural effusion. Head MRI and CT findings were normal. Enhanced CT of Abdomen: large patches of liquid density shadows around the liver and spleen, abdominal cavity, pelvic cavity, and gastric varicose veins. Liver pathology: nodular liver cirrhosis, focal submass parenchymal necrosis, according to severe hepatitis, it is recommended to combine genetic testing to exclude liver metabolic diseases. Gene detection: Sanger sequencing of ATP7B gene identifified a homozygous nonsense mutation c.3955C>T (p.Arg1319Ter) in exon 13. When the child was admitted to the hospital, she was conscious, had vomiting, abdominal distension, and could communicate. We supplement prothrombin complex, vitamin K1, fibrinogen, plasma infusion to improve coagulation, reduced glutathione, hepatocyte growth-promoting hormone, and Simetech for treatment. On the 2nd day of admission, the patient became unconsciousness, irritability, with a Glasgow Coma Scale (GCS) score of 6. Hemoglobin decreased, liver function and coagulation routine continued to deteriorate. Acute liver failure and hepatic encephalopathy were present, so she was transferred to the pediatric intensive care unit for furture treatment, plasma exchange combined with dual plasma adsorption (DPMAS), blood purification were used. We evaluate the changes in the nervous system daily, calculate the liver injury unit score, and evaluate the timing of liver transplantation. Meanwhile, we find the cause of liver failure: the child had a history of fever, abdominal pain, and diarrhea, we should pay attention to enterovirus

infection; the child is an adolescent girl, she did not have joint pains, skin rash, light allergy, joint pain, hair loss. ANA series were normal; She had oral acetaminophen drugs within the normal drug dose. The parents denied the history of toxicosis, so impossibility of poisoning and immune factors; the child had acute liver failure and hemoglobin decrease, considered the existence of non-immune hemolytic anemia, ceruloplasmin 129 mg/l (200-500mg/l), lower than normal, 24 h urinary urinary: 30.18 umol (1886 ug) (normal<100 ug), should be alert Hepatolenticular degeneration, so we send the hepatolenticular gene for furture examination which Got from parents. After six days of treatment, coagulation routine and bilirubin improved, and she was gradually conscious. She can communicate with people normally, express emotions. On the 8th day of admission, she developed dyspnea, and had bloody ascites, bleeding around the drainage tube and deep venous catheterization, and oral mucosa was bleeding. The abdominal color Doppler ultrasound examination showed that the portal vein blood flow direction was away from the liver. Abdominal CT showed gastric varicose veins. The condition continued to deteriorate, she was confusion, and had dyspnea, bleeding. The coagulation routine continued to deteriorate, bilirubin did not decrease significantly. Liver transplantation was considered. Intraoperative liver pictures was shown in Figure 1. Postoperative liver pathology suggested nodular cirrhosis. The gene identified: ATP7B gene mutation is heterozygous mutation, according to the diagnosis of hepatolenticular degeneration. After the operation, she was given anti-infection, glucocorticoid, tacrolimus, mycophenolate mofetil anti-rejection therapy, anticoagulation, prevention of arterial thrombosis, respiratory support. After the operation, her condition improved, she was conscious and the ventilator was removed. The blood flow of the portal vein was normal, no venous thrombi, and no other systemic complications occurred, liver function gradually returned to normal, head MRI were normal. Thity-three days later, she recovered.

Discussion

Hepatolenticular degeneration is a rare autosomal recessive genetic disease. Its related gene ATP7B is located at 13q14.3[2], which encodes a P-type copper transport ATPase. Abnormal function of this enzyme can lead to disorders of copper metabolism in humans[3], excessive copper accumulates in the liver, brain, kidney, cornea, which lead to organ damage[4]. Studies had pointed out that serum ceruloplasmin <200 mg/L indicates WD, and <100 mg/L strongly indicates WD[5]. For clinically insufficient diagnostic evidence, early genetic monitoring is needed to further clarify. Liver biopsy and calculation of liver copper content are not widely used in clinical applications because it is an invasive inspection[6]. Some scholars pointed out that the Wilson index (Table 1) ≥ 4 points, strongly suggesting WD[7]. Combined with the child's Coombs-negative hemolysis, mild mental disorder, ceruloplasmin 129 mg/l, 24 h urine copper increased significantly, a total of 3 scores, possibility of hepatolenticular degeneration, genetic monitoring suggests that mutations in the ATP7B gene on chromosome 13 consistent with hepatolenticular degeneration.

Other scholars had pointed out that personality, mood, and mental state abnormalities can be one of the manifestations of WD. In children and adolescents, we are poor ability to recognize the performance of neurological or mental system abnormalities related to WD. Such manifestations are easily misdiagnosed

as mental disorders[8-10]. The most common psychiatric symptoms include mood swings, personality changes, depression, and cognitive impairment. In this article, the child had irritability, depression, unwilling to communicate with others, the above symptoms improved after liver transplantation.

Acute liver failure caused by hepatolenticular degeneration is a condition that progresses rapidly and is severely life-threatening. There is no specific treatment. Early diagnosis and treatment are the key. There were reports in the literature that it can be achieved through plasma exchange, double plasma adsorption, and blood purification. Plasma replacement is a commonly used method of liver support and has been recognized by WD as a Class I indication for WD American Association of Specialist Physicians (ASFA) in 2013[11]. If the above treatments still cannot reverse the progression of the disease, early liver transplantation is required[12-14]. Indications for liver transplantation (LT) surgery: it provides treatment options for WD patients with acute liver failure or drug resistance. In this article, the child's condition rapidly progressed to liver failure after admission, combined with laboratory tests indicated hepatolenticular degeneration, which is in line with the indications for liver transplantation. After admission, the child was treated with multiple blood purification methods and the condition improved transiently, but later deteriorated again, so the liver transplantation was underwent. LT in WD patients can save lives and cure potential metabolic defects.

Although liver transplantation must be regarded as the ultimate treatment option for these ALF patients, in many cases, temporary treatments such as plasma exchange, dual plasma adsorption and blood purification treatments may become a bridge for liver transplantation[2□15]. Therefore, for these patients with ALF for WD patients, the combined treatment of blood purification technology may play a vital role in saving lives. The experience of this case shows that plasma exchange combined with dual plasma adsorbents and blood purification treatment can improve clinical symptoms. It can remove toxins and drive copper while supplementing coagulation factors to improve coagulation function, and ensure that patients with WD can be treated in critical periods Bridging to late-stage living donor liver transplantation[11,16].

Conclusions

In summary, we report a case of acute liver failure for liver transplantation due to hepatolenticular degeneration.Wilson's disease with acute liver failure has rapid progress, and high mortality. Through this case, we hope to strengthen the study of acute liver failure and hepatolenticular degeneration, and improve clinicians' understanding of the disease. Early diagnosis and treatment to improve prognosis. This case has been approved by the ethics committee and the parents' informed consent.

Declarations

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Authors' contributions

JWL collected the patient data. HBY was a major contributor in writing the manuscript. YML read and approved the final manuscript. All authors read and approved the final manuscript.

Consent for publication

Written informed consent was obtained from the patient’s parents/legal

guardians for publication of this case report and any accompanying images. A copy of the written consent is available for the review by the Editor-in Chief of this journal. Contact author for the form.

Competing interests

Authors have no conflicts of interest to disclose.

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References

1. Ala A, Walker AP, Ashkan K, et al. Wilson’s disease. Lancet. 2007 369(9559):397-408. doi:10.1016/S0140-6736(07)60196-2.
2. Bandmann O, Weiss KH, Kaler SG. Wilson’s disease and other neurological copper disorders. Lancet Neurol. 2015;14(1):103-113. doi:10.1016/S1474-4422(14)70190-5.
3. Ferenci P. Diagnosis of wilson disease. Handb Clin Neurol. 2017;142:171. doi 10.1016/B978-0-444-63625-6.00014-8.
4. Schilsky ML. Wilson disease diagnosis, treatment and follow
5. Clin Liver Dis 2017; 21:755-67. doi:10.1016/j.cld. 2017.06.011.

6. Bandmann O，Weiss KH，Kaler SG. Wilson´s disease and other neurological copper disorders. Lancet Neurol. 2015;14(1):103-113. doi:10.1016/S1474-4422(14)70190-5.

6. Ofliver E A F. EASL Clinical Practice Guidelines: Wilson's disease. Journal of Hepatolog. 2012;56(3):671-685. doi:10.1016/j.jhep.2011.11.007.

7. Ferenci P, Caca K, Loudianos G, et al. Diagnosis and phenotypic classifification of Wilson disease. Liver Int. 2003;23:139-142. doi：10.1034/j.1600-0676.2003.00824.x.

8. Suzan E , Elsayed S M , Abdel G T Y , et al. Phenotypic and Genetic Characterization of a Cohort of Pediatric Wilson Disease Patients. Bmc Pediatrics. 2011;11(1):56-56.doi:10.1186/1471-2431-11-56.

9. Rukunuzzaman M. Wilson's disease in Bangladeshi children: analysis of 100 cases. Pediatr Gastroenterol Hepatol Nutr. 2015;18:121-7. doi：10.5223/pghn.2015.18.2.121.

10. Bayram AK, Gümüş H, Arslan D, et al. Neurological features and management of Wilson disease in children: an evaluation of 12 cases. Turk Pediatri Ars. 2016;51(1):15-21. doi:10.5152/TurkPediatriArs. 2016.3080.

11. Shaz BH: Guidelines on the use of therapeutic apheresis in clinical practice-evidence based approach from the writing committee of the American society for apheresis: the sixth special issue. J Clin Apher. 2013;28(13): 145-284. doi:10.1002/jca.21276.

12. Kido J, Matsumoto S, Momosaki K, et al. Plasma exchange and chelator therapy rescues acute liver failure in Wilson disease without liver transplantation. Hepatol Res. 2016. doi:10.1111/hepr.12711.

13. Motobayashi M, Fukuyama T, Nakayama Y, et al. Successful treatment of fulminant Wilson's disease without liver transplantation. Pediatr Int. 2014;56(3):429-432. doi:10.1111/ped.12291.

14. Rustom N, Bost M, Cour-Andlauer F, et al. Effect of molecular adsorbents recirculating system treatment in children with acute liver failure caused by Wilson disease.J Pediatr Gastroenterol Nutr. 2014, 58(2):160-164. doi:10.1097/MPG.0b013e3182a853a3.

15. Reynolds HV, Talekar CR, Bellapart J, et al. Copper removal strategies for Wilson's disease crisis in the ICU. Anaesth Intensive Care. 2014;42(2):253-257. doi:http://dx.doi.org/.

16. Schaefer B, Schmitt CP.The role of molecular adsorbent recirculating system dialysis for extracorporeal liver support in children. Pediatr Nephrol. 2013;28:1763-1769. doi:10.1007/s00467-012-2348-9.

Tables

Table 1 Scoring system developed at eighth international meeting on Wilson's disease, 2001

Typical symptoms, signs and other tests	Score
Kayser–Fleischer rings	
Present	2
Absent	0
Neurological symptoms (or typical abnormalities on brain MRI)	
Severe	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	
Present	1
Absent	0
Liver copper (in the absence of cholestasis)	
>5×ULN (>4 μmol/g)	2
0.8–4 μmol/g	1
Normal (<0.8 μmol/g)	-1
Rhodamine-positive granules on liver biopsy	1
Urinary copper (in the absence of acute hepatitis)	
Normal	0
1–2×ULN (0.8–1.6 μmol/24 h)	1
>2×ULN (>1.6 μmol/24 h)	2
>5×ULN after penicillamine (>4 μmol/24 h)	2
Mutation analysis	
On both chromosomes detected	4
On 1 chromosome detected	1
No mutations detected	0

Total score	Evaluation
4 or more	Diagnosis
	established
3	Diagnosis possible,
	more tests needed
2 or less	Diagnosis very unlikely
ULN Upper limit of normal	

Figures

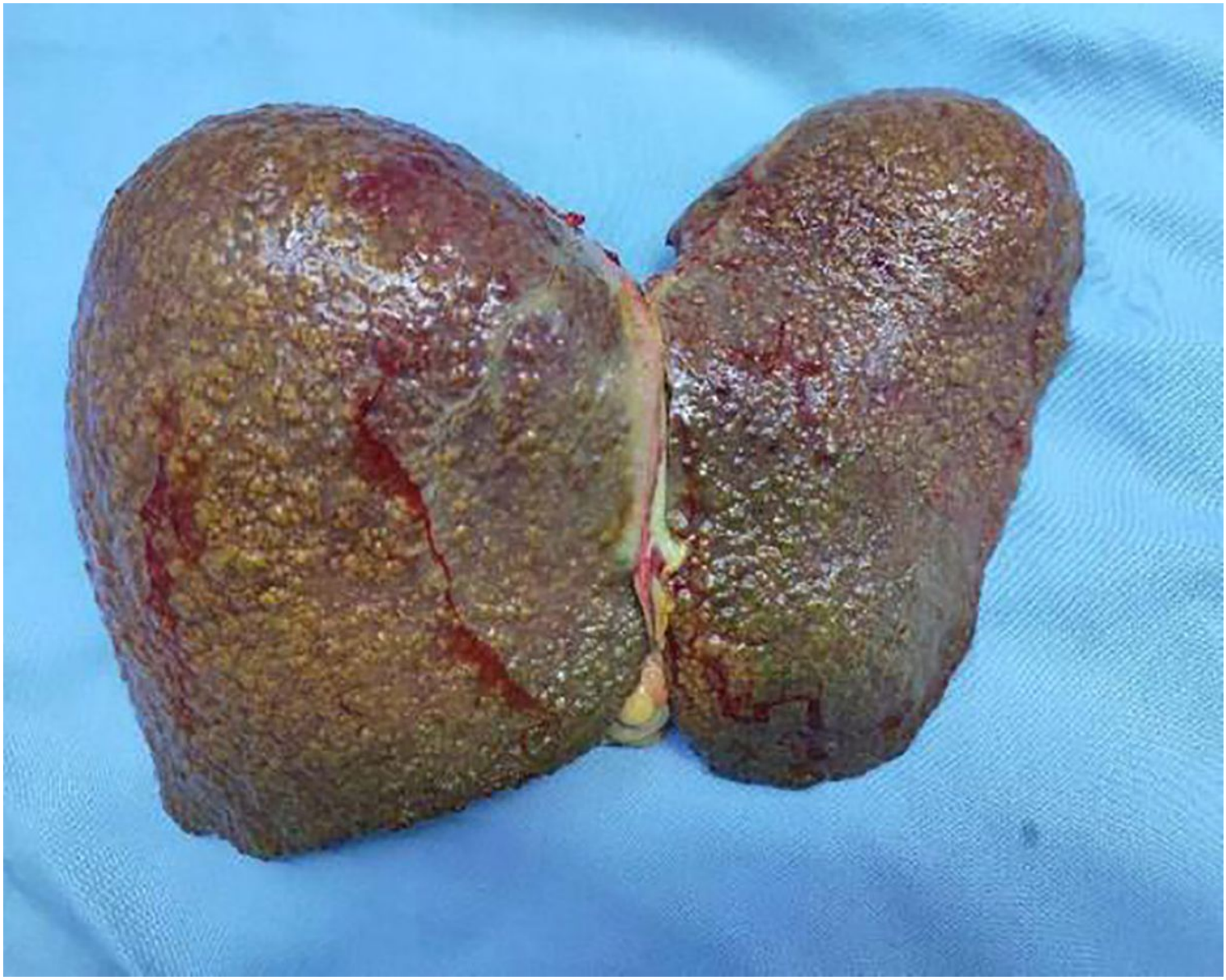

Figure 1

Intraoperative liver pictures

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