



Blood exchange transfusion in viral hepatitis in a small infant: a case report

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ABSTRACT

We report a case of blood exchange transfusion to treat acute liver failure following hepatitis B infection at the Infectious Disease Department of Children's Hospital No.2 in Ho Chi Minh City, Vietnam. A 3.5-month old baby boy was admitted to the hospital with a presentation of progressively worsening jaundice for the past one month. The patient was diagnosed with hepatitis B infection with a positive HBV DNA quantitative assay. Plasma exchange was indicated in view of progressive liver failure and gradually increasing hepatic coma. However, it was impossible to perform plasmapheresis in this case because the patient was small (in terms of age and weight) and there was no suitable plasma exchange filter. Accordingly, the patient was treated with 3 times of blood exchange transfusion in combination with an antiviral drug, lamivudine. After each blood exchange transfusion, the biochemical values (bilirubin, liver enzymes, and coagulation profile) gradually improved and he was discharged after 1 month of treatment. Blood exchange transfusion is an effective procedure for managing acute liver failure, where plasma exchange is not possible while waiting for the recovery of liver functions or liver transplantation.

1. Introduction

Acute liver failure (ALF) or fulminant liver failure (FLF) is a potentially reversible clinical syndrome characterized by severe hepatocellular dysfunction with the onset of coagulopathy (international normalized ratio (INR) ≥ 1.5) and encephalopathy (any degree of altered mental status) that occurs within eight weeks of the first symptom in the absence of preexisting liver disease or cirrhosis [1,2].

Management of ALF includes treatment of the underlying etiologies, intensive supportive care, management of complications, and orthotopic liver transplantation (OLT), in which OLT is the standard therapy for patients with irreversible liver damage [3,4]. However, the availability of OLT is limited hence, alternative bridging therapy should be used to gain time until a suitable organ donor is found. Recent research shows that it is important to eliminate inflammatory mediators by the plasma replacement technique [5]. However, it requires an appropriate

plasma replacement device and a specialized highly trained medical personnel. Exchange blood transfusion which has the same mechanism as plasma exchange can be considered as an alternative. In this case, we would like to introduce a case in which blood exchange transfusion was used to treat acute liver failure caused by hepatitis B virus in a patient who was unable to receive a plasma exchange.

2. Case report

A 3.5 months old male baby with no previous history of liver disease was admitted to the Infectious Disease Department of Children's Hospital No.2 in Ho Chi Minh City, Vietnam after one month of a progressively worsening jaundice (This case report was generated after the patient was discharged from the hospital, so we could not get an informed consent). At the time of admission, his vital signs were stable, and there were no other signs of chronic liver disease and no distention

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Table 1
Clinical and laboratory characteristics of the patient during treatment.

Date of admission	D1	D7	D9 (1 st transfusion)		D12 (2 nd transfusion)		D14 (3 rd transfusion)		D20	D41
			Before	After	Before	After	Before	After		
Total bilirubin (μmol/L)	253.6	577.0	660.0	286.0	362.0	168.0	175.0	93.0	214.0	129.3
Direct bilirubin (μmol/L)	151.0	334.0	407.0	98.5	182.0	82.0	69.6	35.6	132.0	96.2
AST (IU/L)	2982	139	138	107	104	60	112	45	119	210
ALT (IU/L)	1366	177	119	43	53	22	30	16	54	148
Ammonia, NH ₃ (μmol/L)	115	91			139		103		51	
PT (s)	39.6	85.6	70.4	22.7	40.4	29.7	35.6	22.7	23.1	18.1
aPTT (s)	45.0	82.5	73.1	38.8	127.1	52.5	44.8	42.4	42.1	36.8
Fibrinogen (g/L)	0.87	0.40	0.40	1.84	1.27	1.59	1.33	1.76	1.47	1.78
INR	3.16	7.16	5.82	1.76	3.23	2.33	2.83	1.76	1.78	1.39
Platelets (× 10 ³ /ml)	100.0		147.0	78.0	74.3	30.7	65.0	47.7	102.0	103.0
Coma level	I	II	III	III	II	I	I	I	alert	alert

of the jugular vein. His cardiopulmonary examination was normal. On the abdominal examination, his liver was palpable 2 cm below the right costal margin, soft in consistency and tender. There was no ascites noted.

Laboratory tests showed (Table 1) severe hepatocellular necrosis with elevated alanine aminotransferase (ALT) 1366 IU/L, aspartate transaminase (AST) 2982 IU/L and ammonia levels (115 μmol/L). Furthermore, cholestasis observed with increased levels of total (253.6 μmol/L), direct bilirubin (151 μmol/L), alkaline phosphatase (1067 U/L), and gamma-glutamyltransferase (191 U/L). Moreover, coagulopathy was present with prothrombin time (PT) of 39.6 s and international normalized ratio (INR) of 3.16. On the other hand, his serum electrolytes and renal function were normal. An abdominal ultrasound was performed and the result was unremarkable. Serological testing for hepatitis A and C, Epstein-Barr virus, TORCH infections, dengue virus, *Chlamydia*, *Mycoplasma pneumonia* were all negative. However, his HBsAg was positive and the quantitative assay for HBV DNA was 4600 UI/mL (3.66 log₁₀). There was no documented poisoning, metabolic disorders, or excessive use of acetaminophen. The patient was diagnosed with acute hepatic failure caused by acute hepatitis B and was treated with vitamin K, lactulose, and fluid restriction with the correction of glycemia. Moreover, specific treatment of acute hepatitis B infection was introduced with lamivudine 8 mg/kg/day.

During hospitalization, the patient's liver functions continuously deteriorated with progressive hyperbilirubinemia, hyperammonemia, and progressive coagulation disorders (Table 1). On the 8th day of hospitalization, the patient demonstrated signs of grade 2-3 hepatic encephalopathy with drowsiness and decreased awareness. In view of gradually worsened hepatic coma (grade II-III) with the standard treatment, a plasma exchange was indicated. However, the plasma exchange filter in the hospital only available in two different sizes, Primaflx TPE 1000 and TPE 2000 sets (Baxter, USA). Accordingly, bearing in mind that the patient is small, it was not possible to perform a plasma exchange (even with the TPE 1000 available which required priming techniques that were not available at the time, appropriate for a minimal patient weight of 9 kg (https://www.baxter.fi/sites/g/files/ebyasai1556/files/2019-05/NOMG12016-0003_TPE-1000-2000.pdf), so a blood exchange transfusion procedure was performed instead. Double volume exchange transfusion was done three times for this patient as follows: blood transfusion was performed through the right femoral vein using a central catheter (Certofix® Duo Paed). The exchange included 450 mL of a donor's frozen plasma (AB⁺) and 500 mL of packed red blood cells (O⁺) for each time. The procedure was performed within 3 hours, and each cycle (supplied and removed blood volume = 15-20 ml) lasted for 5 - 7 minutes.

After each blood exchange transfusion, the mental status of the patient and the biochemical values (bilirubin, liver enzymes, and coagulation profile) progressively returned to normal (Table 1). Although his ammonia level gradually improved (91,139,103 μmol/L), it did not

return to normal within the third week when the liver functions started to recover (51 μmol/L) (Table 1). Furthermore, PT showed significant improvement after each blood transfusion returning to its lower-most value in D41 (Table 1). Complications of blood transfusion such as hyperglycemia, electrolyte disorders, cardiac arrhythmia, and hypothermia were not observed in this patient. Thrombocytopenia was noted after each blood exchange transfusion because only red blood cells and fresh plasma were transfused (Table 1). However, there were no clinical manifestations of bleeding. The patient's liver functions gradually improved and were normal at discharge with HBV DNA concentration at 286 UI/ml (2.46 log₁₀) and no noticed disability. After being discharge from hospital, the patient continued to receive lamivudine treatment and was followed-up every month.

3. Discussion

For fulminant liver failure with low self-recovery ability, the standard treatment is supportive care for the liver. Plasma exchange is mainly used as a temporary solution for liver transplantation [5] but is not always available. Blood exchange transfusion, which has a similar mechanism to that of plasma exchange, has been practiced in the treatment of acute liver failure for years and a lot of cases have shown favorable outcomes. A study reported the first case of recovery from a hepatic coma after two exchange blood transfusions in a boy aged 13 years old [6] and another recovery from acute hepatic failure after exchange transfusion in a 25-year-old patient was reported [7].

In low-birth-weight infants (< 6 kg), the plasma replacement filter is not suitable, and the procedure must be performed in the intensive care unit environment because of the potential serious side effects. An alternative, which is not less effective but perhaps safer, is total blood transfusion. Blood exchange transfusion is used for the treatment of some diseases, mainly jaundice due to blood group incompatibility in the newborn, sickle cell anemia, and some metabolic disorders. The risk is the same as any blood transfusion procedure, with some occurring more frequently in infants, such as heart failure, hypothermia, hypocalcemia, hyperkalemia, and hypoglycemia [8]. The mechanism of exchange blood transfusion is similar to that of plasma exchange, which includes the removal of bilirubin, bile salts, endotoxins, and cytokines, and the addition of coagulation factors and antibodies. It is important to note that blood transfusion is less effective at reducing blood ammonia (as can be seen in this case), while continuous dialysis can remove this substance quickly within hours [9,10].

There is currently no data on the prognosis of blood exchange transfusion in acute liver failure. Transfusion has been reported in some cases and clinical reports of acute hepatic failure that have been widely accepted. In the absence of means to perform liver transplantation procedure, we recommend performing blood exchange transfusion in acute liver failure until self-recovery of the liver functions or liver transplantation is available.

4. Conclusion

Blood exchange transfusion procedure may be useful in patients with fulminant hepatitis in cases where plasma exchange is not possible. This is a supportive management procedure while waiting for the recovery of liver function or liver transplantation.

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Ethical approval

Informed consent could not be obtained as data collection was retrospective and the patient was discharged at the time of designing the case report. The study was reported at the approval of the Institutional Review Board (IRB).

Disclosure of prior publications or submissions

There are no prior publications or submissions with any overlapping information, including studies and patients.

CRediT authorship contribution statement

Thai Son Pham: Conceptualization, Methodology, Visualization, Investigation. **Abdullah Reda:** Data curation, Writing - original draft. **Thi Thu Ngan Nguyen:** Visualization, Investigation. **Sze Jia Ng:** Validation, Writing - review & editing. **Vuong Thanh Huan:** Validation, Writing - review & editing. **Do Chau Viet:** Supervision, Validation, Writing - review & editing. **Nguyen Tien Huy:** Supervision, Validation, Writing - review & editing.

Declaration of Competing Interest

None.

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