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CASE REPORT

# Cortical Visual Impairment as a Manifestation of Hepatic Encephalopathy in a Young Child: A Case Report

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**Abstract:** Cortical visual impairment (CVI) is an extremely rare manifestation of hepatic encephalopathy (HE), which refers to neuropsychiatric abnormalities as a result of impaired detoxification function of liver. A 16-month-old female Syrian refugee who developed jaundice 4 weeks before referral to our hospital was diagnosed with hepatitis A based on her clinical presentation at a local facility. Overtime, her jaundice worsened, her lower limbs became edematous, and the family noticed sleep disturbances and irritability. On admission to a local hospital, she was deeply jaundiced and irritable, but showed no stigmata of chronic liver dysfunction. During hospitalization, the patient lost the ability to track objects and eventually her sight. However, the results of fundoscopic and neurological examinations were normal, except for a fine tremor. Her laboratory workup showed elevated liver enzymes and ammonia, and a prolongation of prothrombin time. Brain imaging revealed an abnormal signal intensity which is suggestive of metabolic etiology. The patient was diagnosed with CVI secondary to HE and transferred to the pediatric intensive care unit. After a few days of HE management, ammonia levels dropped and vision recovered. In conclusion, CVI may indicate HE in children.

**Keywords:** Cytomegalovirus hepatitis, Cortical visual impairment, Hepatic encephalopathy, Liver biopsy

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## 1. Introduction

Hepatic encephalopathy (HE) refers to neuropsychiatric abnormalities that manifest when the detoxification function of liver is impaired. HE is associated with acute liver failure and affects prognosis and transplant qualifications[1]. Adult HE manifestations are less ambiguous compared to children, especially in non-verbal young children. The diagnosis of HE is established through recognizing specific signs and symptoms that may include sleep and speech disturbances, personality changes, intellectual deterioration, impaired consciousness, and flapping tremor[2]. The pathophysiology of HE is not fully understood. However, an accumulation of neurotoxic materials has been found to be a major contributor. Most of the time, HE manifestations are reversible[3].

In fulminant hepatitis, subclinical visual impairment is well-documented using evoked responses (visual evoked response). Overt visual impairment (cortical blindness) is an extremely rare manifestation of HE[4]. Multiple reports describe cortical blindness in hepatic encephalopathic adult patients[5]. Here, we present the case of a 16-month-old with acute liver failure and encephalopathy who developed reversible cortical visual impairment (CVI).

## 2. Case presentation

A 16-month-old female Syrian refugee was brought to a local hospital with yellowish discoloration of her eyes and skin, abdominal pain, and vomiting. At first, the symptoms were thought to be secondary to hepatitis A infection and would resolve spontaneously without intervention. Two weeks after the onset of symptoms, she was admitted to the local hospital and her laboratory results are as follows: Alanine transaminase 1141 U/L, aspartate transaminase 560 U/L, international normalized ratio (INR) 5, total bilirubin 13 mg/dl, and direct bilirubin 11 mg/dl. During hospitalization, she became progressively irritable and had sleep disturbance. Two days before transfer to our facility, the family noticed that her vision was affected as she could not track objects. The medical history was unremarkable, and she had no family history of similar conditions. Her development was age appropriate. She got three doses of hepatitis B vaccine in accordance with the Jordanian national program.

On admission, she was alert, irritable, and jaundiced. She was not dysmorphic, and her vital signs were stable. Growth parameters were in the 25$^{th}$ centile for weight, height, and head circumference. The abdomen was soft and lax with no distention or organomegaly. There were no stigmata of chronic liver dysfunction.

During neurological examination, we observed no facial asymmetry when she was smiling or closing her eyes. Her gag reflex was intact, the tongue was midline, and she was able to turn her head in both horizontal and vertical directions. She was able to sit alone and bear weight. Deep tendon reflexes were +2/5 with no clonus present. She was able to hold and localize objects that touched her hand. A fine tremor was noted. Her temperature sensation was intact. She had a negative Babinski reflex. Ophthalmological examination revealed equal and reactive pupils. Extraocular movements were intact, but there was no visual tracking. No vertical or rotatory nystagmus was present. The results of fundoscopic examination and other tests were normal.

On admission, the liver enzymes and serum ammonia were elevated, while the prothrombin time (PT) INR was prolonged (**Table 1**). The result of abdominal ultrasound with Doppler flow was normal. Magnetic resonance imaging (MRI) of her brain showed abnormal signal intensity in the deep and periventricular white matter of both frontal and parieto-occipital regions; this finding is consistent with metabolic etiology of her condition. The patient was diagnosed with CVI secondary to HE and transferred to the pediatric intensive care unit (PICU) for further management. She was started on lactulose, oral antibiotics, and Vitamin K. Over the 3 days in PICU, the patient's irritability and sleeping pattern improved. She was transferred back to regular care unit.

The hepatic dysfunction workup confirmed that the hepatitis was secondary to cytomegalovirus (CMV) infection; CMV was detected by polymerase chain reaction (PCR) and CMV IgM test was positive. When coagulopathy and cholestasis persisted, the patient was started on Ganciclovir® and ursodeoxycholic acid. During treatment, her eyesight returned to normal and levels of liver enzymes improved. During follow-up, the liver enzymes were again elevated, leading to the decision to do a liver biopsy. The liver biopsy revealed a chronic hepatitis pattern of injury with marked expansion of the portal areas by mixed inflammatory cells. Most portal tracts exhibited fibrotic expansion (**Figure 1a and b**). CMV stain was negative. Unfortunately, the patient was lost to follow-up and the results were not communicated with the family.

## 3. Discussion

In young children, HE manifestations might be subtle and difficult to diagnose, especially in non-verbalizing toddlers[1-3]. Cortical blindness is a rare manifestation of HE[5]. To the best of our knowledge, our patient is the youngest patient with acute liver failure and HE to develop reversible cortical blindness.

HE pathogenesis is not well understood. Various theories have been proposed to explain HE. The toxin-induced theory is the most widely accepted[1]. Various neurotoxins have been implicated in the development HE. Ammonia has been suggested as the main contributor to low-grade brain edema and neurotoxicity[1,2]. The main goals of treatment are to decrease the accumulated neurotoxins (i.e. ammonia) using lactulose as a cathartic and stool acidifier, and to reduce the fermentation using antibiotics[1,2]. In our case, ammonia was elevated. With treatment, the ammonia levels dropped and the symptoms improved as the levels normalized.

CVI is defined as visual impairment that is based within the brain. CVI replaced the label of cortical blindness as most of the patients retain some visual function. The majority of pediatric patients with CVI are neonates who survived hypoxic-ischemic injuries. Meningoencephalitis, brain tumors, and rarely metabolic insults can cause CVI[6]. In our patient, the ophthalmological examination was unremarkable except for the lack of visual tracking. Interestingly, although the patient had been declared blind, she had photophobia which was associated with CVI[7]. Almost half of all patients with CVI showed some improvement in their vision after diagnosis regardless of the cause[8]. Out of the few reports of CVI with HE, almost

**Table 1.** Results of patient's workup

| | On admission | On discharge | Last follow-up |
|---|---|---|---|
| White blood cells ($10^3$/mm$^3$) | 25.6 | 7.1 | 7.3 |
| Hemoglobin (g/dL) | 10.7 | 10.7 | 10.6 |
| Platelets ($10^3$/mm$^3$) | 344.0 | 174 | 186 |
| Prothrombin time (s) | 31.3 | 25.6 | 19.6 |
| International normalized ratio | 2.36 | 1.93 | 1.50 |
| Partial thromboplastin time (s) | 41.4 | 45.5 | 40.6 |
| Ammonia (µmol/L) | 74.0 | 56.0 | |
| Sodium (mmol/L) | 135.0 | 140.0 | |
| Potassium (mmol/L) | 4.21 | 4.53 | |
| Urea (mmol/L) | 3.0 | 0.9 | |
| Creatinine (µmol/L) | 31.0 | 23.0 | |
| Total protein (g/L) | 65.7 | 55.3 | 65.3 |
| Gamma-glutamyl transferase (U/L) | 73.0 | 25.0 | 50.0 |
| Albumin (g/L) | 41.8 | 32 | 37.9 |
| Alanine transaminase (U/L) | 301.4 | 65.1 | 280.0 |
| Aspartate transaminase (U/L) | 476.2 | 155.6 | 552.0 |
| Total bilirubin (µmol/L) | 288.3 | 105.0 | 23.0 |
| Direct bilirubin (µmol/L) | 243.2 | 89.2 | 18.8 |
| Alkaline phosphatase (U/L) | 373.0 | 410.0 | 441.0 |
| Ferritin (ng/mL) | 91.0 | | |
| Triglycerides (mmol/L) | 1.56 | | 1.50 |
| High-density lipoprotein (mmol/L) | 0.54 | | 0.89 |
| Low-density lipoprotein (mmol/L) | 2.37 | | 2.27 |
| Cholesterol (mmol/L) | 3.23 | | 3.46 |
| Hepatitis A virus antibody, total (IU/L) | 50.0 | | |
| Hepatitis B surface antigen | Non-reactive | | |
| AUSAB (mIU/mL) | 229.8 | | |
| Bean common mosaic virus detection by qualitative PCR | Positive | | Positive |
| CMV IgM (IU/mL) | 44.0 | | |
| CMV IgG (IU/mL) | 28.0 | | |
| HSV-1 and -2 IgM | Negative | | |
| HSV-1 and -2 detection by PCR | Negative | | |
| Epstein–Barr virus detection by PCR | Negative | | |
| Hepatitis C virus antibody | Non-reactive | | |
| Amino acid chromatography of blood and urine | Non-diagnostic, suggestive of liver disease | | |
| Organic acids | Normal | | |
| Reducing substance in urine | Negative | | |
| Succinylacetone in urine | Negative | | |
| Serum copper (µmol/L) | 9.6 | | |
| Lactate (mmol/L) | 2.6 | | |
| Ceruloplasmin (µmol/L) a | 1.08 | 2.16 | |
| Uric acid (µmol/L) | 108.0 | | |
| Antineutrophil cytoplasmic antibodies | Negative | | |
| Antinuclear antibody | Negative | | |

*(Contd...)*

**Table 1.** *(Continued)*

| | On admission | On discharge | Last follow-up |
|---|---|---|---|
| Anti-smooth muscle antibodies | Negative | | |
| Anti-tTG IgA | Negative | | |
| Total IgG (mg/l) | 10,600.0 | | |

PCR, Polymerase chain reaction; CMV, Cytomegalovirus; HSV, Herpes simplex virus; Anti-tTG, Antibodies to tissue transglutaminase, [a]normal range: 1.13–2.25 µmol/L

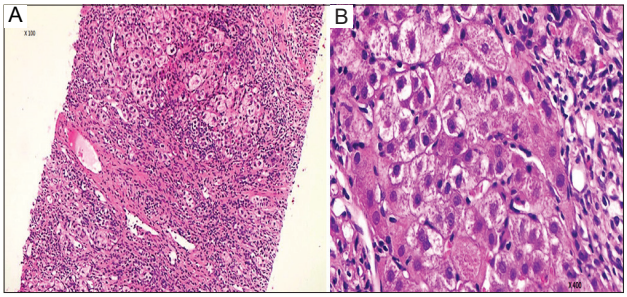


**Figure 1.** (A) Histopathological examination showed chronic hepatitis pattern of injury with marked expansion of portal areas by mixed inflammatory cell infiltration with interface hepatitis (H&E staining, ×100). (B) The lobular areas show feathery degeneration of hepatocytes, significant spotty necrosis, and moderate degree of cholestasis (H&E staining, ×400).

70% completely recovered[5]. Our patient regained her sight, which may reflect the nature of the underlying cause for her vision loss.

In a few reported cases of CVI, brain MRI was used to rule out brain lesions. The most prominent findings were occipitoparietal lesions[9,10]. Our patient showed abnormal signal intensity in the deep and periventricular white matter of both frontal and parieto-occipital regions, suggesting the metabolic etiology of her condition. However, an extensive metabolic workup was negative.

CMV infection is one of the main causes of infantile hepatitis and cholestasis. Serological testing and PCR frequently confirm the diagnosis without the need for a liver biopsy. Most of the patients recover without treatment[11]. Although there are no clear guidelines for antiviral treatment in immunocompetent children, the use of Ganciclovir can be considered in patients with coagulopathy, severe cholestasis, or markedly elevated transaminases[11]. Our patient presented with marked coagulopathy and deep jaundice; therefore, we decided to start Ganciclovir. Min *et al*. reported continuous normalization of liver enzymes for up to 1 year of follow-up[11]. We lost our patient to follow-up 3 months after discharge. This was unfortunate since the enzymes, although improved, did not normalize. Furthermore, the liver biopsy revealed changes consistent with a diagnosis of chronic hepatitis. Despite the short duration of follow-up, we anticipate complete recovery based on previous reports[11,12]. Although other pathologies could have caused the patient's liver injury, the lack of further follow-up visits limited our capacity to explore further possible causes.

## 4. Conclusion

HE manifests as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction. Cortical blindness and visual impairment might indicate HE in children. Improvement of the encephalopathy is associated with complete resolution and regaining of vision.

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## Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

## Author contributions

E.A. and D.S. conceived and drafted the manuscript. M.B. and M.S.A. revised the histopathology topic of the manuscript. All authors reviewed and approved the final manuscript.

## Availability of data and materials

Data won't be deposited at data repository due to the institutional regulations. Data will be available on contacting the corresponding author.

## Ethics approval and consent to participate

This study was reviewed and approved by the Institutional Review Board of Jordan University of Science and Technology and King Abdullah University Hospital, Jordan (7/141/2021), that also waived the need for written informed consent for the publication of this case report.

## Consent for publication

The parents of patient gave their verbal consent for publication of this report and all accompanying images; written informed consent has not been obtained. Highest level of effort has been made to ensure the anonymity of the patient, and none of the images published in this report contain any patient's identifiers.

## References

1. Dara N, Sayyari AA, Imanzadeh F, 2014, Hepatic Encephalopathy: Early Diagnosis in Pediatric Patients with

Cirrhosis. *Iran J Child Neurol*, 8:1–11.

2. Arya R, Gulati S, Deopujari S. 2010, Management of Hepatic Encephalopathy in Children. *Postgrad Med J*, 86:34–40. DOI: 10.1136/pgmj.2009.079467.
3. Toney NA, Bell MJ, Belle SH, *et al*., 2019, Hepatic Encephalopathy in Children with Acute Liver Failure: Utility of Serum Neuromarkers. *J Pediatr Gastroenterol Nutr*, 69:108–15. DOI: 10.1097/mpg.0000000000002351.
4. Sawhney IM, Verma PK, Dhiman RK, *et al*., 1997, Visual and Auditory Evoked Responses in Acute Severe Hepatitis. *J Gastroenterol Hepatol*, 12:554–9. DOI: 10.1111/j.1440-1746.1997.tb00484.x.
5. Cheng-Tagome S, Yamamoto A, Suzuki K, *et al*., 2016. Cortical Blindness Induced by Hepatic Encephalopathy: Case Report and Review of Published Case Reports. *Acute Med Surg*, 4:109–13. DOI: 10.1002/ams2.225.
6. Edmond JC, Foroozan R, 2006, Cortical Visual Impairment in Children. *Curr Opin Ophthalmol*, 17:509–12.
7. Good WV, Jan JE, DeSa L, *et al*., 1994, Cortical Visual Impairment in Children. *Surv Ophthalmol*, 38:351–64.
8. Matsuba CA, Jan JE, 2006, Long-Term Outcome of Children with Cortical Visual Impairment. *Dev Med Child Neurol*, 48:508–12. DOI: 10.1017/s0012162206001071.
9. van Pesch V, Hernalsteen D, van Rijckevorsel K, *et al*., 2006, Clinical, Electrophysiological and Brain Imaging Features during Recurrent Ictal Cortical Blindness Associated with Chronic Liver Failure. *Acta Neurol Belg*, 106:215–8.
10. Arikan C, Tekgul H, Eğilmez S, *et al*., 2003, Stage IV Hepatic Encephalopathy Associated with Acute Blindness after Liver Transplantation. *Pediatr Transplant*, 7:497–500. DOI: 10.1046/j.1397-3142.2003.00118.x.
11. Min CY, Song JY, Jeong SJ, 2017, Characteristics and Prognosis of Hepatic Cytomegalovirus Infection in Children: 10 Years of Experience at a University Hospital in Korea. *Korean J Pediatr*, 60:261–5. DOI: 10.3345/kjp.2017.60.8.261.
12. Manoj MG, Venketeswaran AR, Revathy MS, *et al*., 2014, A Case of Chronic Cytomegalovirus Hepatitis in Immune-Competent. *J Clin Exp Hepatol*, 4:S12.