



CASE REPORT

Hepatitis and Meningoencephalitis due to Enterovirus in a Toddler

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ABSTRACT

Background: Enteroviruses are known for causing wide spectrum of diseases including myocarditis, myopericarditis, myelitis, encephalitis, meningitis, meningoencephalitis, hepatitis and sepsis. The presentation of enteroviral meningoencephalitis predominated with the clinical picture of hepatitis has rarely been recorded in populations other than neonates.

Case Presentation: A male 2-year-old, presenting with a fever of 38 to 40 °C with chills and rigors, lethargy and drowsiness for 6 days. Along with the nausea, vomiting and watery diarrhea, he developed mouth ulcers (peri-oral vesicles) during the stay at the hospital. After extensive workup he was later diagnosed with meningoencephalitis and acute hepatitis due to Coxsackie virus A. After a stay of more than a month he was successfully treated and discharged.

Conclusion: A more thorough evaluation should be carried out for atypical viral infections presenting with clinical presentation of hepatitis and meningoencephalitis.

INTRODUCTION

Enteroviruses are known for causing wide spectrum of diseases including myocarditis, myopericarditis, myelitis, encephalitis, meningitis, meningoencephalitis, hepatitis and sepsis. Enteroviral, are among the most emerging causes of encephalitis in the pediatric population. Acute hepatitis caused by viral organisms which are typically implicated in the cases of encephalitis are rarely reported in literature. The presentation of enteroviral meningoencephalitis predominated with the clinical picture of hepatitis has rarely been recorded in populations other than neonates. (1-3)

CASE REPORT

A tired and lethargic looking 2-year-old boy, presenting with fever of 40 °C with rigors and chills associated with lethargy and sleepiness for 6 days prior to admission. Along with the nausea, non-bilious vomiting and watery diarrhea, he developed mouth ulcers (peri-oral vesicles) during the stay at the hospital. The parents mentioned a contact with birds 6 weeks

prior and drinking raw milk 2 weeks before the development of symptoms. He had Posterior Urethral value at time of birth which caused Nephrogenic Diabetes Insipidus [1], it was then surgically corrected. He had no contact with a sick person, history of travel, bleeding tendencies, any form of adenopathy and/or change in the color of stools or urine. He was born full term by Lower Segment Caesarean section due to an abnormal lie. Birth weight was close to 3 kg and his immunization status was up-to-date. There was no significant pre, peri or postnatal complications in the child and the mother.

He was Alert and oriented on admission. On the 10th day, he experienced drowsiness and altered mental status for 2 weeks. He regained his consciousness one week later. No meningeal signs on admission, but he showed signs Irritability, drowsiness and neck rigidity 8 days later. Power, tone and reflexes were normal during this course. Pupils were regular, round and reactive. He had a chalazion over left eyelid and ptosis during the course of the illness. An ophthalmologist was consulted and treatment was started. His weight and height are at the 50th and 70th percentile respectively. Head circumference is at 47cm (50th percentile). Overall, the child has a normal develop-

Table 1. Complete Blood Count (CBC) Report; Day 1

CBC	Hemoglobin	WBC	Neutrophils	Lymphocytes	MCV	Platelets
	10.9	3.6	50%	42%	81.1	195

Table 2. Liver Function Test report; Day 1

	ALT	AST	ALP	GGT	Total Bilirubin	Direct Bilirubin
Day 1	922	2020	85	27	11.9	2.0
Day 2	946	2190	78	29	13	2.0
Day 4	635	1197	72	52	10	2.1

ment. There was Mild throat congestion and erythema with 2-3 small ulcers on the hard palate, on the cheeks, both of which healed within 3 days. Tympanic membrane looks normal. No cervical lymphadenopathy, thyromegaly. Chest wall was normal. Lungs were normal to percussion and auscultation. S1 and S2 normal. No murmurs, rubs, gallops, or extra sounds. Central and peripheral pulses normal. No JVD. Blood pressure equal in both arms. Abdomen Soft, distended abdomen. Bowel sounds normal; no bruits. Hepatomegaly: 4 cm on admission increased to 6 cm 8 days later and then decreased to 2 cm on after 10 days. Spleen was palpable on admission, increased to 2-3cm and later in course it was not palpable.

Complete blood counts (CBC) (Table 1) and coagulation profiles (Table 3) during the course were reported as normal. A myriad of tests such as blood cultures, urine cultures, ESR, hepatitis virology, Brucella ELISA, bacterial latex agglutination tests, autoimmune tests, chest x-ray and CT brain workup were unremarkable (Figures 1).

Liver function test (Table 2) including Alanine transaminase (ALT), Aspartate transaminase (AST), Total Direct bilirubin, alkaline phosphatase (ALP) and Gamma-glutamyl transferase (GGT) are given below in a table form. Total protein, Albumin levels, C reactive protein (CRP), Glucose and urea electrolytes (U/E) values are given below (Table 4)CSF (Table 5); White blood cells (WBC) and Proteins were increased.

Blood and Urine cultures: Negative

Widal test: Negative

PPD result: Negative

Blood Virology: HAV IgM: Negative, HBsAg: Negative, Anti HCV: Negative, CMV IgM: Negative, serum PCR: Negative (Including Enterovirus, Herpes Simplex Virus).

Brucella agglutination test: Negative

Brucella ELISA Test: IgG, IgA, IgM all Negative.

Serum Ig Levels: Normal

ANA: Negative

CK: 930

Ammonia level: 21.1

Serum Paracetamol Level: 111 (normal 66-198)

Latex Agglutination Test: negative

CSF Bacterial culture and gram stain were negative

Abdomen Ultrasound showed some mild hepatomegaly.

Chest X-Ray was normal throughout the case duration.

CSF-PCR finally showed positive results for coxsackie

A. Serum PCR for all the enteroviruses and HSV did not bear any results.

Table 3. Coagulation profile; Day 1

Coagulation Profile	PT	INR	PTT
Day 1	12.5	1.12	47.7
Day 3	13.9	1.29	52

Table 4. Blood report, Urine Analysis; Day 1

Total	52
Protein	28
Albumin	61.4
CRP	4.2
Glucose	Normal
U/E	

Table 5. (Day 1)

CSF	Colour	RBC	WBC	Glucose	Protein
	Clear	<5	10	3.6 (2.2-3.9)	379.26

Table 6 . Complete blood count; Day 15

CBC	Hemoglobin	WBC	Lymphocytes	MCV	Platelets
Day 15	8.7	11	53.7%	79.3	327

Repeated labs

CRP: 32 (<10)

ESR: 20 (0-22)

LFT	ALT	AST	LDH
Day 15	112	44	652

DIFFERENTIAL DIAGNOSIS

- Other viral hepatitis, EBV, CMV
- CNS infection: Encephalitis and/or Meningitis
- Underlying malignancy
- Infectious: Brucellosis, Tuberculosis.

TREATMENT

Symptomatic management for the fever with paracetamol combined with ibuprofen was initiated. Due to the unusu-

al presentation and lab work, the patient was started on IV cefotaxime (100 mg/kg/dose 6 hourly) and IV acyclovir (10 mg/kg/dose 8 hourly) for first 4 days. Clinical deterioration prompted the need for referral to an infectious disease specialized center, where lab work ruled out viral hepatitis (A, B and C) and changes to the dosages of medication was prescribed. He was admitted back to the floor.

IV vancomycin (15 mg/kg/dose in place of cefotaxime) and IV piperacillin/tazobactam (200 mg/kg/day), were started on day 5 with increase dose of acyclovir (20 mg/kg/dose 8 hourly) because no clinical improvement was noticed. They were carried out for the 10 days then conservative treatment was given for the remaining days of hospital stay.

OUTCOME AND FOLLOW-UP

The complete course of stay in the hospital was 33 days, which also includes the time where the young boy was moved to a referral hospital. He was successfully treated for a case of atypical viral meningitis using CSF-PCR as a diagnostic tool. He was seen in our clinic at 1 and 3 weeks on follow-up and clinical improvement in weight and activity was recorded.

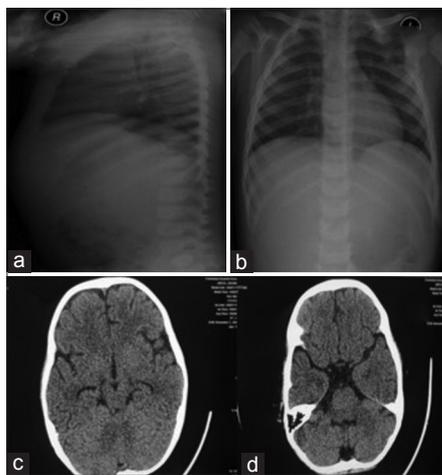


Figure 1. (a) Lateral Chest X-Ray, (b) PA view Chest X-Ray, (c) CT Brain, (d) CT Brain

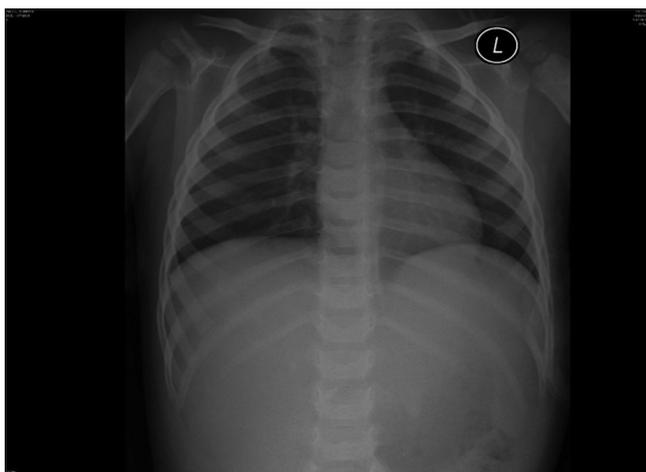


Figure 2. PA view Chest X-Ray

DISCUSSION

Encephalitis is defined by the presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction [1] whereas hepatitis is defined by the presence of an inflammatory process of the Liver. The Coxsackie virus family is enterovirus and is spread by the fecal-oral and respiratory routes. Enteroviruses are RNA viruses of the family Picornaviridae that consists of more than hundred serotypes, which are characterized by a single positive-strand genomic RNA. Ninety percent of enterovirus infections are non-symptomatic or manifest simply as an undifferentiated febrile illness [2]. Twenty-three serotypes from group A and six serotypes from group B have been found. Isolation of Coxsackie virus in cell culture is the standard diagnostic method, but many group A Coxsackie virus grow poorly or not at all in vitro [3].

We present the case of a child from Kuwait who presented in winter with vesicles in the anterior oropharynx fever, altered mental status, drowsiness along with acute hepatitis, and later on developed neck rigidity. Herpetic stomatitis or meningoencephalitis with acute hepatitis was considered as a working diagnosis initially. The possible causes of acute hepatitis including HAV, HBV, and CMV were excluded. On day of admission Serum PCR was done for the possible viral etiologies of meningoencephalitis which came out to be negative. Supportive treatment was advised for the patient and as the altered mental status improved in our patient and the hepatitis subsid-

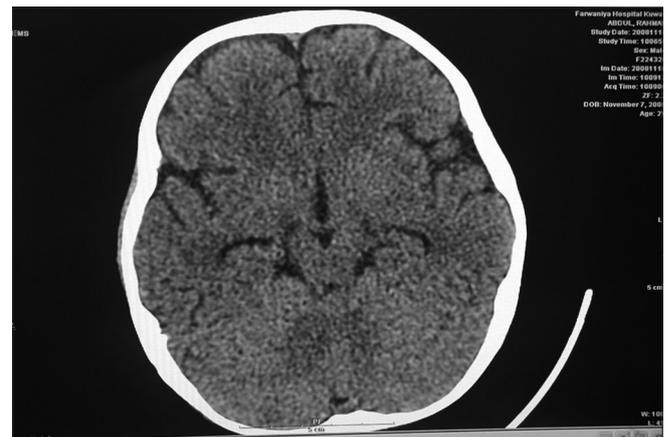


Figure 3. CT Brain



Figure 4. CT Brain

ed as well. The temporal correlation of the manifestation of meningoencephalitis along with hepatitis after excluding the causes of hepatitis, help us to suggest the enteroviral infection was associated with the occurrence of hepatitis in this case.

Although the presence of loose stools was in favor of enteroviral infection, however cases of enteroviral infections predominated with the clinical picture of acute hepatitis except in neonates are rarely found in literature. There is a time limitation towards detection of EV in CSF by PCR. PCR CSF should be done as early as possible in cases of even in slightest suspicion for enteroviral because after 2 days the sensitivity of the test decreases and it can be false negative.

Learning Points/Take Home Messages

- PCR CSF should be done as early as possible in cases of even in slightest suspicion for enteroviral infection.
- CSF PCR is still the best test to diagnose Viral Encephalitis/Meningitis in equivocal or unusual presentation of the disease.
- Hepatitis and Meningoencephalitis can co-occur with infection from Enterovirus.

CONFLICT OF INTEREST

None

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All authors contributed equally.

ETHICAL APPROVAL

Informed consent was obtained from the patient for publication of this case report.

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