



Diagnostic dilemma in reckoning cytomegaloviral infection is prompting increased mortality among abandoned newborns of India

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ABSTRACT

This article emphasizes on an almost untouched aspect of medical adversity concerning the health ordeal of the abandoned newborns in India. The case described here is that of an abandoned female newborn suffering from neonatal hepatitis, respiratory distress, intravascular coagulation and microcephaly. While treating the infant, the practitioners suffered from diagnostic dilemma in identifying the actual cause to be that of Human cytomegalovirus infection. This delay is mostly due to its non-specific clinical presentation and lack of adequate awareness about the virus amongst the practicing physicians. This article being the first of its kind from India aims to provide effective clinical observations and juxtapose the investigative maneuvers vital for differential diagnosis with early treatment initiation and positive outcomes. We also aim to inflict a sociological impact on the issue of abandoning newborn children which leads to their severe diseased fate and acute sufferings.

INTRODUCTION

Child abandonment is a severe issue currently concerning the whole world [1]. India still lacks an efficient administrative system to monitor and prevent this issue. A recent government report (Justice Verma committee) reported that in India more than 60,000 children are being abandoned every year and most of these cases go unnoticed [2]. Viral infections caused by rubella, cytomegalovirus (HCMV) and herpes simplex virus (HSV) account for the major maternal infections causing unfavourable complications during pregnancy and severe consequences for the newborns. HCMV infections are one of the most common congenital infectious diseases in the humans [3,4]. Primary infection of HCMV acquired by women during pregnancy accounts for about half of the morbidity and mortality among neonates; while the remaining results from the reactivation of an old infection. Most infections are caught in utero (congenital HCMV) or postnatally [5, 6]. 80-90% of the women of childbearing age in India demonstrate CMV IgG positive status [7]. Congenital HCMV infection is characterized by hepatitis, sepsis, pneumonitis, microcephaly, periventricular calcifications, hydrocephalus, chorioretinitis, skin lesions, and visceral involvement [8].

Case report

A newborn female child was found abandoned in a dustbin and rescued by locals a few days back. She was immediately rushed to the emergency unit of a local district hospital. On admission in that hospital weight of the child was measured to be about 1.9kgs and gestational age was predicted to be about 35 weeks (estimated by using new Ballard score). The infant showed severe signs of respiratory distress, lethargy, poor sucking reflex and hypothermia at that time. Upon initial investigation, the child was found to be suffering from jaundice prevalent up to the abdomen, petechial rash, hepatosplenomegaly and repeated convulsions. The doctors suspected a case of

neonatal sepsis and the child was put on intravenous fluid therapy.

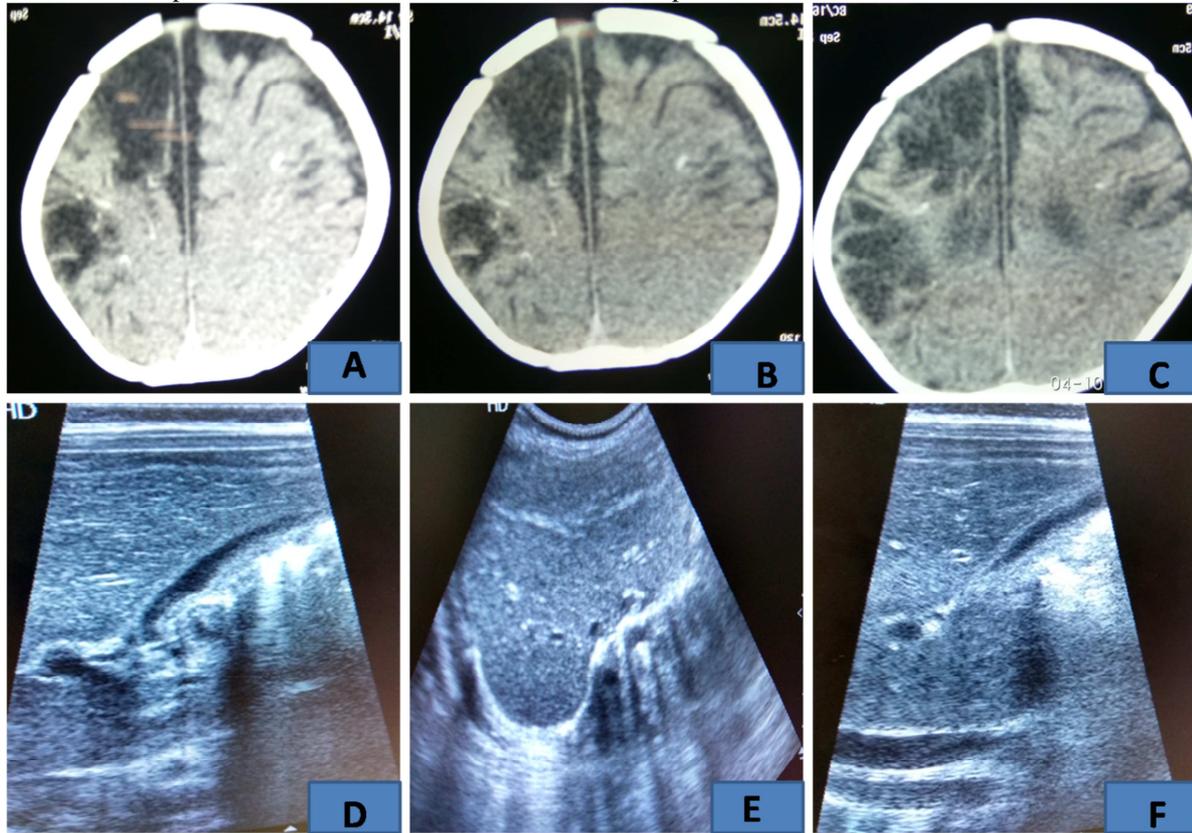


Figure 1 A, B, C- CT scan of brain

- A- Ventricular system appears normal with septum in midline.*
- B- Encephalomalacia present in left frontotemporal region. Effaced basal cistern, cortical sulci and sylvian fissure- suggestive of diffuse brain swelling*
- C- Bilateral sulcal calcification visible at multiple places. Foci of calcification observed at parietal periventricular region.*
- D, E, F- USG of abdomen*
- D- Liver is homogenous in echo texture with a liver span of 9cm (hepatomegaly is present)*
- E- Gall bladder is normal in size.*
- F- No triangular cord sign is noticed, suggestive of cholestatic jaundice.*

Table 1 A complete blood profile analysis and liver profile analysis of the child was presented in the following table

Parameters	Analysis at district hospital	Analysis at B.C.Roy hospital
Haemoglobin	8 gm%	7 gm%
Total WBC	4500/ μ l	6500/ μ l
Neutrophil	1200/ μ l	2300/ μ l
Platelets	44000/ μ l	28000/ μ l
CRP	12.6mg/dl	64mg/dl
Capillary blood glucose	Not done	88mg/dl
Total serum bilirubin	7.8mg/dl	16mg/dl
Conjugated fraction	Not done	13mg/dl
Albumin	Not done	2.1mg/dl
Total protein	2.8mg/dl	4.5mg/dl
Urea	Not done	3.8mg/dl
Creatinine	Not done	0.3mg/dl
SGOT	Not done	152 IU/L
SGPT	196 IU/L	210 IU/L
Alkaline phosphatase	Not done	225 IU/L
Prothrombin Time (PT)	Not done	18 secs (Control-12)
Partial Thromboplastin Time (PTT)	Not done	46 secs(Control-34)
International Normalized Ratio(INR)	Not done	1.68

Antibiotics amoxicillin and gentamycin along with anticonvulsant phenobarbitone was immediately administered. A complete blood profile analysis at this juncture revealed leukocytopenia, thrombocytopenia, neutropenia and elevated C-reactive protein. Liver Function Test showed elevated conjugated hyperbilirubinemia and elevated ALT or SGPT levels. A detailed analysis report has been provided in table 1. In view of the debilitating condition presented with the infant's symptoms the doctors suspected a probable congenital TORCH infection. TORCH screening was immediately performed with the child's blood and gave IgM and IgG positive result for HSV and only IgG positive for HCMV. The newborn was immediately put on a regimen of acyclovir (30mg/kg/day). But no improvement was observed and the child's condition deteriorated further. In the next few days, the infant developed progressive jaundice, abdominal distension and disseminated intravascular coagulation. In view of the limited medical resources and diagnostic manoeuvres available in the district hospital, the child was transferred to the neonatal intensive care unit Dr B.C Roy paediatric government hospital in Kolkata. At the time of admission, the child was suffering from deep jaundice up to the lower limb, recurrent convulsions, breathing difficulty and microcephaly. The liver was found to be 4 cm below right costal margin with a span of 9 cm and multiple purpuric rashes were present all over the body. The child's abdomen was distended with sluggish peristaltic sound. The peripheral capillary oxygen saturation level (Spo₂) of the baby was found to be 60%. The child was immediately placed on mechanical ventilation with oxygen support. Intravenous fluid therapy, anticonvulsant phenytoin and antibiotics meropenem and amikacin were immediately administered. ELISA test for HSV and HCMV specific IgMs with blood serum from the baby gave a low positive result for HSV but high positive result for HCMV. Qualitative PCR detection tests confirmed acute HCMV infection and negative HSV1 infection. Quantitative PCR detected high HCMV viral load in the infant's blood (3890copies/mL). Other serological diagnostic tests performed with the child's blood gave Rubella, toxoplasma, HCV and HBV negative results. No bacterial or fungal infection was observed. Blood profile analysis revealed acute infection with marked leucopenia and thrombocytopenia. Liver function tests showed highly deranged liver function and liver USG suggested hepatic cholestasis. Complete blood analysis report and Liver function test report has been provided in table 1. ABG showed metabolic acidosis. Echocardiogram revealed pulmonary hypertension and moderate hypertrophy of the right ventricle. Head circumference of the baby was 31cm. USG brain showed hypodense areas suggestive of hypoxic-ischemic damage. Skull radiograph and the head ultrasound scan revealed multiple cortical and periventricular calcifications. Ophthalmological examination was within normal limit. The child was immediately put on a stringent regime of intravenous ganciclovir (8mg/kg/day) for about 4 weeks. An improvement was visible after about 20 days treatment and thereafter gradually the symptoms started receding. Quantitative PCR confirmed rapid subsidence of HCMV viral load in the infant's blood. Ganciclovir treatment duration ended and the infant was kept under observation in the intensive care unit for 1 more week. But after about 5 days repeated seizures and convulsions resumed followed by a visible enlargement of the brain. Head circumference increased to 37 cm. The physician performed an immediate CT scan that revealed the cause to be acute hydrocephalus and diffused swelling in the brain. Encephalomalacia was observed to be present in the left fronto-temporal region along with reduced attenuation of brain parenchyma in both cerebral hemispheres. The child expired thereafter while performing VP shunting. The child's parent declined further postmortem examination.

DISCUSSION

Child abandonment is a worldwide social and public health problem, which exerts a multitude of short and long-term consequences on children [9]. The problem of Child abandonment or "baby dumping" in India needs serious consideration, especially among the underprivileged urban and rural communities, where child protection systems are not developed—or do not reach. Prevention of child abandonment is critical for the accomplishment of Millennium Development goals (MDG) and it can't be achieved unless child protection is incorporated as an integral part of program & strategies formulated by the government [10]. Girls in India are more prone to disproportionately experience the abuses of abandonment, infanticide and sex-selective abortion than are boys [10]. This is rooted in a cultural bias against girls in many Indian states. In eastern India, over the last decade, this issue has raised severe concerns for the government about the welfare and wellbeing of the newborns. Every year we receive multiple cases of abandoned newborns admitted with severe viral infections and in most cases, these infants die ascribing to the late diagnosis by the doctors due to their dilemma in identifying the causative organism. Viral pathogens belonging to the herpesviridae family are one the commonest cause of neonatal hepatitis and sepsis [11]. Newborn babies usually catch the infection from maternal birth tract during delivery [12]. Combating congenital infections is in itself extremely difficult and when the antenatal history of the infant is unknown the challenge increases manifold [13, 14]. Neonatal infection caused by HCMV is a highly morbid and fatally dreadful infection [15, 16]. In a poor resource setting with inadequate medical manoeuvres the clinicians face a unique challenge in the

differential diagnosis of congenital HCMV infectivity [17]. There is a significant lack of constructive data regarding the incidence of HCMV infectivity in the Indian population [18]. While working with neonatal subjects from East Indian state of West Bengal we have found that every year a major number of cases of neonatal morbidity can be ascribed to congenital cytomegalovirus infections alone. Here we have selected one of the severe cases to give a glimpse of the ongoing situation at the ground level. The case described here is that of an abandoned female newborn suffering from neonatal hepatitis, respiratory distress, intravascular coagulation and microcephaly. While treating the infant, the practitioners suffered from the diagnostic dilemma in identifying the actual cause to be that of Human cytomegalovirus infection. Though there have been great advances in diagnosis and management of congenital cytomegalovirus infection in last few decades, its morbidity continues to be high due to the greater lag-time between symptoms and diagnosis. This delay is mostly due to its non-specific presentation and lack of adequate awareness about the virus amongst the practising physicians. This article being the first of its kind from India aims to provide fundamentally effective clinical observations and juxtapose the investigative manoeuvres vital for differential diagnosis with early treatment initiation and positive outcomes. We also aim to inflict a sociological impact on the issue of abandoning these newborn children which leads to their severe health complications and intense sufferings.

5. Ethical approval

This work has been ethically approved by the institutional ethical committee of ICMR Virus Unit and is in accordance with the Helsinki Declaration of 1975

6. Conflict of interest

The authors declare no conflict of interest

REFERENCES

- [1] Burke N, Hellman J, Scott B, Weems C. The impact of adverse childhood experiences on an urban pediatric population. *Child Abuse & Neglect*. 2001; 35(6): 408-413.
- [2] Bhakhry S. Children in India and their rights. New Delhi: National Human Rights Commission. 2006
- [3] Stegmann BJ, Carey JC: TORCH infections. Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), and Herpes infections. *Curr Womens Health Rep*. 2002; 2(4):253–258
- [4] Johnson P.M., Barnes RM, Hart, C.A. and Francis W.J. Determinants of Immunological Responsiveness in Recurrent Spontaneous Abortion. *Transplantation*. 1984; 38, 280-284.
- [5] Townsend CL, Forsgren M, Ahlfors K, Ivarsson S-A, Tookey PA, Peckham CS. Long-term Outcomes of Congenital Cytomegalovirus Infection in Sweden and the United Kingdom. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*. 2013;56(9):1232-1239.
- [6] Chakravarty.A, Kashyap B, Rathi K. “The seroepidemiological study on cytomegalovirus in women of childbearing age with special reference to pregnancy and maternal-fetal transmission.” *Indian J Pathol Microbiol*. 2005; 48:518-21.
- [7] Sheevani M, Jindal N, Aggarwal A. “A pilot seroepidemiological study of cytomegalovirus infection in women of childbearing age.” *Indian J Med Microbiol*. 2005;23:34-6.
- [8] Boppana SB, Pass RF, Britt WJ, Stagno S, Alford CA. “Symptomatic congenital cytomegalovirus infection: neonatal morbidity and mortality,” *Pediatr Infect Dis J*. 1992;11(2):93–99.
- [9] Burnstein M. Child abandonment: Historical, sociological and psychological perspectives. *Child Psychiatry & Human Development*. 1981; 11(4): 213-221.
- [10] Unicef. Children and the millenium development goals. 2016
- [11] C. M. Rudnick, “Neonatal herpes simplex virus infections,” *American Family Physician*, 2002;65(6):1138–1143.
- [12] Shorter RG, Baggenstoss AH, Logan GB. Neonatal hepatitis. *AMA J Dis Child*, 1959;98:359-69.
- [13] White JC, Magee SR. Neonatal herpes infection: Case report and discussion. *J Am Board Fam Med*, 2011;24:758-62.
- [14] Hannachi N, Marzouk M, Harrabi I, Ferjani A, Ksouri Z, Ghannem H, Khairi H, Hidar S, Boukadida J: Seroprevalence of rubella virus, varicella zoster virus, cytomegalovirus and parvovirus B19 among pregnant women in the Sousse region, Tunisia. *Bull Soc Pathol Exot*. 2011; 104(1):62–67.
- [15] Gandhoke I, Aggarwal R, Lal S, Khare S. Congenital CMV infection in symptomatic infants in Delhi and surrounding areas. *Indian J Pediatr* 2006, 73: 1095- 1097.

- [16] Enders G, Bader U, Lindemann L, Schalasta G, Daiminger A. Prenatal diagnosis of congenital cytomegalovirus infection in 189 pregnancies with known outcome. *Prenat Diagn.* 2001;21:362–77.
- [17] Alkhwaja S, Ismaeel A, Botta G, Senok AC: The prevalence of congenital and perinatal cytomegalovirus infections among newborns of seropositive mothers. *J Infect Dev Ctries.* 2012; 6(5):410–415
- [18] Sharma A, Rasul ES, Hazarika NK: A serological study of cytomegalovirus infection in pregnant and non-pregnant women at Gauhati Medical College and Hospital. *J Indian Med Assoc.* 2007; 105(6):322–323. 320.