



Case Study

Congenital Cytomegalovirus Infection Causing severe Inclusion Diseases in Infants - Case Report from Eastern India

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Available online at: www.isca.in, www.isca.me

Received 16th November 2016, revised 4th December 2016, accepted 7th December 2016

Abstract

India currently faces a serious challenge to antagonize the increasing number of newborn deaths owing to Human Cytomegalovirus infection every year. Here in this study we report a severe case of congenital HCMV infection causing cytomegalic inclusion disease (CID) affecting the brain and CNS in an infant admitted to the neonatal care unit. This article represents the first documented case from India ascribing the severity of symptomatic congenital HCMV infection manifesting in the form of CID and highlighting the need for improved medical resources in a lower-middle income country like India to timely diagnose and combat this dreaded virus.

Keywords: Human Cytomegalovirus, Inclusion Diseases, Congenital, Cerebral Atrophy, Cortical Calcification.

Introduction

Congenital Human Cytomegalovirus has transpired itself to be one of the major health issues concerning the current population of India. HCMV infection in pregnant women is very common in poor economic hubs and impoverished resource setting, largely visible in many south Asian countries including India. In different regions of India, serological reviews have demonstrated 80-90% frequency of HCMV IgG specific antibodies in pregnant women^{1,2}. The magnitude of this issue in India has been left almost totally unexplored^{3,4}. The most serious manifestation involving the clinical triumph of congenital cytomegaloviral infection is referred to as CID (Cytomegalic Inclusion Diseases) which is generally associated with neurological consequences involving the brain and CNS like microcephaly, ventriculomegaly, cerebral atrophy, chorioretinitis, cerebral palsy, sensori-neural hearing loss, periventricular sequelae and cortical calcifications^{5,6}. Here in this article we present a very challenging case of a CID infected infant rendering from a poor resource setting and discussed the parameters of disease burden along with the attempted medical maneuvers to overcome those barriers.

Case Presentation

An 18 days old male child of a 22 year old mother from her first normal pregnancy was admitted to the neonatal intensive care unit with convulsions and respiratory distress followed by intracranial bleeding and recurrent seizures. High fever and asthenia in the mother highly complicated the course of pregnancy through second trimester. Upon admission the child

was immediately placed under mechanical ventilation and oxygen support. Anti-bacterial therapy with amoxicillin, cefotaxime and amikacin was started promptly however didn't demonstrate any encouraging improvement. The blood from the infant was screened for TORCH infections which gave highly positive result for HCMV but negative results for HSV, Rubella and Toxoplasma. ELISA test for CMV IgM with blood serum from the mother and infant gave positive results indicating acute HCMV infection. High HCMV viral load was found in the newborn child's blood (1990 copies/mL). Bacterial and fungal infections were found to be negative. Liver capacity was abnormally deranged with raised ALT or SGPT (194 IU/L) levels and AST or SGOT (179 IU/L) levels. Other abnormalities included raised C-reactive protein (79mg/L) and conjugated hyper-bilirubinemia. (total serum bilirubin 4.8 mg/dL; direct bilirubin 3.5 mg/dL). Semilateral skull radiograph clearly showed intracranial periventricular and subependymal calcifications. Head ultrasound scan revealed fullness of the ventricular system with multiple cortical calcifications and ventriculomegaly. Intravenous gancyclovir treatment (8mg/kg/d) was initiated immediately following HCMV detection and continued for approximately 4 weeks. After about 20 days treatment slight improvement was found to occur and gradually the intracranial bleeding stopped. HCMV viral load in blood serum was almost negligible which suggested rapid subsidence of the infection. Gancyclovir treatment duration ended and the infant was kept under observation in the intensive care unit for 2 more weeks. But after 1 week the child started suffering from recurrent seizures and the head started to enlarge. An immediate brain CT scan revealed severe hydrocephalus. Reduced attenuation of brain parenchyma in the cerebral

hemispheres and effaced basal cisternae were observed which suggested the presence of permanent sequelae of hypoxic ischaemic injury as well as diffuse brain swelling. Immediately ventriculoperitoneal shunting (VP shunting) was planned to be performed. While performing the procedure shunt blockage occurred and the child expired. The parents of the child declined postmortem examination and brain biopsy (Figure-1).

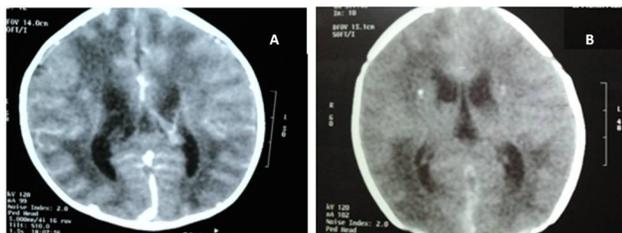


Figure-1

(A) Showing foci of calcification in parietal periventricular region. Effaced basal cistern, cortical sulci and sylvian fissure-suggestive of diffuse brain swelling. (B) Reduced attenuation of brain parenchyma in both cerebral hemisphere-suggestive of hypoxic ischaemic injury. Punctate calcification of right frontal deep white matter

A detailed account of all the symptoms associated with cytomegalic inclusion disease that has been observed in the infant has been listed in the Table-1.

Table-1

A detailed account of all the symptoms associated with Cytomegalic inclusion disease observed in the infant

| Symptoms associated with CID | Observed in the infant |
|--|------------------------|
| Seizures and convulsions | ✓ |
| Cortical calcifications | X |
| Ventricular and sub-ependymal calcifications | ✓ |
| Intracranial bleeding | ✓ |
| Ventriculomegaly | ✓ |
| Ventricular dilation | ✓ |
| Microcephaly | ✓ |
| Cerebral atrophy | ✓ |
| Chorioretinitis | X |
| Cerebral palsy | X |
| Sensori-neural hearing loss | X |
| Ventricular hypertrophy | X |
| Hydrocephalus | ✓ |

Discussion

This article will be the first reported evidence from India to discuss the potentiality of congenital HCMV infection causing serious inclusion diseases like CID in neonates⁷. In reality studies linking the generality of birth defects because of congenital cytomegaloviral diseases are exceptionally constrained in India and henceforth the prevalence of genuine repetitive congenital HCMV infections remains difficult to ascertain.^{8,9} Gancyclovir and valgancyclovir are the main anti-HCMV drugs that have been used in India with considerable success though the exact benefits of this mode of treatment and the effective duration in case of congenital HCMV infection still remain controversial^{10,11}. In the case presented here, initially the infected infant responded to the intravenous gancyclovir therapy (8mg/kg/d on a 3-4 weeks regime) in a positive manner without any genotoxic side effects but due to the time lapse in diagnosis and severity of the infection he died. Administration of gancyclovir can therefore be considered to be appropriate in cases of CID. However, the exact benefits of this treatment cannot be concretely emphasized unless more advanced studies were performed on a bigger cohort. It is very important to understand that CID is associated with a permanent brain or neural damage and hence an unscathed recovery is not possible under any circumstances. Mortality can be prevented only with an early differential diagnosis and stringent anti-HCMV drug treatment regime. General awareness among the public, good personal hygiene and proper medical advice can rapidly reduce the risk of congenital HCMV acquisition and infection.

Conclusion

This study presents the first documented case of congenital cytomegalic inclusion disease from India where we have discussed the concerned severity of the HCMV infection in an infant and have also projected the counter measures to deal with it. This article can, therefore, on one hand be immensely useful for all medical practitioners in India to understand and treat related congenital HCMV infection cases in a economically poor resource setting while on the other hand can be an eye opener to the general public highlighting the aspects of congenital HCMV transmission and measures to avoid infection.

Ethical statement: All experiments have been performed after taking due permission from the institutional ethical committee (ICMR Virus Unit, Kolkata).

Conflict of interest: None to declare.

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