SHORT COMMUNICATION

Cytomegalovirus Infection in Six Neonates

SS YADAV, G NARULA, S NARAYAN*, S BISWAS AND G GUPTA**

*From Department of Pediatrics, INHS Asvini, Colaba, Mumbai, *Department of Pediatrics, Army Hospital (R & R), New Delhi, **Department of Microbiology, Tata Memorial Hospital and Research Center, Mumbai.*

Correspondence to:
Surg Cdr Gaurav Narula,
Assoc Prof (Peds) and Pediatric Hematologist-Oncologist,
Department of Pediatrics, INHS Asvini, Colaba,
Mumbai 400 005, India.
drgauravnarula@gmail.com
Received: September 19, 2007;
Initial review: December 13, 2007;
Accepted: November 4, 2008.

Neonatal cytomegalovirus (CMV) infection is common, has myriad presentations and severe sequelae. Six neonates clinically suspected of CMV infection were confirmed by qualitative PCR (Digene) and evaluated. Those with persistent viremia were treated with Ganciclovir intravenously for 4-6 weeks, and continued orally, if required, with close monitoring. All had prolonged jaundice, hepatosplenomegaly and hematological manifestations in the acute stage. Complications included developmental delay (66%), sensorineural hearing loss (SNHL) (33%), chorioretinitis and obstructive jaundice (18% each). Three cleared viremia spontaneously. The remaining were offered Ganciclovir. One declined, and two completed therapy with clinical resolution and no adverse events. Accurate diagnosis of neonatal CMV enables appropriate treatment with Ganciclovir, which can reverse end-organ damage and limit sequelae.

Keywords: *CMV, Ganciclovir, Management, Neonate.*

Published online: 2009 April 15. PII:S097475590700569-2

Cytomegalovirus (CMV) is the commonest cause of congenital infection worldwide. It maybe transmitted transplacentally, during labor, through breastmilk, and saliva. It manifests with hematological or hepatic manifestations, developmental delay, chorioretinitis and sensorineural hearing loss(1,2). Though antiviral drugs are available, toxicity and lack of oral formulations have limited their use.

METHODS

Cases clinically suspected to have CMV infection in a level III NICU or on early neonatal follow-up between May 2005 and July 2007, were screened by serological tests, and if positive for CMV IgM (enzyme immune assay method), were subjected to CMV DNA by qualitative PCR (Digene hybrid capture). Positive cut-off values were 16000 RLU (Relative light units). Confirmed cases were studied. Acute manifestations were managed symptomatically. Growth, development and clinical parameters were closely monitored. Hearing evaluation by brainstem evoked response audiometry (BERA), and eye examinations were done. Those with persistent viremia and end-organ damage in CNS, eye, hearing or hematological manifestations were treated with Ganciclovir (10 mg/kg IV for 2-3 weeks, reduced to 5 mg/kg for 4-6 weeks) against monitoring of clinical parameters, viremia and toxicity (blood counts twice weekly, bio-chemistry weekly). Oral ganciclovir was continued if end-organ damage persisted after clearance of viremia. Renal function was monitored by ^{99}Technetium scans after 6-8 wk of therapy and 4-6 wk after completion.

RESULTS

Six neonates were eligible for study. All had hyperbilirubinemia, hepatosplenomegaly and hematological manifestations. Developmental delay, sensorineural hearing loss, chorioretinitis, and obstructive jaundice was present in four, two, one and one children, respectively. Three children had persistent viremia, anemia and end-organ damage. Ganciclovir was started at this stage in one child and sometime later in another. Both these patients had significant decline in viremia after 8 weeks.

WHAT THIS STUDY ADDS?

- All confirmed cases of neonatal CMV infection do not require antiviral therapy.

Ganciclovir was stopped in the first following complete clearance of choreo-retinitis, and in the other following normalization of hematological parameters. Both showed catch- up in development.

At follow-up of 8-26 months (mean 13 mo) post-diagnosis, two cases, who spontaneously cleared the virus are asymptomatic and thriving well. One child, who spontaneously cleared the virus but had significant comorbidities, has mental retardation, spasticity and profound SNHL. The first child who received ganciclovir had severe SNHL for which a cochlear implant was given followed by speech therapy, with encouraging response. The other case which received ganciclovir is asymptomatic and thriving, with no evidence of end-organ damage.

DISCUSSION

Controversy exists when to treat CMV infection, as symptoms, especially in cases presenting acutely, are often transient and reversible. Those showing end-organ damage with significant viremia should be treated with ganciclovir, which causes reduction of viral load and reversal of manifestations(3). Schedules vary in literature and fewer still have monitored therapy against viral loads(3-5). Our schedule was dictated by clinical response and viral monitoring but reflected reported regimes. Outcomes ranged from spontaneous clearance of the virus and clinical resolution to severe SNHL.

Treatment was well tolerated. Complications were mild and no episodes of treatment related neutropenia occurred. A mild increase in viral loads was seen on cessation of therapy, which has also been reported earlier(3). We practiced selective screening followed by confirmatory qualitative estimation of CMV-DNA, where the RLU reading indirectly also gave a guide to viral load. Unnecessary treatment in patients with decreasing levels and clinical resolution could be avoided.

We conclude that treatment of neonatal CMV should be reserved for those with persistent viremia, progressive disease and end-organ damage.

Contributors: SSY, GN and SN: record keeping, collection of data and analysis. GN and SN: study design and protocols. GN, SB and GG: manuscript preparation and critical review. GN will act as guarantor.

Funding: None

Competing interests: None stated.

REFERENCES

1. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007; 17: 253-276.
2. Burchett SK. Viral Infections. In: Cloherty JP, Eichenwald EC, Stark AR, editors. Manual of Neonatal Care. 5th ed. Philadelphia: Lippincot, Williams and Wilkins; 2003. p.255-259.
3. Tanaka-Kitajima N, Sugaya N, Futatani T, Kanegane H, Suzuki C, Oshiro M, *et al.* Ganciclovir therapy for congenital cytomegalovirus infection in six infants. Pediatr Infect Dis J 2005; 24: 782-785.
4. Nigro G, Scholz H, Bartmann U. Ganciclovir therapy for symptomatic congenital cytomegalovirus infection in infants: a two-regimen experience. J Pediatr 1994; 124: 318-322.
5. Michaels MG, Greenberg DP, Sabo DL, Wald ER. Treatment of children with congenital cytomegalovirus infection with ganciclovir. Pediatr Infect Dis J 2003; 22: 504-509.