OPEN

Severe Postnatal Cytomegalovirus Enterocolitis in Immunocompetent Term Infants Requiring Total Parenteral Nutrition

*†Annaleise R. Howard-Jones, ‡Giancarlo H. Cristerna-Tarrasa, §Rabia Khan, †§Michael Stormon, †‖Susan Arbuckle, and *†Philip N. Britton

Abstract: Postnatal cytomegalovirus enterocolitis is uncommon in immunocompetent infants. We report a 10-week-old term boy with severe and prolonged secretory diarrhea, leading to dependence on total parenteral nutrition and a 10-week hospitalization. Cytomegalovirus enterocolitis was diagnosed based on duodenal biopsy in the context of marked viremia, and the child recovered promptly on initiation of ganciclovir. Collated case reports reveal delayed diagnoses as the norm but rapid improvement with antiviral treatment. Cytomegalovirus enterocolitis should be considered early as a differential diagnosis in infants with refractory diarrhea.

Key Words: cytomegalovirus, enterocolitis, ganciclovir, immunocompetent, secretory diarrhea

What Is Known

- Severe secretory diarrhea in infants is uncommon, with causes including allergic enteropathies, congenital diarrheal disorders & immune dysregulation, polyendocrinopathy with enteropathy, X-linked.
- Cytomegalovirus has been associated with fulminant disease in immunocompromised hosts but typically causes mild infection in immunocompetent term infants.

What Is New

- Cytomegalovirus can cause severe, refractory diarrhea in immunocompetent infants, necessitating prolonged hospitalization and total parenteral nutrition.
- In cytomegalovirus-induced enterocolitis, response to ganciclovir is rapid and sustained.

Translational Impact

- In an infant with severe secretory diarrhea, early screening for cytomegalovirus by nucleic acid testing of urine should be followed promptly by cytomegalovirus blood titers and endoscopic biopsy to avoid delays in diagnosis.
- Given the prompt response to ganciclovir initiation in cytomegalovirus enterocolitis, a short 7–10 days trial of ganciclovir should be considered as an adjunctive diagnostic tool and for therapeutic purposes.

INTRODUCTION

Severe, protracted diarrhea in immunocompetent term infants is most frequently due to cow's milk protein intolerance, allergic colitis, or other rarer conditions such as congenital diarrheal disorders. It may also herald the presence of an undiagnosed primary immunodeficiency, such as immune dysregulation, polyendocrinopathy with enteropathy, X-linked or common variable immunodeficiency, very early onset inflammatory bowel disease, or autoimmune enteritis.

Cytomegalovirus (CMV) is a betaherpes virus, which is ubiquitous worldwide (1). Between 45% and 100% of the population has been exposed to CMV by adulthood, with South America, Asia, and Africa reporting the highest rates (2). In immunosuppressed individuals, severe primary or reactivation CMV disease may manifest in almost any organ system or as a disseminated infection. In immunocompetent hosts, infection often occurs without symptoms, with mild nonspecific features or as an infectious mononucleosis-like illness (3).

Although CMV infection is common in childhood, severe end-organ disease is rare in immunocompetent term infants. In the gastrointestinal tract, other causes of chronic diarrhea are more common, including cow's milk protein intolerance or allergic enterocolitis, leading to marked delays in diagnosis (4). Diagnosis of CMV enterocolitis in this population group requires a high degree of clinician awareness due to the infrequency of this condition.

METHODS

A search of Medline using keywords (cytomegalovirus OR CMV) AND (infant OR neonate) AND (enterocolitis OR gastroenteritis OR diarrhea OR colitis), while excluding references with keywords (immunocompromised OR immunologic deficiency syndromes OR human immunodeficiency virus) was used to collate manuscripts of relevance. Articles in languages other than English were excluded where translation was not feasible. Patients were excluded if they were born prematurely (before 37 wk of gestation), showed clinical features of congenital CMV such as chorioretinitis,

Received November 20, 2020;accepted June 10, 2021.

From the *Department of Infectious Diseases & Microbiology, The Children's Hospital at Westmead, Westmead, New South Wales, Australia; †Discipline of Child and Adolescent Health, University of Sydney, The Children's Hospital at Westmead, Westmead, New South Wales, Australia; ‡Department of Infectious Diseases, Instituto Nacional de Pediatría, Mexico City, Mexico; §Department of Gastroenterology, The Children's Hospital at Westmead, Westmead, New South Wales, Australia; and ‖Department of Histopathology, The Children's Hospital at Westmead, Westmead, New South Wales, Australia.

The authors report no conflicts of interest.

Correspondence: Annaleise R. Howard-Jones, Department of Infectious Diseases & Microbiology, The Children's Hospital at Westmead, Hawkesbury Road, Westmead, NSW 2145, Australia. E-mail: annaleise.howard-jones@health.nsw.gov.au

JPGN Reports (2021) 2:3(e110)
ISSN: 2691-171X
DOI: 10.1097/PG9.0000000000000110

or if onset of symptoms occurred within the first 21 days of life as this time frame implies prenatal acquisition of CMV.

Results Illustrative Case

A previously well, term, 10-week-old boy presented with 3 days of watery diarrhea without vomiting or fever (Fig. 1). His father and older sibling had been unwell with gastrointestinal symptoms 1 week prior. The patient was exclusively breastfed and thriving (weight on the 67th centile for age) with no feeding or developmental concerns. He was the third child to consanguineous parents (first cousins) with no family history of inflammatory bowel disease, autoimmune conditions, immunodeficiency, or congenital diarrheal disorders.

He was febrile (38.6 °C), tachycardic, and clinically dehydrated with concerns for sepsis. Inflammatory markers were raised (C-reactive protein 34 mg/L, white cell count 17.2 × 10^9/L, and neutrophils 11.8 × 10^9/L), and liver enzyme levels were normal. Lactic acidosis (pH 7.17, lactate 6.3, base excess –12) corrected with rehydration. A gastrointestinal pathogen polymerase chain reaction (PCR) panel on stool was negative (including targets for adenovirus, norovirus, rotavirus, *Salmonella*, and *Shigella* spp.). Respiratory pathogen PCR panel on a nasopharyngeal aspirate (Seegene Allplex) revealed rhinovirus (with negative results for enterovirus and adenovirus PCR targets). Blood, urine, stool, and cerebrospinal fluid cultures were all negative. He received 48 hours of intravenous antibiotics (ampicillin, cefotaxime, and single dose of gentamicin), then a subsequent 5 days of ampicillin and cefotaxime (with a single dose of gentamicin) for fever recrudescence raising suspicion for infection.

Fevers resolved, but profuse, green, watery diarrhea continued, worsening each time carbohydrates were reintroduced, whether breastmilk or modular formula. A provisional diagnosis of allergic colitis such as cows' milk protein intolerance was made.

Dependence on total parenteral nutrition (TPN) developed by week 2 of admission, alongside a secretory diarrhea (stool osmotic gap 30 mOsm/kg). He became hypoalbuminemic (nadir of 17 g/L, normal range 31–46 g/L) with elevated stool alpha-1-antitrypsin levels (3.1 mg/g dry weight, normal range <1.5 mg/g dry weight), consistent with a protein-losing enteropathy. A urine metabolic screen was normal, and plasma amino acids were uniformly reduced. Inflammatory markers (erythrocyte sedimentation rate >120 mm/h, C-reactive protein 37 mg/L) remained elevated.

Genetic testing for *FOXP3* mutations was negative, excluding immune dysregulation, polyendocrinopathy with enteropathy, X-linked. Immunoglobulins and T- and B-cell subsets were normal, as was the regulatory T-cell profile. There was no peripheral blood eosinophilia.

Mild thrombocytopenia was noted on day 13 of admission (platelet count nadir 122 × 10^9/L). Hepatomegaly with elevated liver enzyme levels (3–5 times upper limit of normal) evolved on day 30 of admission, with abdominal ultrasound demonstrating homogenous increased echogenicity of the liver that was mildly enlarged. The patient did not have seizures or focal neurological signs, and neuroimaging was not performed. Ophthalmology review revealed no evidence of chorioretinitis.

Endoscopy with biopsy on day 35 of admission revealed chronic gastritis and duodenitis with a mixed inflammatory infiltrate, marked villous atrophy, and irregular crypts (Fig. 2), notable loss of Goblet cells and sparse Paneth cells. Occasional viral inclusion bodies and a small number of cells staining positive for CMV by immunohistochemistry were seen on the duodenal sections. The biopsy findings prompted further investigations for CMV infection. CMV was detected in the blood by PCR with a high viral load (log10 4.6), and CMV IgM was positive.

Although the mucosal histopathological features were not striking with regard to CMV preponderance, the balance of evidence favored an empiric trial of ganciclovir for diagnostic and therapeutic purposes. Ganciclovir was commenced on day 39 of admission with a rapid drop in blood CMV viral load (titer 0 following first 7 days of therapy) and normalization of transaminase levels over a period of 3 weeks. Gradual introduction of modular feeds with added carbohydrate occurred concurrently, and the pattern of stooling improved over the first 2 weeks (Fig. 1). TPN was weaned entirely 5 weeks after commencement of ganciclovir.

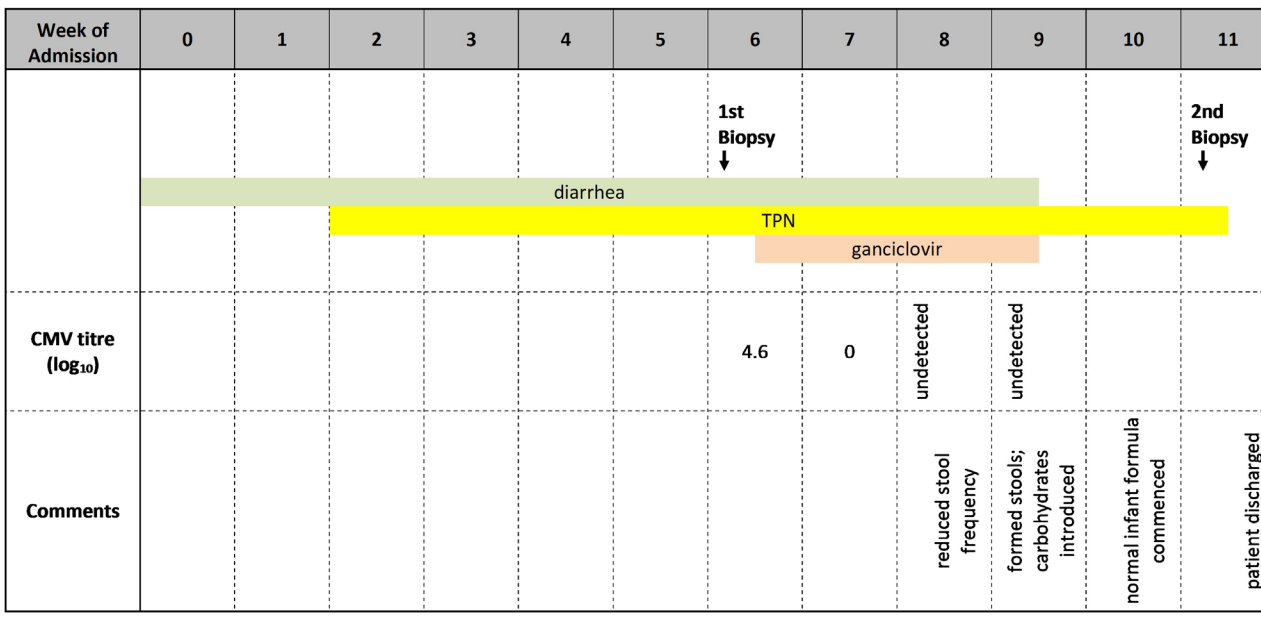

FIGURE 1. Timeline of clinical progress of illustrative case, highlighting duration of diarrhea, and temporal association of ganciclovir course with CMV viral load, symptom resolution, and reintroduction of feeds. CMV = cytomegalovirus; TPN = total parenteral nutrition.

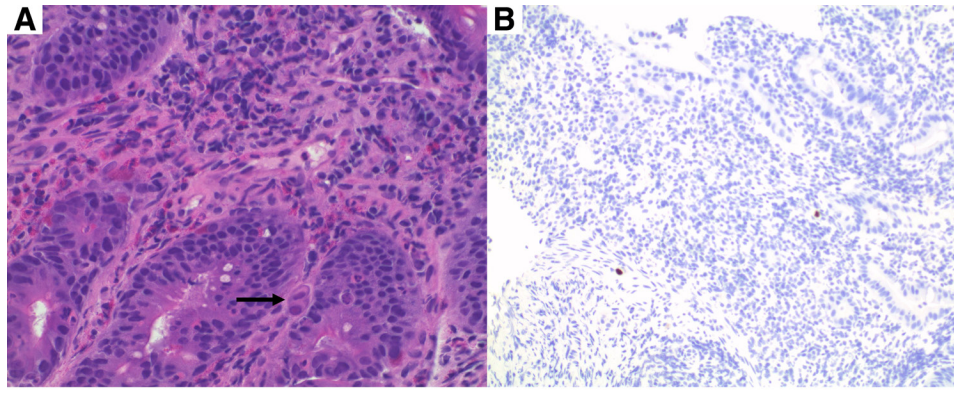

FIGURE 2. Histopathology of duodenal biopsy specimens. (A) Viral inclusion body (indicated by arrow) on hematoxylin and eosin staining and (B) sparse cells staining positive for CMV by immunohistochemistry. CMV = cytomegalovirus.

Taken in the context of marked CMV viremia, the profound enterocolitis with suggestive histopathological findings, associated hepatitis, and thrombocytopenia were together highly suggestive of acute CMV infection. While it is not possible to pinpoint the exact time of acquisition, the infant's pattern of disease and timing of symptom onset at 10 weeks of age was most consistent with postnatal acquisition of CMV.

The secretory diarrhea with protein-losing enteropathy seen in this child is curious in the presence of marked villous blunting and crypt irregularities. It is possible that endoscopy with biopsy earlier in the illness may have given more diagnostic information regarding the etiology of the secretory diarrhea as well as delineating further the role of CMV as a cause of these mucosal changes.

Ganciclovir was ceased after 3 weeks once symptoms had completely resolved and blood viral loads remained suppressed. Repeat biopsy was performed at the end of the ganciclovir course, which demonstrated resolving inflammatory changes and regeneration. No inclusion bodies were seen, and CMV immunohistochemical staining was negative. The infant was discharged on normal infant formula after a 10-week admission.

The infant was well up to the age of 8 months, demonstrating no gastrointestinal symptoms and normal growth and development. His blood CMV viral load remained suppressed up to 4 months following cessation of ganciclovir.

Case Compilation

Postnatally acquired CMV enterocolitis is rare in immunocompetent term infants with 24 case reports identified in infants up to 3 months of age (Table 1). Median age at presentation is 7.5 weeks (range, 3–12 wk) with a male preponderance (male:female ratio 3.4:1). The disease typically manifests as watery or bloody diarrhea, with additional features including vomiting, lethargy, and abdominal distension. Secretory diarrhea may only develop later in the illness. In line with the current case series, the association between protein-losing enteropathy and CMV infection has been previously described (28), further highlighting the role of CMV as a possible driver of this clinical phenotype.

As in the aforementioned illustrative case, marked villous atrophy and crypt distortion were common features, but CMV immunohistochemical findings more variable (6, 14, 23). The number of inclusion bodies and intensity of immunohistochemical staining did not always correlate with other features including severity of diarrhea or degree of protein-losing enteropathy or hypoalbuminemia.

Given the prevalence of cow's milk protein intolerance in this age group and the necessity for invasive testing to ascertain presence of CMV in tissue, diagnosis is frequently delayed with a median delay of 3 weeks (range, 5 d to 7.5 wk) in the collated case reports. Diagnostic challenges are exacerbated by difficulties in interpreting a high blood CMV titer in this age group since historical studies suggest asymptomatic acquisition of CMV occurs in 12% of infants by the age of 3 months (29).

Long-term outcomes were favorable among the collated cases. Only 1 of the infants had a recurrence of symptoms that responded to reinitiation of valganciclovir (14). Survival was 89% in those cases for which follow-up data were available (17 of 19); the 2 fatalities did not receive ganciclovir due to rapid disease progression or lack of availability of this agent at the time of publication. Ganciclovir was well tolerated with only 1 case of neutropenia among the 14 term infants treated (14). In those followed beyond 6 months of age, the children were universally thriving with no further infective complications.

Breastfeeding has been implicated as a risk factor for postnatal CMV acquisition (30), but prospective data are lacking to enable firm conclusions, particularly in the term infant population. In patients in our case series for whom data were available, 16 of 18 infants were exclusively or partially breastfed, consistent with other reports in mixed term/preterm populations (30). Given the relative rarity of this condition compared with the number of breastfed infants in the community, the absolute risk of breastfeeding as a cause for CMV end-organ disease in the term immunocompetent population remains extremely low.

DISCUSSION

Postnatally acquired CMV enterocolitis is a well described entity in immunocompromised children but is rare in immunocompetent term infants up to 3 months of age. This report describes an immunocompetent term infant with profound secretory diarrhea in association with postnatal CMV acquisition. The close temporal association between initiation of ganciclovir and rapid clinical improvement suggests that CMV was a key driver of inflammation in this child.

Notwithstanding this, postviral enterocolitis with secondary carbohydrate intolerance can be severe even without the complicating CMV infection. The high basal metabolic requirements of infancy, compounded by infection, may impede timely recovery of the bowel epithelium under conditions of stress. This phenomenon can improve over time with conservative management and nutritional support; hence, the singular role of ganciclovir in gut recovery in this child cannot be unequivocally proven. However, as demonstrated in Figure 1, the delay in undertaking a diagnostic biopsy resulted in a significant period of diarrhea, which did not improve with TPN,

TABLE 1. Reported cases of postnatally acquired CMV enterocolitis in immunocompetent term infants

Case no.	Country, year	Age, sex	Diagnosis	Time to diagnosis (d)	Treatment	Time to symptom improvement	Comments at follow-up (age at follow-up)	References
1	Thailand, 2018	5 wk, male	CMV enterocolitis	Not specified	Ganciclovir, then valganciclovir (6 mo)	Not specified	Well (12 mo)	Osatakul et al (5)
2	United States, 2016	8 wk, male	CMV colitis, hepatitis	Not specified	Ganciclovir 4 wk, then valganciclovir 4 wk	3 d	Well (1.5 mo)	Sue et al (6)
3	Korea, 2015	8 wk, female	CMV enterocolitis with intussusception	5	Nil	Not specified	Unknown	Park et al (7)
4	United States, 2014	7 wk, male	CMV esophagitis, hepatitis	28	Ganciclovir, then valganciclovir (total 4 wk)	Not specified	Unknown	Hanisch and Belani (8)
5	Germany, 2014	2 mo, male	CMV colitis with stricture	Not specified	Ganciclovir 6 wk; steroids and IVIG for colonic stricture	Not specified	Well (12 mo)	Novakova et al (9)
6	France, 2014	10 wk, male	CMV colitis	8	Nil	Not specified	Unknown	Louazon et al (10)
7	United Kingdom, 2012	6 wk, female	CMV enterocolitis, disseminated CMV	Not specified (postmortem)	Nil	NA	Died day 3 after admission	Refai et al (11)
8	Italy, 2011	10 wk, male	CMV colitis	Not specified	Ganciclovir 3 wk	3 d	Well (24 mo)	Berardi et al (12)
9	Germany, 2011	8 wk, male	CMV duodenitis	Not specified	Ganciclovir, then valganciclovir (2 wk)	2 d	Unknown	Breil et al (13)
10	Italy, 2010	3 mo*	CMV enterocolitis	Not specified	Ganciclovir 3 wk, valganciclovir 6 mo later for 2 mo	Not specified	Well (54 mo)	Nigro et al (14)
11	Italy, 2010	1 mo*	CMV enterocolitis	Not specified	Ganciclovir 3 wk, valganciclovir 2 mo later for 2 mo	Not specified	Well (60 mo)	Nigro et al (14)
12	Spain, 2009	12 wk, male	CMV enterocolitis	28	Ganciclovir 2 wk	Not specified	Well (6 mo)	Ramos Boluda et al (15)
13	United Kingdom, 2008	12 wk, female	CMV colitis	28	Ganciclovir 2 wk	3 d	Well (60 mo)	Abdulhannan et al (16)
14	France, 2006	7 wk, female	CMV enterocolitis with volvulus related to Meckel's diverticulum	Not specified	Nil	Not specified	Unknown	Bonnard et al (17)
15	United States, 2005	5 wk, male	CMV colitis	Not specified	Ganciclovir 2 mo	Not specified	Well (not specified)	Richardson et al (18)
16	United States, 2004	8 wk, male	CMV enterocolitis	21	Ganciclovir	5 d	Well (12 mo)	Rongkavilit et al (19)
17	United Kingdom, 2004	2 mo, male	CMV enterocolitis	>21	Nil	Not specified	Well (10 mo)	Hinds et al (20)
18	Canada, 2001	6 wk, male	CMV esophagitis	6	Nil	Not specified	Well (15 mo)	Weinstein et al (21)
19	United States, 1999	2 mo, male	CMV enterocolitis	10	Ganciclovir	2 d	Well (6 mo)	Quiros-Tejeira et al (22)
20	United States, 1999	5 wk, male	CMV enterocolitis	21	Ganciclovir 3 wk, then valganciclovir 1 wk	Several days	Well (11 mo)	Fox et al (23)
21	Netherlands, 1997	5 wk, male	CMV enterocolitis	35	Nil	Not specified	Underlying CMPI (12 mo)	Jonkhoff-Slok et al (24)
22	United States, 1997	7 wk, male	CMV enterocolitis with colonic stricture	14	Nil	Not specified	Well (9 mo)	Reyes et al (25)
23	Taiwan, 1996	6 wk, female	CMV enterocolitis with ileal stricture	19	Nil	Not specified	Well (10.5 mo)	Huang et al (26)
24	Spain, 1975	6 wk, male	CMV enterocolitis	52	Nil	Nil	Died at age 8 wk, intractable diarrhea	Alvarez et al (27)

CMPI = cow's milk protein intolerance; CMV = cytomegalovirus; d = days; mo = month; NA = not available; wk = week.
*Gender not specified.

making it difficult to ignore the clinical impact of introducing ganciclovir therapy.

Control of CMV infection requires intact function of both the innate and adaptive immune systems (31). Control of CMV replication is limited in early life (11), and thus infants may show enhanced vulnerability to severe manifestations of CMV infection, as exemplified by CMV-related necrotizing enterocolitis in the preterm population (32). A range of hypotheses have been proposed for this phenomenon including apparent functional exhaustion of effector CD8 and CD4 T-cells following primary CMV infection in infants (32).

In CMV enterocolitis, lengthy delays to diagnosis are unfortunately commonplace, causing significant morbidity and distress to families. This burden contrasts to the prompt and profound response to ganciclovir once treatment is initiated and the favorable long-term disease outcomes. We suggest greater clinician awareness and a lower threshold to diagnosis and treatment.

CMV enterocolitis should be considered in infants with protracted secretory diarrhea and feeding intolerance as an adjunct to standard algorithms (4). Following initial PCR screening of the urine for CMV, viral titers in blood and endoscopic biopsy should be initiated early to avoid delays in diagnosis. Direct evidence of CMV in the gastrointestinal mucosa may be sparse, particularly if inflammation has been longstanding. Elevated CMV blood titers are not diagnostic in isolation but can be confirmatory if the clinical picture and histopathology are suggestive.

In this child, as in the other 24 collated cases, response to ganciclovir initiation was rapid, enabling weaning from TPN and discharge on full formula feeds with normal growth and development at follow-up. Given the prompt response to ganciclovir, clinicians should expect symptom improvement within a week, enabling use of a short 7–10 day trial of ganciclovir therapy as an adjunctive diagnostic tool.

ACKNOWLEDGMENTS

We would like to thank Dr Melanie Wong and Dr Juliana Puppi for helpful discussions. Parents provided informed patient consent for publication of the case details. A.R.H.-J. conception, design, data collection & data interpretation; drafting & review of article; approval of final version of article; and agreement to be accountable for all aspects of this work, including accuracy and integrity. G.H.C.-T. conception & data collection; review of article; approval of final version of article; and agreement to be accountable for all aspects of this work, including accuracy and integrity. R.K. conception & data interpretation; review of article; approval of final version of article; and agreement to be accountable for all aspects of this work, including accuracy and integrity. M.S., S.A., and P.N.B. conception, design & data interpretation; review of article; approval of final version of article; and agreement to be accountable for all aspects of this work, including accuracy and integrity.

REFERENCES

1. Gugliesi F, Coscia A, Griffante G, et al. Where do we stand after decades of studying human cytomegalovirus? *Microorganisms*. 2020;8:E685.
2. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol*. 2010;20:202–213.
3. Dioverti MV, Razonable RR. Cytomegalovirus. *Microbiol Spectr*. 2016;4. doi: 10.1128/microbiolspec.DMIH2-0022-2015.
4. Thiagarajah JR, Kamin DS, Acra S, et al; PediCODE Consortium. Advances in evaluation of chronic diarrhea in infants. *Gastroenterology*. 2018;154:2045–2059.e6.
5. Osatakul S, Chanpong A, Pruekprasert P. Congenital cytomegalovirus infection presenting with isolated secretory diarrhoea mimicking a congenital diarrhoeal disorder. *J Paediatr Child Health*. 2018;54:460.
6. Sue PK, Salazar-Austin NM, McDonald OG, et al. Cytomegalovirus enterocolitis in immunocompetent young children: a report of two cases and review of the literature. *Pediatr Infect Dis J*. 2016;35:573–576.
7. Park H, Park S, Hong YJ, et al. Cytomegalovirus-associated intussusception with florid vascular proliferation in an infant. *J Pathol Transl Med*. 2015;49:270–273.
8. Hanisch BR, Belani K. CMV esophagitis as a cause of failure to thrive. *Minn Med*. 2014;97:50.
9. Novakova V, Hamprecht K, Müller AM, et al. Severe postnatal CMV colitis with an extensive colonic stenosis in a 2-month-old male immunocompetent term infant infected via breast milk. *J Clin Virol*. 2014;59:259–263.
10. Louazon T, Collardeau S, Lachaux A. [Cytomegalovirus colitis in an immunocompetent child]. *Arch Pediatr*. 2014;21:1016–1019.
11. Refai Z, Nicholls S, Garg A. Infant death due to CMV enterocolitis. *BMJ Case Rep*. 2012;2012:bcr1120115080.
12. Berardi A, Rossi C, Fiorini V, et al. Severe acquired cytomegalovirus infection in a full-term, formula-fed infant: case report. *BMC Pediatr*. 2011;11:52.
13. Breil T, Longerich T, Bettendorf M, et al. An unusual intestinal infection causing intractable diarrhoea of infancy. *J Clin Virol*. 2011;50:97–99.
14. Nigro G, Pietrobattista A, Divito S, et al. Oral gancyclovir therapy for immunocompetent infants with cytomegalovirus-associated hemorrhagic or intractable enterocolitis. *J Pediatr Gastroenterol Nutr*. 2010;50:111–113.
15. Ramos Boluda E, Molina Arias M, Sarría Osses J, et al. [Cytomegalovirus infection causing protracted diarrhea in an immunocompetent child]. *An Pediatr (Barc)*. 2009;70:582–585.
16. Abdulhannan P, Sugarman ID, Wood P, et al. Primary CMV colitis in an immunocompetent infant, successfully treated by gancyclovir. *J Pediatr Gastroenterol Nutr*. 2008;47:203–205.
17. Bonnard A, Le Huidoux P, Carricaburu E, et al. Cytomegalovirus infection as a possible underlying factor in neonatal surgical conditions. *J Pediatr Surg*. 2006;41:1826–1829.
18. Richardson B, Singer JI, Walter J. Case records of Wright State University. Fever in a 5-week-old male. *Pediatr Emerg Care*. 2005;21:130–133.
19. Rongkavilit C, Bedard MP, Ang JY, et al. Severe cytomegalovirus enterocolitis in an immunocompetent infant. *Pediatr Infect Dis J*. 2004;23:579–581.
20. Hinds R, Brueton MJ, Francis N, et al. Another cause of bloody diarrhoea in infancy: cytomegalovirus colitis in an immunocompetent child. *J Paediatr Child Health*. 2004;40:581–582.
21. Weinstein M, Ford-Jones E, Cutz E. Esophagatis and perinatal cytomegalovirus infection. *Pediatr Infect Dis J*. 2001;20:545–546.
22. Quiros-Tejeira RE, Ament ME, Rivera-Penera T, et al. Cytomegalovirus enterocolitis in an immunocompetent infant host: another cause of treatable intractable diarrhea in infancy. *J Pediatr Gastroenterol Nutr*. 1999;29:86–90.
23. Fox LM, Gerber MA, Penix L, et al. Intractable diarrhea from cytomegalovirus enterocolitis in an immunocompetent infant. *Pediatrics*. 1999;103:E10.
24. Jonkhoff-Slok TW, Veenhoven RH, de Graeff-Meeder ER, et al. An immunocompetent infant with cow's milk allergy and cytomegalovirus colitis. *Eur J Pediatr*. 1997;156:528–529.
25. Reyes C, Pereira S, Warden MJ, et al. Cytomegalovirus enteritis in a premature infant. *J Pediatr Surg*. 1997;32:1545–1547.
26. Huang YC, Lin TY, Huang CS, et al. Ileal perforation caused by congenital or perinatal cytomegalovirus infection. *J Pediatr*. 1996;129:931–934.
27. Alvarez I, Polanco I, Ruiz A, et al. [Chronic diarrhea and intestinal cytomegalic inclusion (author's transl)]. *An Esp Pediatr*. 1975;8:603–608.
28. Nakase H, Itani T, Mimura J, et al. Transient protein-losing enteropathy associated with cytomegalovirus infection in a noncompromised host: a case report. *Am J Gastroenterol*. 1998;93:1005–1006.
29. Peckham CS, Johnson C, Ades A, et al. Early acquisition of cytomegalovirus infection. *Arch Dis Child*. 1987;62:780–785.
30. Bar-Meir M, Farrow KN, Melin-Aldana H, et al. Cytomegalovirus enterocolitis mimicking necrotizing enterocolitis: case reports and review of the literature. *J Pediatric Infect Dis Soc*. 2013;2:71–75.
31. Picarda G, Benedict CA. Cytomegalovirus: shape-shifting the immune system. *J Immunol*. 2018;200:3881–3889.
32. Huygens A, Dauby N, Vermijlen D, et al. Immunity to cytomegalovirus in early life. *Front Immunol*. 2014;5:552.