CASE REPORT

Listeria monocytogenes Meningitis Complicating Rotavirus Gastroenteritis in an Immunocompetent Child

Takuma Ohnishi,^{1,2} Akiko Kawano,² Mayumi Araki,² Yuko Hamahata,² Machiko Usui,² Motoko Shimoyamada,² Takuya Tamame,² Masayuki Akashi² and Seiji Sato²

¹ Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan

² Department of Pediatrics, Saitama City Hospital, Saitama, Japan

(Received for publication on July 2, 2016)

(Revised for publication on October 9, 2016)

(Accepted for publication on November 28, 2016)

(Published online on April 7, 2017)

Listeria monocytogenes only occasionally causes bacterial meningitis in immunocompetent children. We report a case of *L. monocytogenes* meningitis associated with rotavirus gastroenteritis. The patient was a previously healthy 20-month-old girl who was admitted because of sustained fever and lethargy after suffering from gastroenteritis for 6 days. The patient's peripheral white blood cell count was 18,600/ μ L and the C-reactive protein level was 2.44 mg/dL. A stool sample tested positive for rotavirus antigen. A cerebrospinal fluid (CSF) sample showed pleocytosis. Cultures of the CSF and stool samples revealed the presence of *L. monocytogenes*. The patient was successfully treated with ampicillin and gentamicin. We speculate that translocation of enteric flora across the intestinal epithelium that had been damaged by rotavirus gastroenteritis might have caused bacteremia that disseminated into the CSF. Both listeriosis and secondary systemic infection after rotavirus gastroenteritis are rare but not unknown. Initiation of appropriate treatment as soon as possible is important for all types of bacterial meningitis. This rare but serious complication should be taken into consideration even if the patient does not have any medical history of immune-related problems. (doi: 10.2302/kjm.2016-0007-CR; Keio J Med 66 (2) : 25–28, June 2017)

Keywords: *Listeria monocytogenes*, meningitis, rotavirus

Introduction

Listeria monocytogenes, a gram-positive facultative intracellular bacterium, is known to infect humans through ingestion of contaminated food. Listeriosis mainly affects neonates, the elderly, and immunocompromised patients, and rarely affects healthy children. Around 20%–25% of listeriosis cases correspond to central nervous system infections such as meningitis, meningoencephalitis, and rhombencephalitis.¹ Some case reports have been published on secondary systemic bacterial infections, mostly caused by gram-negative rods, as a complication of rotavirus gastroenteritis.^{2–14} However, we could find in the English literature no description of listeria meningitis as

a complication of rotavirus infection. Herein, we report a case of *L. monocytogenes* meningitis associated with rotavirus gastroenteritis in an otherwise healthy child.

Case Presentation

A 20-month-old girl was admitted to our hospital because of persistent fever and lethargy. She had had fever, vomiting, and watery diarrhea 6 days prior to admission. Although the vomiting and diarrhea had disappeared by the 5th day of illness, the fever continued. She was previously healthy and had no known medical history suggestive of immunodeficiency. On admission, her temperature was 40°C and her heart rate was 168/min. A

Table 1. Laboratory analysis on admission

Complete blood count		Blood chemistry		CSF analysis	
WBC	18,600 / μ L	CRP	2.44 mg/dL	WBC	1056 / μ L
Hb	11.4 g/dL	T. Bil	0.5 mg/dL	Neutrophil-to-lymphocyte ratio	
Plt	352,000 / μ L	Alb	4.9 g/dL	4:2	
Serum Electrolytes		AST	35 IU/L	Protein	100 mg/dL
		ALT	17 IU/L	Glucose	75 mg/dL
Na	130 mmol/L	LDH	423 IU/L	Bacterial cultures	
K	3.8 mmol/L	UA	2.2 mg/dL	Blood 1st set	Negative
Cl	94 mmol/L	BUN	2.8 mg/dL	Blood 2nd set	Negative
Ca	9.1 mg/dL	Cr	0.22 mg/dL	Stool	<i>Listeria monocytogenes</i>
		Glucose	128 mg/dL	CSF	<i>Listeria monocytogenes</i>
		Ig G	670 mg/dL		
		Ig A	90 mg/dL		
		Ig M	146 mg/dL		

notable finding of the physical examination was nystagmus without consciousness disturbance. The patient had no meningeal signs such as nuchal rigidity, Brudzinski's sign, or Kernig's sign. Her abdomen was flat and soft without tenderness. The results of laboratory analyses on samples taken on admission are given in **Table 1**. Brain computed tomography revealed no abnormal findings. Examination of the cerebrospinal fluid (CSF) obtained by lumbar puncture revealed 1,056 cells/ μ L (neutrophil-to-lymphocyte ratio, 5:4), with glucose and protein concentrations of 75 and 100 mg/dL, respectively. No bacteria were observed on Gram staining of the CSF. Rotavirus antigen was detected in the patient's stool sample by use of immunochromatographic analysis. Rotavirus was also subsequently detected by polymerase chain reaction. Two sets of samples were obtained for blood culture on admission. Analysis of these samples did not reveal the presence of any pathogens. Empirical antimicrobial and antiviral therapies were started with ceftriaxone (100 mg/kg/day), vancomycin (60 mg/kg/day), and acyclovir (30 mg/kg/day). Intravenous dexamethasone (0.15 mg/kg every 6 h) was initiated before administering antibiotics and was continued for 2 days. The patient's clinical course in the hospital is shown in **Fig. 1**. Her clinical condition improved rapidly, but the fever did not subside after the commencement of therapy. On day 3 of hospitalization, CSF sample culture revealed a gram-positive rod; consequently, ampicillin (400 mg/kg/day) was additionally administered. On day 6 of hospitalization, *L. monocytogenes* was recovered from the CSF sample culture. The strain was sensitive to ampicillin, imipenem, erythromycin, minocycline, vancomycin, and levofloxacin, but resistant to cefotiam, cefotaxime, and clindamycin. Ampicillin therapy was maintained, but ceftriaxone, vancomycin and acyclovir were stopped. On day 7 of hospitalization, the fever had still not subsided, and so gentamicin (7 mg/kg/day)

was additionally administered. On hospitalization day 10, contrast magnetic resonance imaging of the head was performed, and it revealed no abnormal findings. The patient completed 21 days of ampicillin therapy and 17 days of gentamicin therapy. Follow-up blood and CSF sample cultures were sterile. The patient was discharged and appeared to be in excellent health on her follow-up visit. We continued to check her health every 6 months until she reached 3 years of age. She has no developmental delay and has not had any subsequent infectious disease. Epidemiological assessment revealed that she had visited a farm with her family the day before the onset of symptoms of gastroenteritis, but the source of infection with *L. monocytogenes* remains unclear.

Discussion

We experienced a rare case of listeria meningitis associated with rotavirus gastroenteritis in a previously healthy 20-month-old girl. Listeria infection is generally an opportunistic infection in immunocompromised patients such as infants, the elderly, and people with malignancies or immunosuppression. Our patient had no medical history that suggested immunodeficiency. Even though *L. monocytogenes* is a known foodborne pathogen causing meningitis and encephalitis, listeria meningitis accounts for only a small percentage of cases of bacterial meningitis. In Japan, Shinjoh *et al.*¹⁵ reported a pediatric epidemiological survey of bacterial meningitis from January 2009 to December 2010. The survey revealed that among 314 patients with bacterial meningitis, only 3 (less than 1%) had listeria meningitis. Improperly processed dairy products and contaminated vegetables are known to be sources of *Listeria* infection.¹⁶ Our patient had visited a farm on the day before the onset of the gastroenteritis symptoms, but the relationship of the condition with lis-

Fig. 1 The patient's clinical course in the hospital. WBC, white blood cells; CRP, C-reactive protein.

Fig. 2 Possible pathogenesis of *Listeria monocytogenes* meningitis complicating rotavirus gastroenteritis. Intestinal villi are damaged by rotavirus gastroenteritis. Such damage facilitates the translocation of *L. monocytogenes*, leading to secondary bacteremia. Finally, *L. monocytogenes* reaches the central nervous system.

teriosis remains unknown.

Secondary bacteremia complicating rotavirus gastroenteritis has rarely been reported, with a prevalence rate of only 0.22%–3.8%.^{4,10} Its pathological mechanism is not fully understood. Rotavirus gastroenteritis might lead to columnar-to-cuboidal epithelial metaplasia, shortening and stunting of the villi, and denudation of the enterocytes in the villous tips.¹⁷ Such damage to the small intestine could facilitate the translocation of *L. monocytogenes*, leading to secondary bacteremia, particularly in the relatively vulnerable intestinal wall of infants. Our patient's stool showed rotavirus and *L. monocytogenes*, which was suggestive of translocation of *Listeria* across the intestinal epithelium damaged by rotavirus gastroenteritis, which could lead to bacteremia. *Listeria* reached the central nervous system by crossing the blood–brain barrier. This possible mechanism is shown in Fig. 2.¹⁸

In patients with listeria meningitis, Gram staining of CSF revealed the causative organism in less than 50% of cases, which is clearly lower than that for other pathogens.¹⁹ Although *L. monocytogenes* was found in the CSF culture, our patient also had negative Gram staining results. None of the blood cultures obtained during the treatment course showed any causative organisms. Nevertheless, we should not exclude listeriosis even if the CSF sample Gram staining result is negative.

When a patient is suspected of having bacterial meningitis, empirical antimicrobial therapy should be administered immediately. For infants with bacterial meningitis, a therapeutic regimen of ceftriaxone and vancomycin is recommended to target the most common pathogens, namely *Streptococcus pneumoniae* and *Haemophilus influenzae*.²⁰ *L. monocytogenes* culture isolated from the CSF specimen from our patient was resistant to ceftriaxone but sensitive to vancomycin. Administration of intravenous ampicillin alone or in combination with gentamicin therapy is recommended for the treatment of listeriosis.¹⁶ In vitro studies have shown that aminoglycoside synergistically enhances the bactericidal activity of ampicillin against *L. monocytogenes*.²¹

To our knowledge, this is the first reported case of *L. monocytogenes* meningitis related to rotavirus gastroenteritis. It is important to obtain not only a blood culture but also a CSF specimen when a child with rotavirus gastroenteritis shows worsening symptoms and neurological symptoms. Awareness of this rare but serious complication is important during rotavirus gastroenteritis, even in a previously healthy child.

References

1. Disson O, Lecuit M: Targeting of the central nervous system by *Listeria monocytogenes*. *Virulence* 2012; **3**: 213–221. [Medline] [CrossRef]

2. Adler A, Wollach B, Kilman A, Gottesman G: Enteric gram-negative sepsis complicating rotavirus gastroenteritis in previously healthy infants. *Clin Pediatr (Phila)* 2005; **44**: 351–354. [Medline] [CrossRef]
3. Lowenthal A, Livni G, Amir J, Samra Z, Ashkenazi S: Secondary bacteremia after rotavirus gastroenteritis in infancy. *Pediatrics* 2006; **117**: 224–226. [Medline] [CrossRef]
4. Gonzalez-Carretero P, Noguera A, Fortuny C: Rotavirus gastroenteritis leading to secondary bacteremia in previously healthy infants. *Pediatrics* 2006; **118**: 2255–6.
5. Carneiro NB, Diniz-Santos DR, Amorim C, Galeno C, Raposo J, Brandão L, Magalhães M, Cathalá R, Sardeiro S, Mello C, Silva LR: Septic shock complicating acute rotavirus-associated diarrhea. *Pediatr Infect Dis J* 2006; **25**: 571–572. [Medline] [CrossRef]
6. Cicchetti R, Iacobini M, Midulla F, Papoff P, Mancuso M, Moretti C: *Pantoea agglomerans* sepsis after rotavirus gastroenteritis. *Pediatr Infect Dis J* 2006; **25**: 280–281. [Medline] [CrossRef]
7. Mel E, Nahum E, Lowenthal A, Ashkenazi S: Extended spectrum beta-lactamase-positive *Escherichia coli* bacteremia complicating rotavirus gastroenteritis. *Pediatr Infect Dis J* 2006; **25**: 962. [Medline] [CrossRef]
8. Kashiwagi Y, Sato S, Nakamura M, Kuboshima S, Numabe H, Kawashima H, Takekuma K, Hoshika A, Matsumoto T: *Klebsiella oxytoca* septicemia complicating rotavirus-associated acute diarrhea. *Pediatr Infect Dis J* 2007; **26**: 191–192. [Medline] [CrossRef]
9. Nakatani K, Koizumi H, Nagano R: Septicemia complicating rotavirus gastroenteritis in 5-year-old child. *Pediatr Infect Dis J* 2009; **28**: 555–556. [Medline] [CrossRef]
10. Ciftçi E, Tapisiz A, Ozdemir H, Güriz H, Kendirli T, Ince E, Doğru U: Bacteraemia and candidaemia: a considerable and underestimated complication of severe rotavirus gastroenteritis. *Scand J Infect Dis* 2009; **41**: 857–861. [Medline] [CrossRef]
11. Longmore DK, Batch JA, McMahon SK, Conwell LS: *Klebsiella pneumoniae* bacteraemia complicating rotavirus gastroenteritis in two infants with glucocorticoid deficiency. *J Pediatr Endocrinol Metab* 2010; **23**: 293–295. [Medline] [CrossRef]
12. Yao TC, Chiu CY, Tsai YC, Huang JL: Viridans streptococcal bacteremia secondary to viral gastroenteritis in a healthy infant. *Pediatr Int* 2010; **52**: e108–e110. [Medline] [CrossRef]
13. Scheier E, Aviner S: Septicemia following rotavirus gastroenteritis. *Isr Med Assoc J* 2013; **15**: 166–169. [Medline]
14. Zlomy M, Kofler S, Orth D, Wurzner R, Heinz-Erian P, Streng A, Prelog M: The impact of rotavirus mass vaccination on hospitalization rates, nosocomial rotavirus gastroenteritis and secondary blood stream infections. *BMC Infect Dis* 2013; **13**: 112,2334–13-112.
15. Shinjoh M, Iwata S, Sato Y, Akita H, Sunakawa K: [Childhood bacterial meningitis trends in Japan from 2009 to 2010]. *Kansenshogaku Zasshi* 2012; **86**: 582–591. [Medline] [CrossRef]
16. Baltimore RS, Murray TS: *Listeria monocytogenes*. In: Kliegman RM, Stanton BF, eds, *Nelson Textbook of Pediatrics*, 20th ed, Philadelphia, Elsevier, 2016; 1349–1352.
17. Lundgren O, Svensson L: Pathogenesis of rotavirus diarrhea. *Microbes Infect* 2001; **3**: 1145–1156. [Medline] [CrossRef]
18. Estes MK, Greenberg HB: Rotaviruses. In: Knipe DM, Howley PM, Cohen JI, eds, *Fields Virology*, 6th ed, Philadelphia, Lippincott Williams & Wilkins, 2013; 1347–1401.
19. Gray LD, Fedorko DP: Laboratory diagnosis of bacterial meningitis. *Clin Microbiol Rev* 1992; **5**: 130–145. [Medline] [CrossRef]
20. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ: Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis* 2004; **39**: 1267–1284. [Medline] [CrossRef]
21. Azimi PH, Koranyi K, Lindsey KD: *Listeria monocytogenes*: synergistic effects of ampicillin and gentamicin. *Am J Clin Pathol* 1979; **72**: 974–977. [Medline] [CrossRef]