Ventriculoperitoneal Shunt Infection Caused by *Enterococcus gallinarum* in a Pediatric Patient: A Case Report

Kacie Clark¹ Deborah Maka²

¹Department of Pharmacy, Florida Hospital Orlando, Orlando, Florida, United States

²Department of Pediatric Pharmacy, Florida Hospital for Children, Orlando, Florida, United States

Address for correspondence Kacie Clark, PharmD, Department of Pharmacy, Florida Hospital Orlando, 601 E Rollins St, Orlando, FL 32803, United States (e-mail: kacie.clark91@gmail.com).

J Pediatr Intensive Care 2019;8:100–102.

Abstract

Keywords

- *Enterococcus*
- ventriculoperitoneal shunt
- meningitis

Enterococcus gallinarum is a common colonizer of the gastrointestinal tract that expresses intrinsic vancomycin resistance. This case report describes an *E. gallinarum* ventriculoperitoneal (VP) shunt infection in a pediatric patient. A 4-year-old female patient presented with cerebrospinal fluid (CSF) cultures from a VP shunt significant for *E. gallinarum*. The patient received ampicillin and synergistic gentamicin. She completed a total of 16 days of therapy following 2 weeks of negative CSF and blood cultures with full clinical cure of infection. The patient was successfully treated following a 2-week course of antibiotics. Awareness of *Enterococcus* species with intrinsic vancomycin resistance should be increased.

Introduction

Enterococcus species are an uncommon pathogen in meningitis, accounting for only 0.3 to 4% of cases.¹ *Enterococci* remain a relevant healthcare-associated concern due to the rise in vancomycin-resistant organisms. *Enterococcus casseliflavus* and *Enterococcus gallinarum* are common colonizers of the gastrointestinal tract that express intrinsic vancomycin resistance via the VanC gene. This case report describes an *E. gallinarum* ventriculoperitoneal (VP) shunt infection in a pediatric patient.

Case Report

A 4-year-old female patient presented to the hospital with fever and redness along her VP shunt track. Her past medical history was significant for Seckel syndrome, dwarfism, hydranencephaly, VP shunt placement (at 1 year of age), gastroesophageal reflux disease (GERD), gastro-jejunal (GJ)-tube dependent, and tracheostomy with home mechanical ventilation at night. The patient's mother reported no lethargy, but an

increase in irritability. Diagnostic work-up was significant for white blood count (WBC) $28.5 \times 10^3/\text{mm}^3$, bands 32%, and a negative respiratory polymerase chain reaction (PCR). Initial procalcitonin level and C-reactive protein (CRP) count were 7.97 ng/mL and 95.7 mg/L, respectively. Chest X-ray showed no local consolidation and head computed tomography (CT) showed no acute changes from a comparison image 2 months prior. She was initiated empirically on ceftriaxone 50 mg/kg intravenously every 12 hours and vancomycin 20 mg/kg every 6 hours.

Neurosurgery was consulted for a shunt tap. Nine mL of clear cerebrospinal fluid (CSF) was aspirated under low pressure and was sent for analysis and cultures. Fluid analysis was clear and showed nucleated cells 280×10^6 cells/L, red blood cells 20, negative xanthochromia, neutrophils 99%, glucose 12 mg/dL, and protein 44 mg/dL. CSF Gram stain was significant for Gram-positive cocci, and the patient was taken to the operation room (OR) for a left frontal VP shunt removal and a left frontal external ventricular drain (EVD) placement. Final cultures were significant for *E. gallinarum*. Sensitivities for *E. gallinarum* showed vancomycin resistance (minimum

received

June 23, 2018

accepted after revision

August 17, 2018

published online

October 11, 2018

Copyright © 2019 by Georg Thieme Verlag KG, Stuttgart · New York

DOI <https://doi.org/10.1055/s-0038-1672194>.
ISSN 2146-4618.

inhibitory concentration [MIC] 8) and susceptibility to ampicillin (MIC ≤ 2), linezolid (MIC 1) and were negative for gentamicin high-level resistance. Of note, the original culture was reported as *E. casseliflavus*. Subsequent positive cultures were reported as *E. gallinarum*; therefore, a co-infection was thought to be present. This was not corrected by the laboratory until hospital day 6 when *E. gallinarum* was reported by the laboratory as the sole organism.

The patient was started on ampicillin 75 mg/kg intravenously every 6 hours. Gentamicin was added for synergy at a dose of 2.5 mg/kg intravenously every 8 hours. Target peak levels were established as 8 to 12 μ /mL, and target trough levels were ≤ 1.5 μ /mL. She maintained goal levels throughout her course of therapy. There were no fluctuations in serum creatinine or urine output. The CSF cultures from ampicillin/gentamicin day 3 and onward were consistently negative. There were no fevers documented throughout admission, and procalcitonin levels trended down to 0.13 ng/mL by hospital day 15. On hospital day 17, the patient underwent a repeat VP shunt insertion with Delta valve (performance level III) and re-internalization on the right side. She completed a total of 16 days of ampicillin and gentamicin following 2 weeks of negative CSF and blood cultures.

Discussion

Enterococcus gallinarum was first isolated in 1978 as a subspecies of *Streptococcus* before being renamed, along with *casseliflavus*, as part of the *Enterococcus* genus in 1984.¹ A diagnostic test for these organisms did not exist until 1989. They are commonly referred to as motile *Enterococcus* species. While rare isolation in humans may be due to detection and isolation limitations, the clinical impact of a pathogenic strain is not well understood. Retrospective studies have reported a 1% occurrence of *Enterococcus* bacteremia with mortality of approximately 2%.

Enterococci present with intrinsic resistance to antimicrobials utilized for other gram-positive cocci infections. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria report MIC ranges for *E. gallinarum* as 1 to 32 mg/L for ampicillin, 0.5 to 16 mg/L for imipenem, 0.5 to 16 mg/L for piperacillin, and 0.032 to 0.25 mg/L for tigecycline. MIC distributions for *E. casseliflavus* are 0.5 to 32 mg/L for ampicillin, 0.25 to 16 mg/L for imipenem, and 0.032 to 0.25 mg/L for tigecycline.² Unfortunately, ampicillin resistance may be increasing based on a 2008 study that reported a 15% ampicillin resistance rate for non-*faecalis*, non-*faecium* *Enterococci*.³ Inference of susceptibility to anti-enterococcal beta-lactam agents from ampicillin sensitivity should also be done with caution. Britt and Potter found a higher rate of reoccurrence and microbiological failure in *E. gallinarum* and *E. casseliflavus* bacteria when treated with anti-enterococcal beta-lactam agents, such as piperacillin-tazobactam, versus an anti-vancomycin-resistant enterococci (VRE) agent (linezolid or daptomycin).⁴ While *E. gallinarum* and *E. casseliflavus* carry low levels of resistance to aminoglycosides, it is cornerstone practice to utilize these agents for synergistic purposes.

Both *E. gallinarum* and *E. casseliflavus* exhibit intrinsic resistance to vancomycin.¹ The VanC phenotype of these organisms weakens vancomycin binding to the novel pentapeptide, blocking its mechanism of action. *E. gallinarum* will typically have high vancomycin resistance (MIC ≥ 8 mg/L). While *E. casseliflavus* shows lower MIC values (2–4 mg/L), it still expresses higher distribution than do other *enterococci*. There has been documentation that *E. gallinarum* has demonstrated other vancomycin-resistant phenotypes, such as VanA and VanB. In regards to these organisms harboring intrinsic low-level resistance, clinicians should recognize that some antimicrobial susceptibility tests might report these vancomycin MIC values as “susceptible.” This is especially important for some *E. casseliflavus* strains (MIC 2–4 mg/L) as EUCAST reports *Enterococcus* species vancomycin resistance as MIC > 4 mg/L.² Despite vancomycin susceptibility, vancomycin monotherapy has been reported with high clinical failure in previous studies.^{5,6}

Two pediatric cases have been previously described. Takayama et al described the case of a 12-year-old male in 1995 who developed *E. gallinarum* meningitis following a tumor resection and VP shunt insertion.⁷ He received an 8-week course of ampicillin (2 g every 12 hours) with full clinical cure. A 2018 case report of a 2-day-old neonate male utilized a 2-week course of linezolid that resulted in reoccurrence 10 days after discharge.⁸ The patient was treated with a second 3-week course of linezolid with full clinical cure. Two adult cases, one with a VP shunt, utilized a 3-week course of ampicillin (12 g/day) and synergistic gentamicin.^{9,10} Both patients had either intermediate or resistant sensitivity to vancomycin.

A literature review found only a single case report of *E. casseliflavus* meningitis. A 77-year-old female patient presented with meningitis-like symptoms with no recent surgery or head trauma.¹¹ Her past medical history was significant for rheumatoid arthritis treated with steroids and methotrexate. CSF analysis was indicative of bacterial meningitis. She was empirically started on meropenem, cotrimoxazole, acyclovir, and dexamethasone. *E. casseliflavus* was isolated via culture showing sensitivity to penicillin, ampicillin-sulbactam, imipenem, teicoplanin, tetracyclines, and linezolid. It exhibited intermediate sensitivity to vancomycin (MIC ≥ 8 μ /mL) and high resistance to gentamicin (MIC $\geq 2,000$ μ /mL). Ampicillin-sulbactam 3 g every 6 hours was added to meropenem and the patient completed a 2-week antimicrobial course. A colonoscopy revealed multiple erosions via ulcerative lesions, which were likely the source of *E. casseliflavus*. The authors acknowledge that there was not a true indication for the addition of meropenem to ampicillin-sulbactam for the patient's treatment.

The patient discussed above had a known risk factor for *Enterococcus* meningitis. While she did not present with hallmark meningitis symptoms, the presence of a VP shunt should place enterococcal meningitis in the diagnostic work-up due to the risk of gastrointestinal translocation. The association of gastrostomy feeding tubes (GT) in the presence of VP shunts has also been associated with infectious complications. Gassas et al¹² evaluated approximately 1,100 children with brain

tumors who had concomitant VP shunts and a GT. While not statistically significant, the study found a 23.5% VP shunt infection rate versus 8.8% in the control group and concluded that GT complications in the setting of a VP shunt could result in a higher infection risk.

As *E. gallinarum/casseliflavus* meningitis has so few case reports in literature, predicting an organism with intrinsic vancomycin resistance in a patient with no history would be extremely challenging. Therefore, an empiric course of vancomycin and ceftriaxone was appropriate. Transition to standard-of-care ampicillin plus aminoglycoside synergy occurred on hospital day 3, and CSF sterility was observed. While more recent adult cases extended therapy to 3 weeks, clinical success was seen in this patient with only 2 weeks of therapy from the first negative culture. Due to significant rises in antimicrobial resistance and emphasis on stewardship, a reduction in 7 days of therapy could be considered clinically significant for both adult and pediatric patients. The laboratory update of an *E. casseliflavus* co-infection to *E. gallinarum* as a solitary cause of the patient's infection are not clinically significant in regard to choice of therapy, but it is important to recognize the intrinsic vancomycin resistance for both organisms.

Conclusion

To the authors' knowledge, this is the first case report of an *E. gallinarum* meningitis in a pediatric patient treated with standard-of-care ampicillin and synergistic gentamicin. Patient history, treatment, and outcomes should aid in guidance of therapy to ensure appropriate coverage of motile *Enterococcus* species. Awareness of *Enterococcus* species with intrinsic vancomycin resistance should be increased, especially for applicability of patients with known risk factors.

Conflict of Interest
None declared.

References

- Monticelli J, Knezevich A, Luzzati R, Di Bella S. Clinical management of non-faecium non-faecalis vancomycin-resistant enterococci infection. Focus on *Enterococcus gallinarum* and *Enterococcus casseliflavus/flavescens*. J Infect Chemother 2018; 24(04):237–246
- The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 8.1, 2018. Available at: <http://www.eucast.org>
- Brown DF, Hope R, Livermore DM, et al; BSAC Working Parties on Resistance Surveillance. Non-susceptibility trends among enterococci and non-pneumococcal streptococci from bacteraemias in the UK and Ireland, 2001–06. J Antimicrob Chemother 2008;62 (Suppl 2):ii75–ii85
- Britt NS, Potter EM. Clinical epidemiology of vancomycin-resistant *Enterococcus gallinarum* and *Enterococcus casseliflavus* bloodstream infections. J Glob Antimicrob Resist 2016;5:57–61
- Choi SH, Lee SO, Kim TH, et al. Clinical features and outcomes of bacteremia caused by *Enterococcus casseliflavus* and *Enterococcus gallinarum*: analysis of 56 cases. Clin Infect Dis 2004;38(01):53–61
- Reid KC, Cockerill FR III, Patel R. Clinical and epidemiological features of *Enterococcus casseliflavus/flavescens* and *Enterococcus gallinarum* bacteremia: a report of 20 cases. Clin Infect Dis 2001; 32(11):1540–1546
- Takayama Y, Sunakawa K, Akahoshi T. Meningitis caused by *Enterococcus gallinarum* in patients with ventriculoperitoneal shunts. J Infect Chemother 2003;9(04):348–350
- Li X, Fan S, Lin X, et al. The first case report of *Enterococcus gallinarum* meningitis in neonate: a literature review. Medicine (Baltimore) 2018;97(07):e9875
- Antonello VS, Zenkner FM, França J, Santos BR. *Enterococcus gallinarum* meningitis in an immunocompetent host: a case report. Rev Inst Med Trop São Paulo 2010;52(02):111–112
- Kurup A, Tee WS, Loo LH, Lin R. Infection of central nervous system by motile *Enterococcus*: first case report. J Clin Microbiol 2001;39(02):820–822
- Iaria C, Stassi G, Costa GB, Di Leo R, Toscano A, Cascio A. Enterococcal meningitis caused by *Enterococcus casseliflavus*. First case report. BMC Infect Dis 2005;5(01):3
- Gassas A, Kennedy J, Green G, et al. Risk of ventriculoperitoneal shunt infections due to gastrostomy feeding tube insertion in pediatric patients with brain tumors. Pediatr Neurosurg 2006;42 (02):95–99