

Enterococcal Meningitis/Ventriculitis: A Tertiary Care Experience

Abstract

Context: Enterococcal meningitis is very rare among bacterial meningitis and has variable clinical outcomes. **Aims:** The purpose of the current study is to evaluate clinical features, therapeutic options with susceptibility profile, and outcomes of enterococcal meningitis in a tertiary care hospital. **Settings and Design:** We retrospectively reviewed medical records of all patients with enterococcal meningitis over the periods of 4 years. **Subjects and Methods:** The clinical and laboratory data of all patients with enterococcal meningitis were evaluated between 2013 and 2016. **Results:** Six cases of enterococcal meningitis were found (three infant and three adults). All patients developed meningitis after neurosurgical procedures, and majority of patients (four out of six) had central nervous system (CNS) devices *in situ* at the time of development of meningitis. The causative organism isolated from cerebrospinal fluid (CSF) culture of all patients was *Enterococcus* species only. All *Enterococcus* spp. were resistant to ampicillin, Amoxicillin-clavulanate, and oxytetracycline and two isolates were also resistant to vancomycin. Four patients with vancomycin-sensitive *Enterococcus* spp. were treated with vancomycin alone for mean periods of 18 days (14–21 days). One patient with vancomycin-resistant *Enterococcus* (VRE) meningitis was treated with linezolid alone, and another one requires combination with rifampicin to achieve microbiological clearance of CSF. CNS devices were removed in all patients. No mortality was reported in current case series. **Conclusions:** Enterococcal meningitis is very uncommon, mostly associated with neurosurgical intervention. Early treatment is associated with favorable outcomes. Removal of CNS devices is recommended to achieve a clinical cure.

Keywords: *Enterococcus* species, nosocomial meningitis, vancomycin-resistant *Enterococcus*

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Introduction

Enterococcus, a normal commensal of human gastrointestinal and genitourinary tract, is now increasingly being recognized as one of the causative agents of healthcare-associated infections such as surgical site infections and urinary tract infections over the past few decades.^[1,2] The management of infections secondary to *Enterococcus* species (*Enterococcus* spp) is difficult because *Enterococcus* not only possesses intrinsic resistance to many antimicrobial agents but also has the ability to acquire resistance against antibiotics through genetic mutation.^[3]

Enterococcal meningitis is very rare among bacterial meningitis and mostly nosocomial in origin.^[4,5] Risk factors for enterococcal meningitis are neurosurgical procedures, underlying immunosuppression, enterococcal infection, or colonization at other sites of the body and central nervous system (CNS) devices.^[4-6] CNS infections

secondary to *Enterococcus* spp. are associated with high mortality.^[5-7]

In this study, we have looked at the clinical features, therapeutic options with antimicrobial susceptibility, and outcomes of enterococcal meningitis in a tertiary care hospital.

Subjects and Methods

We retrospectively reviewed medical records of all patients with acute bacterial meningitis admitted to our hospital over the periods of 4 years, i.e., from 2013 to 2016.

Patient's clinical records, microbiology and other laboratory data were reviewed. In the present study, the criteria of acute bacterial meningitis were as follows:

- Patients with clinical presentation of acute bacterial meningitis including fever, seizure, altered mental status, and headache
- Positive cerebrospinal fluid (CSF) culture in patients with clinical presentation of acute bacterial meningitis.

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CSF parameters:

- Leucocytes count ≥ 10
- CSF glucose $< 2/3$ of blood glucose or < 45 mg/dl if no simultaneous blood glucose available.

Nosocomial or healthcare-associated meningitis or ventriculitis was defined as clinical features and CSF findings not present at the time of admission and developed 48 hrs after admission. Mixed infection was defined as at least two or more than two organisms isolated from CSF culture (exclusion criteria of study). The antibiotics susceptibility was based on Clinical Laboratory Standard Institute document M-100.

Results

Demographic data

During the study period from years 2013 to 2016, a total of six patients were diagnosed with identified as enterococcal meningitis/ventriculitis including three children (age from 2–12 months) and 3 adults (age range from 40 to 71 years). All patients had single pathogen isolated from CSF that is *Enterococcus* spp.

Clinical features of the subjects

All of the patients developed meningitis after neurosurgical procedures such as craniotomy, repair of myelomeningocele, and ventriculoperitoneal (VP) shunt. Majority of patients (4 out of 6) had CNS devices *in situ* at the time of development of meningitis. Clinical features and management are given in Table 1.

Organism isolated and antibiotic sensitivity and resistance

Blood cultures and other body site cultures were negative for *Enterococcus* as well as other organisms. The causative organism isolated from CSF culture of all patients was

Enterococcus spp. only and none of the patients had mixed bacterial infection. The organism was present in Gram stain of CSF and isolated on blood agar culture medium. It was identified by conventional biochemical reactions, API 20 STREP (BIOMERIEUX), and its intrinsic resistance to ceftriaxone and clindamycin. The antibiotic susceptibility was checked on Muller-Hinton agar by disk diffusion method and vancomycin minimum inhibitory concentration was checked with E-strip (gradient diffusion method).

In all patients, *Enterococcus* spp. was resistant to ampicillin, Amoxicillin-clavulanate, and oxytetracycline. Vancomycin-resistant *Enterococcus* (VRE) was also isolated in CSF of two of our patients; however, VRE strains showed sensitivity to linezolid and chloramphenicol.

Outcome

All patients treated with antibiotics according to culture and sensitivities and cured as repeat CSF cultures were negative. Only two patients became neurologically dependent because of their associated neurological condition and no mortality reported in the current case series.

Discussion

Postoperative CNS infection after neurosurgical procedures is a serious problem with a reported incidence of 0.8%–8%.^[8–11] The common bacterial pathogens associated with nosocomial meningitis after neurosurgical interventions are *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, Gram-negative bacilli such as *Pseudomonas aeruginosa*, *Acinetobacter*, and *Propionibacterium acnes*.

Intracranial device can predispose to infections that could be due to contamination and/or colonization of implanted devices.^[4–6] Additional risk factors include the presence of infection with *Enterococcus* spp. in other sites of the body,

Table 1: Clinical data of patients with enterococcal meningitis

Patient	Age/sex	Infection pattern	Underlying condition	Clinical features	Microorganisms	Treatment with duration	Outcome
1	40 years/ female	Nosocomial	Craniotomy secondary to meningioma	Fever, vomiting	<i>Enterococcus</i> species	Ceftriaxone \times 4 days and vancomycin for 14 days	Cured
2	1 year/ male	Nosocomial	MMC repair, VP shunt	Fever, vomiting	VRE	Meropenem \times 5 days, linezolid \times 21 days	Cured
3	2 months/ male	Nosocomial	MMC repair, VP shunt	Fever, neck stiffness, altered conscious level	<i>Enterococcus</i> species	Meropenem \times 7 days, vancomycin \times 21 days	Cured
4	52 years/ female	Nosocomial	DM, craniotomy sec to intracranial bleed, EVD	Fever, headache, vomiting, altered conscious level	<i>Enterococcus</i> species	Meropenem \times 6 days, vancomycin for 21 days	Cured
5	1 year/ female	Nosocomial	MMC repair	Fever, vomiting, seizures	<i>Enterococcus</i> species	Meropenem \times 4 days, vancomycin \times 14 days	Cured
6	71 years/ female	Nosocomial	Intracranial bleed, EVD	Fever, altered conscious level	VRE	Linezolid \times 27 days and rifampicin \times 17 days	Cured

MMC – Myelomeningocele; VP shunt – Ventriculo-peritoneal shunt; VRE – Vancomycin resistant *Enterococcus*; DM – Diabetes mellitus; EVD – External ventricular drainage

underlying chronic illnesses, and immunosuppressive states such as diabetes and steroids therapy.^[5,6,12,13]

The emergence of resistant *Enterococcus* strains has complicated the management of enterococcal infection. The invasive enterococcal infections such as endocarditis require a combination of cell wall-active agents with other susceptible antimicrobials such as aminoglycoside to achieve synergistic bactericidal activity. The simultaneous use of a cell wall-active agent raises the permeability of the cell so that an intracellular bactericidal concentration of accompanying antibiotic can be achieved.^[14] Even though previously published cases of enterococcal meningitis were treated with beta-lactam, glycopeptides, or other susceptible antibiotics either alone or in combination,^[5,13] vancomycin can be used as a single agent with good clinical response.

Vancomycin-resistant enterococcal meningitis/ventriculitis (VRE meningitis/ventriculitis) is very rare and only reported in the form of case report and case series in literature. Limited therapeutic options are available for vancomycin-resistant CNS infections and best possible therapy has not been established.^[15,16] VRE infections are successfully treated with antibiotics such as linezolid, daptomycin, quinupristin-dalfopristin, rifampicin, and gentamicin.^[17-19] The first case of treatment of VRE meningitis with linezolid was reported in 2001. Linezolid has good meningeal penetration and is used alone or in combination with other susceptible antibiotics for VRE meningitis/ventriculitis with favorable clinical outcome.^[20-23]

Intrathecal or intraventricular antibiotics have been increasingly utilized in cases of nosocomial meningitis/ventriculitis when systemic therapy is unable to sterilize CSF. Antibiotics used for intrathecal or intraventricular route for cases of VRE meningitis/ventriculitis are linezolid, gentamicin, daptomycin, chloramphenicol, and quinupristin/dalfopristin.^[15,24-27] Removal of infected hardware like VP shunt is also recommended for better treatment outcome.^[28] Although reported mortality is high with enterococcal CNS infection,^[5,13] timely initiation of appropriate therapy improves outcomes.

Conclusions

Enterococcal meningitis should be suspected in patients who developed CNS infection during hospital stay, especially after neurosurgical procedures. As enterococcal meningitis is associated with significant mortality, early recognition and appropriate therapeutic intervention have prime importance for good clinical outcome.

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Conflicts of interest

There are no conflicts of interest.

References

- Giridhara Upadhyaya PM, Ravikumar KL, Umapathy BL. Review of virulence factors of *Enterococcus*: An emerging nosocomial pathogen. *Indian J Med Microbiol* 2009;27:301-5.
- Olawale KO, Fadiora SO, Taiwo SS. Prevalence of hospital-acquired enterococci infections in two primary-care hospitals in Osogbo, Southwestern Nigeria. *Afr J Infect Dis* 2011;5:40-6.
- Hollenbeck BL, Rice LB. Intrinsic and acquired resistance mechanisms in *Enterococcus*. *Virulence* 2012;3:421-33.
- Laguna Del Estal P, García Zubiri C, García Madero R, Gil Navarro M. Enterococcal meningitis in adults. *Neurologia* 2009;24:245-8.
- Pintado V, Cabellos C, Moreno S, Meseguer MA, Ayats J, Viladrich PF, et al. Enterococcal meningitis: A clinical study of 39 cases and review of the literature. *Medicine (Baltimore)* 2003;82:346-64.
- Lu Y, Huang C, Lu C, Chang W, Chen N, Chuang Y. Clinical characteristics and therapeutic outcomes of adult enterococcal meningitis. *J Int Med Taiwan* 2014;25:424-31.
- Dhanalakshmi TA, Vijaya S, Sharieff S. Spontaneous enterococcal meningitis: A case report. *J Med Sci Health* 2015;1:1-2.
- McClelland S 3rd, Hall WA. Postoperative central nervous system infection: Incidence and associated factors in 2111 neurosurgical procedures. *Clin Infect Dis* 2007;45:55-9.
- Chen C, Zhang B, Yu S, Sun F, Ruan Q, Zhang W, et al. The incidence and risk factors of meningitis after major craniotomy in China: A retrospective cohort study. *PLoS One* 2014;9:e101961.
- van de Beek D, Drake JM, Tunkel AR. Nosocomial bacterial meningitis. *N Engl J Med* 2010;362:146-54.
- Erdem I, Hakan T, Ceran N, Metin F, Akcay SS, Kucukercan M, et al. Clinical features, laboratory data, management and the risk factors that affect the mortality in patients with postoperative meningitis. *Neurol India* 2008;56:433-7.
- Hebbbar S, Upadhyaya S. A case of enterococcal meningitis in a healthy infant. *Int J Infect Dis* 2004;4:1-3.
- Stevenson KB, Murray EW, Sarubbi FA. Enterococcal meningitis: Report of four cases and review. *Clin Infect Dis* 1994;18:233-9.
- Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr., Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A Scientific statement for healthcare professionals from the American Heart Association. *Circulation* 2015;132:1435-86.
- Wang JS, Muzevich K, Edmond MB, Bearman G, Stevens MP. Central nervous system infections due to vancomycin-resistant enterococci: Case series and review of the literature. *Int J Infect Dis* 2014;25:26-31.
- Knoll BM, Hellmann M, Kotton CN. Vancomycin-resistant *Enterococcus faecium* meningitis in adults: Case series and review of the literature. *Scand J Infect Dis* 2013;45:131-9.
- Heintz BH, Cho S, Fujioka A, Li J, Halilovic J. Evaluation of the treatment of vancomycin-resistant enterococcal urinary tract infections in a large academic medical center. *Ann Pharmacother* 2013;47:159-69.
- Patel R, Gallagher JC. Vancomycin-resistant enterococcal bacteremia pharmacotherapy. *Ann Pharmacother* 2015;49:69-85.
- Erlandson KM, Sun J, Iwen PC, Rupp ME. Impact of the more-potent antibiotics quinupristin-dalfopristin and linezolid on outcome measure of patients with vancomycin-resistant *Enterococcus* bacteremia. *Clin Infect Dis* 2008;46:30-6.

20. Luque S, Grau S, Alvarez-Lerma F, Ferrández O, Campillo N, Horcajada JP, *et al.* Plasma and cerebrospinal fluid concentrations of linezolid in neurosurgical critically ill patients with proven or suspected central nervous system infections. *Int J Antimicrob Agents* 2014;44:409-15.
21. Steinmetz MP, Vogelbaum MA, De Georgia MA, Andrefsky JC, Isada C. Successful treatment of vancomycin-resistant *Enterococcus* meningitis with linezolid: Case report and review of the literature. *Crit Care Med* 2001;29:2383-5.
22. Qiu JJ, Tang J, Li DL. Success of linezolid therapy for post neurosurgical ventriculitis due to vancomycin-resistant *Enterococcus faecium*: Case report and literature review. *Chin Neurosurg J* 2015;1:18.
23. da Silva PS, Monteiro Neto H, Sejas LM. Successful treatment of vancomycin-resistant *Enterococcus* ventriculitis in a child. *Braz J Infect Dis* 2007;11:297-9.
24. Lich BF, Conner AK, Burks JD, Glenn CA, Sughrue ME. Intrathecal/Intraventricular linezolid in multidrug-resistant *Enterococcus faecalis* ventriculitis. *J Neurol Surg Rep* 2016;77:e160-1.
25. Mueller SW, Kiser TH, Anderson TA, Neumann RT. Intraventricular daptomycin and intravenous linezolid for the treatment of external ventricular-drain-associated ventriculitis due to vancomycin-resistant *Enterococcus faecium*. *Ann Pharmacother* 2012;46:e35.
26. Tan TY, Pitman I, Penrose-Stevens A, Simpson BA, Flanagan PG. Treatment of a vancomycin-resistant *Enterococcus faecium* ventricular drain infection with quinupristin/dalfopristin and review of the literature. *J Infect* 2000;41:95-7.
27. Hartmann C, Peter C, Hermann E, Ure B, Sedlacek L, Hansen G, *et al.* Successful treatment of vancomycin-resistant *Enterococcus faecium* ventriculitis with combined intravenous and intraventricular chloramphenicol in a newborn. *J Med Microbiol* 2010;59:1371-4.
28. Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Michael Scheld W, *et al.* 2017 infectious diseases society of America's clinical practice guidelines for healthcare-associated ventriculitis and meningitis. *Clin Infect Dis* 2017;64:e34-e65.