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Original Article

Enterococcal Meningitis/Ventriculitis: A Tertiary Care Experience

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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*

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:

a. Leucocytes count ≥10
b. 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	*Enterococcus* species	Ceftriaxone × 4 days and vancomycin for 14 days	Cured
2	1 year/ male	Nosocomial	MMC repair, VP shunt	Fever, vomiting	VRE	Meropenem × 5 days, linezolid × 21 days	Cured
3	2 months/ male	Nosocomial	MMC repair, VP shunt	Fever, neck stiffness, altered conscious level	*Enterococcus* species	Meropenem × 7 days, vancomycin × 21 days	Cured
4	52 years/ female	Nosocomial	DM, craniotomy sec to intracranial bleed, EVD	Fever, headache, vomiting, altered conscious level	*Enterococcus* species	Meropenem × 6 days, vancomycin for 21 days	Cured
5	1 year/ female	Nosocomial	MMC repair	Fever, vomiting, seizures	*Enterococcus* species	Meropenem × 4 days, vancomycin × 14 days	Cured
6	71 years/ female	Nosocomial	Intracranial bleed, EVD	Fever, altered conscious level	VRE	Linezolid × 27 days and rifampicin × 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.

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