

RESEARCH ARTICLE

Enterococcal meningitis/ventriculitis in Qatar—Experience with eight patients

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ABSTRACT

Background & objectives: Enterococcal meningitis/ventriculitis (EMV) is a relatively rare condition that usually affects patients with underlying diseases. This study was designed to describe the clinical profile, laboratory parameters, treatment, and outcomes of EMV in patients admitted to Hamad General Hospital, Qatar.

Methods and material: This retrospective hospital-based study described the patients with EMV from 2009 to 2013.

Results: Eight patients were recruited for the study. Their median age was 42 years (21.50–53.75 years). Six patients (75%) were males, and two (25%) were females. Fever was the most common presenting symptom being present in seven (87.5%) cases. Six patients (75%) had nosocomial EMV, and all acquired the infection after placement of an external ventricular drain (EVD). The isolated species include seven (87.5%) *E. faecalis* and one (12.5%) *E. gallinarum*, and all of them were sensitive to ampicillin and vancomycin. In all patients with nosocomial EMV, the infected EVDs were removed, and the eight patients received empirical antibiotics that were modified upon receipt of culture results. All patients were cured, and no mortality was reported.

Conclusions: EMV is a recognized complication related to the introduction of EVD, whereas community-acquired enterococcal meningitis was reported among children who had no established risk factors or immunosuppression. Because of its nonspecific clinical presentation, treating physicians should have a high suspicion index.

Keywords: meningitis; ventriculitis; external ventricular drain; *Enterococcus* species; ampicillin; and vancomycin

INTRODUCTION

Enterococci are gram-positive bacteria belonging to the genus *Enterococcus*.¹ These ubiquitous bacteria can be found in the normal gut microbiota of humans and many animals. In contrast, in hospitalized patients, the main colonization sites are soft tissue wounds, ulcers, and the gastrointestinal tract.² Enterococci are traditionally considered to be low-virulent pathogens. However, in recent years, the *Enterococcus* species have emerged as significant causes of both nosocomial and community-acquired infections in adults and children,^{1,3,4} reflecting a possible change in the epidemiology of the bacteria. Enterococcal meningitis/ventriculitis (EMV) is a relatively rare disease that accounts for 0.3%–4% of bacterial meningitis cases.⁵ Affected patients generally have underlying diseases and most have a history of neurosurgery, immunosuppression, or prolonged antibiotic therapy.^{1,4–8} Few studies describe the clinical pattern of EMV, and most data come from case reports.

In Qatar, EMV is uncommon, representing 6.8% of bacterial meningitis cases.⁹ This study aimed to describe the clinical presentation, laboratory data, treatment, and outcomes of this clinical condition in patients admitted to Hamad General Hospital.

METHODS AND MATERIALS

This secondary *post-hoc* analysis was performed on data collected from the previous study, Acute Bacterial Meningitis in Qatar: A Clinical Study from 2009 to 2013,⁹ with different objectives. All EMV cases were identified from the primary study and the collected data were reanalyzed. The primary study was approved by the medical research committee at Hamad Medical Corporation (#13254/13).

The diagnosis of EMV was considered if *Enterococcus* was recovered from cerebrospinal fluid (CSF) in the setting of clinical and laboratory evidence of meningitis.⁶ In all patients with an external ventricular drain (EVD), bacteria were isolated from CSF obtained from the ventricles. All EVDs used were simple, and the placement procedure was performed in the operating room without antibiotic administration. The isolation of *Enterococcus* from CSF with normal cell counts and the absence of clinical symptoms were designated as contaminants.⁷

EMV was considered nosocomial if the diagnosis was made after more than 48 hours of hospitalization or within a short period (i.e., usually within one month after

discharge from the hospital where the patient had received an invasive procedure, especially a neurosurgical procedure). On the other hand, EMV was considered community-acquired if the diagnosis was made within the first 48 hours of hospitalization, and the patient was not hospitalized in the preceding month. The case was considered cured when two successive cultures were negative for enterococci species, and the clinical signs of infection (fever and meningism) were absent during therapy or when therapy was discontinued.⁹ Cases with polymicrobial isolates were excluded. Empirical antimicrobial therapy was started no later than 24 hours after taking the CSF sample for the culture in accordance with hospital guidelines.⁹

Data were reported as the median with the interquartile range (IQR) for quantitative variables, whereas qualitative variables were described as numbers and percentages.

RESULTS

Of the eight cases recruited in this study, six (75%) were males, and two (25%) were females with a median age of 42 years (IQR: 21.50–53.75 years). Fever was the most common presenting symptom and presented in seven (87.5%) cases. Other symptoms and signs in the order of their decreasing frequency were mental alterations five (62.5%), vomiting four (50%), headache three (37.5%), seizures two (25%), focal neurological signs one (12.5%), meningism one (12.5%), and bulging fontanelle one (12.5%). Table 1 describes the clinical characteristics of the eight patients enrolled in this series.

Six (75%), cases were nosocomially acquired, and often after EVD insertion. The median time between EVD insertion and infection acquisition was 13.5 days (IQR: 9.25–17.75 days).

The CSF showed pleocytosis in all cases with a polymorphonuclear predominance (Table 1). The median percentage of neutrophils was 63% (IQR: 21.75%–81.50%). Elevated total protein levels with a median of 66 g/dL (51.75–98 g/dL) and low glucose levels with a median of 2.80 mg/dl (1.73–3.0mg/dl) were also noted. The isolated species included seven (87.5%) *E. faecalis* and one (12.5%) *E. gallinarum*. Antimicrobial susceptibility is described in Table 2. All isolates were sensitive to ampicillin and vancomycin.

All patients with nosocomial EMV had infected EVDs removed. Moreover, the eight patients receiving

Table 1. Clinical and cerebrospinal fluid characteristics at the time of presentation of involved patients

Variable	Value N (%) / Median (IQR)
Fever	7 (87.5%)
Mental alteration	5 (62.5%)
Vomiting	4 (50%)
Headache	3 (37.5%)
Seizures	2 (25%)
Focal neurological signs	1 (12.5%)
Meningism	1 (12.5%)
Bulging fontanel	1 (12.5%)
Cerebrospinal fluid	
WBCs/ μ L, median (IQR)	276.50 (21.50–53.75)
Neutrophils %, median (IQR)	63 (21.75–81.50)
Lymphocytes %, median (IQR)	28 (12.5–73.57)
Total protein (g/dl), median (IQR)	66 (51.75–98)
CSF glucose (mg/dl), median (IQR)	2.80 (1.73–3)
Positive gram stain	7 (87.5%)
Positive culture	8 (100%)

WBC: white blood cells; CSF: cerebrospinal fluid; and IQR: interquartile range

empirical antibiotics had them modified upon receipt of culture results. All patients were cured, and no mortality was reported.

DISCUSSION

Although *Enterococci* can produce infections at multiple anatomic sites, EMV is an uncommon condition commonly caused by *E. faecalis* and *E. faecium*.⁴ Other enterococcal species such as *E. gallinarum* and *Enterococcus casseliflavus* have been infrequently described as causes of EMV.^{1,10}

To our knowledge, this study is the first to describe EMV in the state of Qatar. Consistent with other reports, *E. faecalis* was the most common causative enterococcal species in this study, accounting for 87.5% of cases, whereas *E. gallinarum* was isolated in only one patient.

As noted in this series and other reports,^{5–8,11–13} most cases were nosocomial. All nosocomial cases in this study had a neurosurgical condition as the preceding event and neurosurgical devices, namely EVDs, as predisposing factors, which coincides with previously published studies.^{5–7,11–13} This study's findings support the view that EVDs, which are commonly used to monitor intracranial pressure or temporarily remove CSF in the management of elevated intracranial pressure associated with various conditions, provide a potential entry portal for microorganisms. Risk factors associated with EVD-

related infection include subarachnoid or intraventricular hemorrhage, concurrent systemic infections, longer catheterization duration, CSF leakage, and frequent manipulation of the EVD system.¹⁴ In this study, three patients had subarachnoid and/or intraventricular hemorrhage. However, none of them had a concurrent systemic infection or CSF leakage. Moreover, the time between EVD insertion and infection occurrence in this study varied between seven and 20 days. Due to the retrospective design of this study, it was not feasible to determine whether it was manipulated frequently or not.

On the other hand, community-acquired enterococcal meningitis is uncommon compared to nosocomial infection. Based on previously published cases, it is common among children and usually associated with severe underlying diseases, such as prematurity, congenital or acquired heart disease, meningomyelocele, pulmonary disease, chronic renal failure, diabetes, and immunosuppression due to corticosteroid or immunosuppressive therapy, malignancy, and human immunodeficiency virus infection.^{5,6,15,16} However, community-acquired enterococcal meningitis is also reported among healthy children.¹⁶ In this series, the affected patients did not have established risk factors or immunosuppression.

As noted in this and other reports,^{5,6,11,12,15,16} the most consistent clinical features of EMV are fever and disturbed level of consciousness, which are non-

Table 2. Clinical characteristics, microbiological findings, treatments, and outcomes of the reported cases of EMV in this series

Patient Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age (year)/sex	54/M	53/F	46/M	0.9/F	38/M	1.5/M	60/M	0.25/M
Nationality	Pakistani	Filipino	Sri Lankan	Qatari	Sri Lankan	Yemeni	Qatari	Qatari
Infection onset after procedures (days)	7	12	15	10	20	NA	17	NA
Underlying neurological condition	No	No	Yes	No	Yes	No	No	No
Traumatic head injury	Yes	No	No	No	No	No	Yes	No
Intracerebral hg	No	Yes	No	No	No	No	No	No
Subarachnoid hg	No	No	No	No	No	No	No	No
Hydrocephalus	No	No	No	Yes	No	No	No	No
Associated bacteremia	No	No	No	No	No	No	No	No
Infection setting	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Community	Nosocomial	Community
External ventricular drain (EVD)	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Indication for EVD placement	Reduction of intracranial hypertension	Reduction of intracranial hypertension	Intracranial pressure monitoring	Reduction of intracranial hypertension	Intracranial pressure monitoring	NA	Reduction of intracranial hypertension	NA

Table 2 – continued

Other comorbidities	No	No	No	No	No	No	No	No
Diabetes mellitus	Yes	No	No	No	No	No	No	No
Hypertension	No	No	No	No	No	No	No	No
Malignancy								
Enterococci species	E. faecalis	E. faecalis	E. gallinarum	E. faecalis	E. faecalis	E. faecalis	E. faecalis	E. faecalis
Antimicrobials susceptibility	R	R	S	R	ND	S	S	ND
Gentamycin	S	S	S	S	S	S	S	S
Vancomycin	S	S	ND	ND	ND	ND	S	ND
Tazocin	ND	ND	S	ND	ND	ND	ND	ND
Meropenem	S	S	S	S	S	S	S	S
Ampicillin								
Empirical therapy	Ceftriaxone + Vancomycin	Ampicillin + Gentamycin	Ampicillin + Meropenem	Ampicillin	Ceftriaxone + Vancomycin	Ampicillin + Vancomycin	Ceftriaxone + Vancomycin	Ampicillin + Ceftriaxone + Vancomycin
Duration of therapy (days)	3	4	3	3	4	3	3	5
Definitive therapy	Ampicillin + Vancomycin	Ampicillin + Vancomycin	Ampicillin + Meropenem	Ampicillin	Ampicillin	Ampicillin	Ampicillin	Ampicillin + Vancomycin
Duration of therapy (days)	14	10	10	16	10	12	10	11
EVD removal	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Outcome	Cured	Cured	Cured	Cured	cured	Cured	Cured	Cured

R: resistant; S: sensitive; ND: not done; M: male; F: female; EMV: Enterococcal meningitis/ventriculitis

specific and can be found in other infections, such as septicemia. Therefore, the doctor must require a high index of suspicion when he/she encounters patients who have undergone neurosurgery and who subsequently have a fever, changes in consciousness, headache, and seizures.

All the isolates in this series were sensitive to ampicillin and vancomycin, which facilitated the therapeutic approach used. All patients received intravenous antibiotics empirically that was changed upon receipt of culture sensitivity test results. Intrathecal or intraventricular antibiotics have been increasingly utilized in cases of nosocomial meningitis/ventriculitis, especially in vancomycin-resistant *Enterococcus meningitis/ventriculitis*.^{3,11,17,18} Fortunately, the isolates in this series were sensitive to ampicillin and vancomycin. All patients showed a good response to intravenous ampicillin alone or in

combination with vancomycin, which undoubtedly played a major role in the nonmortality in this series. The limitations of this study were its retrospective design, small sample size (attributed to the low incidence of EMV), and implementation at a single-center, which makes it difficult to generalize the study results.

CONCLUSION

In conclusion, EMV is a recognized EVD-related complication, whereas community-acquired enterococcal meningitis was reported among children who had no established risk factors or immunosuppression. Because of its nonspecific clinical presentation, treating physicians should have a high suspicion index for EMV, especially in patients who have undergone neurosurgery and subsequently have a fever, headache, consciousness changes, and seizures.

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