

Adult Coagulase-Negative Staphylococcal Meningitis in Qatar: Clinical Characteristics and Therapeutic Outcomes

Abstract

Background and Objectives: Coagulase-negative staphylococci (CoNS) have emerged as a major pathogen in nosocomial meningitis. This study was designed to describe the clinical profile, laboratory parameters, treatment, and outcomes of CoNS meningitis in patients admitted to Hamad General Hospital, Qatar. **Materials and Methods:** This retrospective hospital-based study described the patients with CoNS meningitis from 2009 to 2013. **Results:** Twelve patients were recruited for the study, of which there were 10 (83.3%) males and 2 (16.7%) females with a median age of 39 years (interquartile range [IQR]: 29–46 years). Fever was the most common presenting symptom being present in all patients, followed by mental alterations 7 (58.3%). All CoNS meningitis cases in this study were nosocomially acquired after neurosurgery and in most cases after external ventricular drain (EVD) insertion. The median time between the procedure and acquisition of infection was 13 days (IQR: 10–15.7 days). The isolated species include 8 (66.7%) *Staphylococcus epidermidis*, 2 (16.7%) *Staphylococcus capitis*, and 2 (16.7%) *Staphylococcus haemolyticus*. All CoNS isolates were sensitive to vancomycin while 75% of them were oxacillin resistance. In the eight patients with EVDs, the infected EVDs were removed, while all patients received empirical antibiotics involving mainly vancomycin and ceftriaxone that were modified upon receipt of culture results. All patients were cured, and no mortality was reported. **Conclusions:** CoNS meningitis is a recognized complication related to the introduction of neurosurgical devices. Because of its nonspecific clinical presentation, treating physicians should have a high suspicion index. If CoNS meningitis is highly suspected, vancomycin is the empirical treatment of choice while awaiting results of sensitivity.

Keywords: Coagulase-negative *Staphylococcus*, meningitis, neurosurgical device, vancomycin

Fahmi Yousef Khan

Department of Medicine, Hamad General Hospital, Doha, Qatar

Introduction

Acute bacterial meningitis is a serious central nervous system infection that has various etiologies depending on the age of patients, status of vaccination, geographical distribution, surgical conditions, underlying medical conditions, means of contraction, and the receipt of different treatments in the community.^[1] Coagulase-negative staphylococci (CoNS) are recognized as causative agents of bacterial meningitis worldwide.^[1,2] In one study, it was found in 11% of adult bacterial meningitis.^[3] In another study, it was found in 10.5% of bacterial meningitis cases.^[4]

CoNS rarely cause community-acquired acute bacterial meningitis, but they are a frequent cause of nosocomial meningitis. In general, CoNS meningitis is related to trauma or direct implantation of foreign

bodies and the presence of a cerebrospinal fluid (CSF) shunt.^[1] A review of the literature showed few studies describing CoNS meningitis, while most of the data have been obtained from case reports.

In Qatar, adult CoNS meningitis is common accounting for 10.3% of bacterial meningitis cases.^[2] However, recent data on detailed demographic and clinical information on these cases are lacking. We performed a secondary analysis of our previous data to fill this gap, with the aim of describing the clinical presentation, laboratory data, treatment, and outcome of this clinical condition in adult patients admitted to Hamad General Hospital.

Methods and Patients

A secondary *post hoc* analysis was performed on data collected from a previous study, “Acute Bacterial Meningitis in Qatar:

Address for correspondence:

Dr. Fahmi Yousef Khan,
Department of Medicine, Hamad General Hospital, Doha, Qatar.
E-mail: fakhnqal@yahoo.co.uk

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A Clinical Study from 2009 to 2013,^[2] with different objectives. All adult CoNS meningitis cases (≥ 18 years) were identified from the primary study and the collected data such as demographic, clinical, and investigations, predisposing factors, the onset of infection (either hospital or community-acquired), and the outcome of treatment were reanalyzed. The primary study was approved by the medical research committee at Hamad Medical Corporation (#13254/13).

In this series, a confirmed diagnosis of adult CoNS bacterial meningitis met all three of the following criteria: (a) isolation of CoNS from at least two separate CSF studies or the tip of an indwelling neurosurgical device; (b) a clinical presentation compatible with acute bacterial meningitis such as fever, consciousness disturbance, seizures, or signs of meningeal irritation; (c) at least one of the following CSF parameters: (1) a leukocyte count of $>0.25 \times 10^9/l$ with predominantly polymorphonuclear cells; (2) a lactate concentration of >3.5 mmol/l; (3) a glucose concentration <45 mg/dL.^[2,4,5]

Blood culture was considered positive only when multiple blood cultures grew CoNS,^[5] while patients with polymicrobial isolates were excluded from this study.

CoNS bacterial meningitis was considered nosocomial if the diagnosis was made after more than 48 h of hospitalization or within a short period (i.e., usually within 1 month after discharge from the hospital where the patient had received an invasive procedure, especially a neurosurgical procedure). The case was considered cured when two successive cultures were negative for CoNS, and clinical signs of infection (fever and meningism) were absent during therapy or when therapy was discontinued.^[2] The empirical antimicrobial therapy was started no later than 24 h after taking the CSF sample for the culture in accordance with hospital guidelines.^[2]

For quantitative variables, the data were reported as median with the interquartile range (IQR) or mean \pm standard deviation, while qualitative variables were described as numbers and percentages.

Results

A total of 12 cases were recruited in this study, of which there were 10 (83.3%) males and 2 (16.7%) females with a median age of 39 years (IQR: 29–46 years). All patients were non-Qataris with various nationalities. Fever was the most common presenting symptom being present in all patients, followed by mental alterations 7 (58.3%). Table 1 describes the clinical characteristics of the 12 patients enrolled in this study.

All CoNS meningitis cases in this study were nosocomially acquired after neurosurgery and in most cases after external ventricular drain (EVD) insertion. The median time between the procedure and acquisition of infection was

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

Variable	Value, n (%)/ median (IQR)
Fever	12 (100)
Cough	7 (58.3)
Mental alteration	7 (58.3)
Headache	5 (41.7)
Vomiting	5 (41.7)
Seizures	1 (8.3)
Focal neurological signs	1 (8.3)
Cerebrospinal fluid	
WBCs/ μ L, median (IQR)	493.50 (193.75–613.75)
Neutrophils, median (IQR)	84.8 (74.00–92.25)
Lymphocytes, median (IQR)	10 (7.25–14.75)
Total protein (g/dl), median (IQR)	90.5 (54.75–107.25)
CSF glucose (mg/dl), median (IQR)	52.2 (30.6–66.2)
Positive gram stain	12 (100)
Positive culture	12 (100)

WBCs – White blood cells; CSF – Cerebrospinal fluid; IQR – Interquartile range

13 days (IQR: 10–15.7 days). In all patients with an EVD, the CSF was obtained from the ventricles through the drain, while in patients with shunts, ventricular fluid was obtained by aspiration of the shunt reservoir or tubing. As described in Table 1, CSF showed pleocytosis in all cases with polymorphonuclear predominance; the median of neutrophils percentage was 84.8% (IQR: 74.0%–92.25%). Elevated total protein levels with a median of 90.5 (IQR: 54.75–107.25 g/dL) and low glucose levels with a median of 52.2 mg/dL (IQR: 30.6–66.2 mg/dL) were also noted. The isolated species include 8 (66.7%) *Staphylococcus epidermidis*, 2 (16.7%) *Staphylococcus capitis*, and 2 (16.7%) *Staphylococcus haemolyticus*. Antimicrobial susceptibility is described in Table 2. All isolates were sensitive to vancomycin, while 9 (75%) of CoNS strains were methicillin resistant.

In the eight patients with EVDs, the infected devices were removed, while all patients received empirical antibiotics involving mainly vancomycin and ceftriaxone that were modified upon receipt of culture results. The mean duration of treatment was 17.4 ± 2.9 days (range: 14–24 days). During therapy, patients were clinically evaluated, and their CSF samples were analyzed regularly. The duration of therapy was influenced by clinical improvement and obtaining 2 consecutive-negative CSF cultures for CoNS. All patients were treated successfully, and no mortalities have been reported.

Discussion

CoNS are considered low-virulent and common contaminant microorganisms isolated from a fluid specimen such as blood, CSF, hydrothorax, and ascites. In recent years, however, CoNS have emerged as significant nosocomial

Table 2: Clinical characteristics, microbiological findings, treatment, and outcome of the of CoNS meningitis in our series

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12
Age (years)/sex	32/male	40/female	28/male	21/male	38/male	39/female	24/male	43/male	56/male	47/male	39/male	54/male
Nationality	Nepalese	Filipino	Sri Lankan	Nepalese	Bangladeshi	Indonesian	Nepalese	Nepalese	Iraqi	Jordanian	Nepalese	Cyprus
Infection onset after procedures (days)	10	16	18	22	15	11	7	13	14	13	14	14
Underlying neurosurgical condition	No	Yes	No	Yes	No	No	No	No	No	No	No	No
Head injury	No	No	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes
Intracerebral hg	Yes	No	No	No	No	No	No	No	No	No	No	No
Brain tumor	Yes	No	Yes	No	No	Yes	No	No	Yes	No	No	No
Hydrocephalus	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No
Associated bacteremia	No	No	Yes	No	No	No	No	No	No	No	Yes	No
Infection setting	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial	Nosocomial
Neurosurgical device	VP shunt	EVD	VP shunt	EVD	EVD	VP shunt	EVD	EVD	VP shunt	EVD	EVD	EVD
Comorbidities	No	Yes	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes
Hypertension	No	No	No	No	No	No	No	No	No	No	No	No
AVM	S.	S.	S.	S.	S. capitis	S.	S.	S.	S.	S.	S.	S. capitis
<i>Staphylococcus</i> species	<i>epidermidis</i>	<i>epidermidis</i>	<i>haemolyticus</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>epidermidis</i>	<i>haemolyticus</i>	<i>epidermidis</i>
Antimicrobials susceptibility	R	R	R	S	R	R	S	ND	R	R	R	R
Amoxicil/calv	S	S	S	S	S	S	S	S	S	S	S	S
Vancomycin	R	R	R	R	R	R	R	R	R	R	R	R
Tazocin	ND	ND	ND	ND	ND	ND	ND	ND	S	S	S	ND
Linezolid	ND	S	S	S	S	S	S	S	S	S	S	ND
Teicoplanin	R	R	R	R	R	R	R	R	R	R	R	R
Oxacillin	R	R	R	R	R	R	R	R	R	R	R	R
Ceftriaxone	R	R	R	R	R	R	R	R	R	R	R	R
Empirical therapy	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Meropenem + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin	Ceftriaxone + vancomycin
Duration of therapy (days)	3	6	5	5	4	5	4	3	4	3	3	6
Definitive therapy	Vancomycin	Vancomycin	Linezolid	Cloxacillin	Vancomycin	Vancomycin	Cloxacillin	Cloxacillin	Vancomycin	Linezolid	Vancomycin	Vancomycin
Duration of therapy (days)	14	15	10	12	10	12	20	13	10	14	14	14
EVD removal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Outcome	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured	Cured

R – Resistant; S – Sensitive; ND – Not done; EVD – External ventricular drain; VP – ventriculoperitoneal; S. capitis – *Staphylococcus capitis*; S. epidermidis – *Staphylococcus epidermidis*; S. haemolyticus – *Staphylococcus haemolyticus*; AVM – Arteriovenous malformation

infections, especially in patients with catheter-related meningitis.^[6] To the best of our knowledge, this study is the first to describe CoNS meningitis in Qatar and Arab countries, and it is a new addition to the limited studies available in the literature on CoNS meningitis.

This study highlights several important findings.

First, as noted in all cases, CoNS meningitis occurred after neurosurgery and in association with neurosurgical devices, and the median time between the procedure and acquisition of infection was 13 days, which is approximately similar to one report in the literature.^[5] CoNS meningitis in adults has been almost exclusively associated with neurosurgical procedures and head trauma. However, a review of the literature revealed that few cases of CoNS meningitis without a neurosurgical device have been reported.^[7,8]

Second, the clinical picture of CoNS meningitis in this study was found to be indistinguishable from other bacterial meningitis. Given this finding, isolation of CoNS strains in such patients poses a diagnostic challenge for clinicians who must make a clinical decision on whether the positive finding is likely to be a pathogen or a contaminant. Therefore, in an adult patient with fever and delayed recovery of consciousness after a neurosurgical procedure, isolation of CoNS from the patient's CSF should be interpreted with caution and in the context of other CSF tests for meningitis.

Third, *S. epidermidis* was the most common CoNS strain isolated from the CSF of the patients involved in this study, which is consistent with other reports.^[1,3,5,6] It was found that *S. epidermidis* never failed to colonize any type of inserted or implanted foreign body,^[6,9,10] which explains the predominance of this microorganism as the main pathogen that causes several nosocomial infections such as surgical site infections, intravenous catheter-related bloodstream infections, peritoneal dialysis-related infections, and neurosurgical device infections.

Forth, this study demonstrated that 75% of all CoNS strains were oxacillin resistant, while all strains were sensitive to vancomycin, which is consistent with the findings from other countries.^[3,5,6] These findings have resulted in therapeutic challenges for the treating physicians in the choice of initial empiric antibiotics. Although some reports do not recommend using vancomycin alone due to limited data,^[5] six of the patients in this study have received intravenous vancomycin alone as definitive therapy, with surprisingly excellent outcomes.

Fifth, although there is no consensus among researchers regarding the optimal duration of treatment for CoNS meningitis, the duration of antibiotic therapy in this study ranged from 14 days to 24 days, whereas in another study,^[5] the duration of antibiotic therapy ranged from 6 days to 38 days.

Finally, in contrast to many reports,^[3-6] which showed high overall mortalities, there was no mortality in this study. The reason for this is not clear, however, early recognition of CoNS meningitis with prompt initiation of vancomycin empirically could have led to the surprisingly excellent outcomes in this series.

This study is limited by its retrospective design, the small sample size, and being implemented in a single center, which makes it difficult to generalize the results. Moreover, this study lacks data on the molecular epidemiology of CoNS isolates. However, along with the few studies available in the literature, this study provided important conclusions regarding resistance patterns among CoNS isolates, which has implications for future work.

Conclusions

CoNS meningitis is a recognized postneurosurgical complication associated with neurosurgical device placement. Due to its nonspecific clinical presentation, treating physicians should have a high index of suspicion for CoNS meningitis, especially in patients who have undergone neurosurgery and subsequently develop fever, headache, changes in consciousness, and seizures. Therefore, CSF analysis is needed to confirm the diagnosis. If CoNS meningitis is highly suspected, vancomycin is the empirical treatment of choice while awaiting results of sensitivity.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Azimi T, Mirzadeh M, Sabour S, Nasser A, Fallah F, Pourmand MR. Coagulase-negative staphylococci (CoNS) meningitis: A narrative review of the literature from 2000 to 2020. *New Microbes New Infect* 2020;37:100755.
2. Khan FY, Abu-Khattab M, Almaslamani EA, Hassan AA, Mohamed SF, Elbuzdi AA, *et al.* Acute Bacterial meningitis in qatar: A hospital-based study from 2009 to 2013. *Biomed Res Int* 2017;2017:2975610.
3. Chang WN, Lu CH, Huang CR, Chuang YC, Tsai NW, Chen SF, *et al.* Epidemiology of adult staphylococcal meningitis in southern Taiwan: A clinical comparison of *Staphylococcus aureus* infection and coagulase-negative staphylococcal infection. *Jpn J Infect Dis* 2007;60:262-6.
4. Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness VS Jr., *et al.* Acute bacterial meningitis in adults. A review of 493 episodes. *N Engl J Med* 1993;328:21-8.
5. Huang CR, Lu CH, Wu JJ, Chang HW, Chien CC, Lei CB, *et al.* Coagulase-negative staphylococcal meningitis in adults: Clinical characteristics and therapeutic outcomes. *Infection* 2005;33:56-60.
6. Zheng G, Li S, Zhao M, Yang X, Zhang Y, Deng J, *et al.* Time to positive culture can differentiate post-neurosurgical coagulase-negative Staphylococci other than *S. epidermidis* meningitis from contamination: A case-control observational

- study. J Clin Lab Anal 2020;34:e23447.
7. Oud L. Community-acquired meningitis due to *Staphylococcus capitis* in the absence of neurologic trauma, surgery, or implants. Heart Lung 2011;40:467-71.
 8. Drinkovic D, Pottumarthy S, Knight D, Morris AJ. Neonatal coagulase-negative staphylococcal meningitis: A report of two cases. Pathology 2002;34:586-8.
 9. von Eiff C, Peters G, Heilmann C. Pathogenesis of infections due to coagulase-negative staphylococci. Lancet Infect Dis 2002;2:677-85.
 10. Davidson RJ, Low DE. *Staphylococcus epidermidis* and other coagulase-negative staphylococci. In: Yu VL, Weber R, Raoult D, editors. Antimicrobial Therapy and Vaccines. New York: Apple Trees Productions; 2002. p. 659-73.