

Case report

***Enterococcus gallinarum* meningitis: a case report and literature review**

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Abstract

We report a case of *Enterococcus gallinarum* meningitis in a 53-year-old female who was admitted to our hospital with a fever, headache, and consciousness disturbance one week after a life-saving craniotomy operation. There was obvious neck stiffness; lumbar puncture was performed and cerebrospinal fluid parameters were consistent with bacterial meningitis. The patient was given ceftriaxone and vancomycin for bacterial meningitis. Cerebrospinal fluid culture yielded an isolate which was identified as *Enterococcus gallinarum*. The isolate was sensitive to ampicillin, ampicillin/clavulanate, linezolid, moxifloxacin and teicoplanin, but it showed intermediate sensitivity to vancomycin and quinopristin-dalfopristin. Intravenous linezolid, 600 mg every 12 hours, was started. Three days after starting treatment, the patient became afebrile; a repeat lumbar puncture two weeks later showed no white blood cells in cerebrospinal fluid and no bacterial growth. Treatment with linezolid was continued for a total therapy duration of three weeks, after which the patient was discharged in a good condition.

Key words: Enterococcal meningitis; linezolid; bacterial meningitis; *Enterococcus gallinarum*

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Introduction

Enterococci are gram-positive bacteria belonging to the genus *Enterococcus*. These organisms are found in the normal bowel microbiota of humans and many animals. In hospitalized patients the main sites of colonization are soft tissue wounds, ulcers, and the gastrointestinal tract [1]. These ubiquitous bacteria have traditionally been regarded as low-grade pathogens but have become recognized increasingly as important causes of both nosocomial and community-acquired infections in adults and in children [1-3]. Important clinical infections caused by enterococci include urinary tract infections, bacteremia, intraabdominal and intrapelvic abscesses, post-surgery wound infections, bacterial endocarditis, diverticulitis, and rarely central nervous system infections [1,3]. Enterococci are clearly unusual etiological agents of bacterial meningitis, which occurs rarely as a complication of neurosurgical procedures.

In this report, we present a case of meningitis caused by *Enterococcus gallinarum* after a life-saving craniotomy in a 53-year-old female patient. The patient responded well to a 21-day course of linezolid. To our knowledge, this is the first reported case of *E. gallinarum* meningitis which was

successfully treated with intravenously administered linezolid.

Case report

A 53-year-old Pakistani female living in Qatar was admitted to our hospital with a one-week fever, headache, and consciousness disturbance. The patient was known to have diabetes mellitus and hypertension, for which she was under treatment with regular follow-up.

The patient had traveled to Pakistan four weeks prior to her admission. One week after her arrival she developed right-sided weakness and was diagnosed with a cerebellar hemorrhagic stroke. The patient was hospitalized in Pakistan where she underwent life-saving decompression craniotomy to relieve a life-threatening intracranial hypertension. One week after the craniotomy the patient developed fever and headache followed by deterioration in her level of consciousness. Repeat brain computerized tomography (CT) was unremarkable. Lumbar puncture was performed, and cerebrospinal fluid (CSF) culture and other septic workups were negative, as mentioned by her husband (no documents). During her stay in the hospital in

Pakistan, she received many antibiotics empirically but with no benefit.

Two weeks after the craniotomy, the family decided to bring this lady back to Al Doha to continue her treatment. Upon arrival at the Al Doha airport, the patient was brought directly to our hospital. On examination, the patient was febrile, conscious and oriented. There was obvious neck stiffness, but Kernig's and Brudzinski's signs, typically indicative of meningitis, were negative. She had dense right-sided hemiplegia with right-sided upper motor neuron facial palsy. The right side was spastic with hyperreflexia and up-going planter reflex. The rest of her examination was unremarkable. Blood investigations found a hemoglobin level of 10 g/dL, a total leukocyte count of 15,000 /mm³ (60% neutrophils, 31% lymphocytes), an adequate number of platelets, and an erythrocyte sedimentation rate (ESR) of 73 mm/hour. Blood chemistry, liver profile, and coagulation studies were within normal limits. A malaria parasite smear was negative and the urine dipstick and microscopy were normal. Blood and urine samples were sent for cultures. Urgent brain CT showed right occipital craniotomy with cerebellar changes. Lumbar puncture was performed. The opening pressure was 150 mmH₂O, and analysis of CSF revealed the following values: white blood cell (WBC) count of 1,190 cells/mm³ (89% segmented neutrophils and 9% lymphocytes); glucose level 1.8mmol/L; and protein level, 3.01 g/L. The patient was admitted to the medical ward with a provisional diagnosis of acute bacterial meningitis and received ceftriaxone and vancomycin while CSF culture was pending. The following additional studies were obtained after admission: tuberculin skin test, human immunodeficiency virus enzyme-linked immunosorbent, and Widal test, all of which were negative.

The CSF specimen was cultured on a blood agar, chocolate agar, and pediatric blood culture bottle. Cultures yielded bacteria identified as *Enterococcus* spp., further identified using a Phoenix machine (Becton Dickson, Sparks, Maryland, USA) as *E. gallinarum*. Identification was confirmed by API strep (bioMerieux, Marcy l'Etoile, France) and by doing a motility test and pigment production. [4] The isolate was sensitive to ampicillin (MIC < 2 µg/mL), ampicillin/clavulanate (MIC < 2 µg/mL), linezolid (MIC < 0.75 µg/mL), moxifloxacin (MIC < 0.5 µg/mL) and teicoplanin (MIC < 2 µg/mL). It exhibited intermediate sensitivity to quinopristin-

dalfopristin (MIC 2 µg/mL) and vancomycin (MIC > 8 µg/mL), and was resistant to erythromycin (MIC > 4 µg/mL) and tetracycline (MIC > 8 µg/mL).

Discussion

Enterococcus faecalis and *Enterococcus faecium* are responsible for most enterococcal infections in humans, while *E. gallinarum* and *Enterococcus casseliflavus* are not frequently reported [1-3]. *Enterococci* are clearly unusual etiological agents of bacterial meningitis, and they account for 0.3–4% of reported cases of bacterial meningitis [5]. *E. faecalis* and *E. faecium* are the two species most frequently isolated during the course of meningitis, whereas *E. gallinarum* is extremely rare. A PubMed (<http://www.ncbi.nlm.nih.gov/pubmed?term=Enterococcus%20gallinarum%20meningitis>) search identified only five cases of *E. gallinarum* meningitis reported in the literature [6-9], summarized along with this study in Table 1. The low incidence of *E. gallinarum* meningitis may be attributed to an underestimation of the cases due to misidentification.

Based on a clinical spectrum of symptoms and findings, enterococcal meningitis can be found in two clinical forms, postoperative and spontaneous. Postoperative meningitis appears as a nosocomial infection usually associated with neurosurgical procedures and shunt devices [5]. Our patient underwent a life-saving craniotomy, which was considered as a risk factor for her enterococcal meningitis. Patients with spontaneous enterococcal meningitis have a higher frequency of community-acquired infections which are usually associated with severe underlying diseases such as prematurity, congenital or acquired heart disease, meningomyelocele [10], pulmonary disease, chronic renal failure, diabetes and immunosuppression due to corticosteroid or immunosuppressive therapy, malignancy, and human immunodeficiency virus infection [11,12].

In most instances, the presentation of enterococcal meningitis is a rapid onset of fever, altered mental status, headache, seizures, and signs of meningeal irritation. Clinical features such as coma, septic shock, focal neurological deficit, or petechial rash are very unusual findings. Our patient presented with fever, altered mental status, and neck stiffness. No significant clinical differences have been noted among children and adults in postoperative cases, whereas in spontaneous cases children present with a lower incidence of fever, headache, altered mental status, and meningeal signs. The most common

Table 1. Clinical characteristics of the reported cases of meningitis caused by *Enterococcus gallinarum*

Reference	Age/sex	Predisposing factor	Presenting symptoms/signs	Susceptibility to vancomycin	Treatment	Outcome
Antonello <i>et al.</i> [6]	53 y/M	Alcoholism	Fever, confusion / neck stiffness	Resistant	i.v. Ampicillin & i.v. Gentamycin for 3 weeks	Cured
Kurup <i>et al.</i> [7]	64 y/M	VP shunt	Fever/ lethargy	Intermediate sensitivity	i.v. Ampicillin & i.v. Gentamycin for 3 weeks	Cured
Roca <i>et al.</i> [8]	51 y/F	Previous lumbar puncture	Fever and headache	Resistant	i.v. Ampicillin and rifampin for 3 weeks	Cured
Takayama <i>et al.</i> [9]	57 y/M	VP shunt and RA	Fever/neck stiffness	Intermediate sensitivity	i.v. Teicoplanin 4 weeks + VP shunt removal	Cured
Takayama <i>et al.</i> [9]	12 y/M	Post astrocytoma Resection+ VP shunt	Fever, drowsiness and limb cramps	Intermediate sensitivity	i.v. Ampicillin for 8 weeks + VP shunt removal	Cured
Khan <i>et al.</i> (Present case)	53 y/F	Cerebral hemorrhage with craniotomy	Fever, headache and consciousness disturbance /neck stiffness	Intermediate sensitivity	i.v. Linezolid for 3 weeks	Cured

i.v: intravenous VP: ventriculo-peritoneal RA: rheumatoid arthritis

complications of enterococcal meningitis include hydrocephalus, brain abscess, and stroke [5]. Obviously, our patient did not develop such complications.

The diagnosis is usually suspected from the clinical data, especially the presence of predisposing and risk factors, and is confirmed by the laboratory analysis of CSF. In enterococcal meningitis, CSF findings are usually consistent with bacterial infection demonstrated by pleocytosis, elevated protein levels, and hypoglycorrhachia. In contrast to other bacterial meningitis, the lower yield of CSF Gram stain smears in enterococcal meningitis (29%–45%) has been reported [5,11,13]. In our patient, as well as in the five reported cases of *E. gallinarum* meningitis, the CSF studies were consistent with bacterial meningitis. For most clinical microbiological laboratories, the primary method of identifying *Enterococcus* spp. strains relies on phenotypic characterization [14]. In our patient, an automated identification system was used to identify the isolate as *E. gallinarum*, confirmed by API strip, motility test and pigment production.

Treatment of enterococcal meningitis includes administration of appropriate antibiotics that have *in vitro* activity against the strain, and efficiently

penetrate the cerebrospinal fluid, in addition to the elimination of the predisposing factor if necessary.

Ampicillin or penicillin is considered the standard therapy for most enterococcal infections since enterococci are classically sensitive to cell wall active antibiotics such as beta-lactams. Combination therapy using a cell wall active agent (*e.g.* ampicillin, penicillin) and an aminoglycoside (*e.g.* gentamicin) is necessary to adequately treat enterococcal meningitis. Glycopeptides such as vancomycin should be reserved for patients allergic to penicillin or for penicillin resistant strains [5]. In recent years, increasing rates of vancomycin resistant enterococci (VRE) have been documented in many hospitals [15,16]. Meningitis caused by VRE represents a therapeutic challenge due to limited treatment options because of the frequent multidrug resistance of VRE and difficulty in reaching therapeutic drug concentrations in the CSF. The risk factors for clinically significant VRE infections are underlying malignancies, seriously ill hospitalized patients, immunosuppression, renal insufficiency, long duration of broad-spectrum antibiotic therapy, and frequent use of oral or intravenous vancomycin in the hospital setting. [17] It is noteworthy that motile species of enterococci such as *E. gallinarum* are

naturally resistant to glycopeptides. In all reported cases of meningitis caused by *E. gallinarum* (including ours) the isolates were either resistant or intermediately sensitive to vancomycin, whereas five of the strains were sensitive to ampicillin (Table 1). Cephalosporins are not active against enterococci, either vancomycin-susceptible or vancomycin-resistant, and should never be used for *E. gallinarum* infections.

The United States Food and Drug Administration (FDA) have recently approved antimicrobial agents with activity against VRE, such as linezolid and quinupristin/dalfopristin. Linezolid also has been approved in our hospital. It is an oxazolidinone antibiotic, bacteriostatic against enterococci with good CSF penetration. Our patient received linezolid because she developed severe allergic reaction to ampicillin, and the isolated strain exhibited intermediate sensitivity to vancomycin. Although we were unable to measure the concentration of linezolid in the patient's cerebrospinal fluid to assess penetration, our patient responded well to this drug. The outcome of the treatment of *E. gallinarum* meningitis is unclear due to the paucity of the cases, but as described in Table 1, it seems positive, since all patients had clinical improvement.

In conclusion, *E. gallinarum* meningitis should be considered in any patient who develops fever after neurosurgical procedures or shunt devices. Since all reported cases of *E. gallinarum* meningitis were either resistant or intermediately sensitive to vancomycin, linezolid emerges as a useful option for treating such cases.

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