Clinical Case Report

Medicine®

OPEN

The first case report of *Enterococcus gallinarum* meningitis in neonate

A literature review

Xiaoquan Li, MD[a,*], Shujuan Fan, MD[a], Xiaojie Lin, MD[a], Li Liu, MD[a], Jie Zheng, MD[b], Xihui Zhou, MD[a], Axel Heep, MD[c]

Abstract

Rationale: Enterococcus gallinarum meningitis (EGM) is rarely found in normal adults and even rarer in children. To our knowledge, EGM in neonate has not been reported previously.

Patients concerns: Here we reported the first case of EGM in neonate. Prolonged fever was the only manifestation for the case after admission.

Diagnoses: Cerebrospinal fluid cultures showed that the isolate was *Enterococcus gallinarum* and sensitive to linezolid.

Interventions: Ceftriaxone, beta lactam type, and vancomycin were used respectively, but not effective.

Outcomes: The temperature went down to normal after linezolid was used and the baby was discharged in good condition in the end.

Lessons: This case indicated that EGM could also occur in neonate and fever could be the only obvious manifestation. Thus, the effective antibiotics and adequate duration are very important and linezolid is a potential good choice, especially for vancomycin-resistant patients.

Abbreviations: CRP = C-reactive protein, CSF = cerebrospinal fluid, EGM = *Enterococcus gallinarum* meningitis, FDA = Food and Drug Administration, Hgb = hemoglobin, RBC = red blood cell, WBC = white blood cell.

Keywords: *Enterococcus gallinarum* meningitis, linezolid, neonate

1. Introduction

Enterococci are facultative anaerobic, gram-positive cocci, which are usually found in urinary tract infection, bacterial endocarditis, and diverticulitis. Central nervous system infection of enterococci is rarely found.[1,2] Enterococcus gallinarum, which belongs to enterococcus, is a dominant bacterium in poultry gastrointestinal tracts. The infections of *Enterococcus gallinarum* and *Enterococcus casselifavus* uncommonly occur in clinical practice. *Enterococcus gallinarum* meningitis (EGM) occurs occasionally in postneurosurgery and immunocompromised patients. Six EGM cases have been reported around the world so far, but none has been reported in the neonate. We would share the first case of EGM in the neonate.

1.1. Ethical statement

Ethics committee approval is not included as it is commonly accepted that case reports do not require such an approval. Because our work did not use the patients' data that would allow identifying them, informed consent is not necessary.

2. Case report

A 2-day-old baby boy, presented with jaundice without fever, was admitted to the First Affiliated Hospital of Xi'an Jiaotong University for 1 day before the hospitalization. Physical examination at the admission showed that the baby with normal axillary temperature was in good condition and the jaundice was extended to the proximal limb. Laboratory examination results were: direct antiglobulin test negative, release test positive, free test weakly positive, red blood cell (RBC) count 3.46×10^{12}/L, white blood cell (WBC) count 11.7×10^{9}/L, and hemoglobin 110 g/L with a mild anemia. Then the blue-ray phototherapy was adopted at the day of the admission.

The baby presented fever (axillary temperature of 38.5°C) without nuchal rigidity and mental confusion at the seventh day after admission. WBC count 27.2×10^{9}/L, neutrophils count 20.3×10^{9}/L and C-reactive protein (CRP) count 23 mg/L (The normal reference value is <10 mg/L) went up, too. Blood culture was negative at this time. Intravenous ceftriaxone, 75 mg/kg every 24 hours, was used and the fever was reduced but went up

Editor: N/A.

The authors have no conflicts of interest to disclose.

[a] Department of Neonatology, [b] Clinical Research Center, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China, [c] Neonatal Unit, North Bristol NHS Trust, Bristol, The United Kingdom.

[*] Correspondence: Xiaoquan Li, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China (e-mail: lxqxianchina@outlook.com).

Medicine (2018) 97:7(e9875)

Received: 27 November 2017 / Received in final form: 19 January 2018 / Accepted: 24 January 2018

http://dx.doi.org/10.1097/MD.0000000000009875

again at the 10th day after admission. Vancomycin, 15 mg/kg every 8 hours, was given to the baby intravenously in addition to the use of ceftriaxone for 4 days. The axillary temperature fluctuated between 36.5°C and 38.4°C.

A lumbar puncture was performed on the 15th day after admission. Double cerebrospinal fluid (CSF) specimens' culture grew *E gallinarum* and the isolate was sensitive to linezolid, vancomycin, and tetracycline. Cranial ultrasound and computer tomography scan were normal. So intravenous linezolid, 10 mg/kg every 12 hours, was given to the baby instead of the combination therapy of vancomycin and ceftriaxone. The temperature was down to the normal range 4 days later and the CRP went down to 15 mg/L. The lumbar puncture was performed again 10 days later with negative CSF culture and the CRP went down to 6 mg/L, with the WBC count 11.2×10^9/L and neutrophils count 4.3×10^9/L. The baby was discharged from the hospital with normal temperature after a 2-week course of linezolid treatment.

The baby presented fever again 10 days after being discharged. The temperature was up to 39.6°C. Ceftriaxone, 75 mg/kg every 24 hours, was given to the baby for 5 days in another hospital but the fever was still running. The baby was transferred to our hospital then. CSF and blood culture was negative. Intravenous linezolid was used again and the course of treatment was extended to 3 weeks. Fever faded on the third day of the treatment. The baby, who has been followed up for 2 years since then, stayed in good condition and no fever and neurological abnormality were observed.

3. Discussion

EGM is rarely found in normal adults. Enterococcus meningitis, occurring occasionally in postneurosurgery, immunocompromised patients and patients with nervous system defects and trauma, accounts for 0.3% to 4% of meningitis. While the occurrence of *E faecalis* meningitis and *E faecium* meningitis accounts for about 90% of enterococcus meningitis. Only 6 EGM cases were reported (details shown in Table 1),[2] including 4 cases secondary to neurosurgery, 1 case secondary to lumbar puncture, and 1 alcoholism patient,[3–5] and the youngest patient was 12 years old. We reported a case of a 9-day-old baby with neonatal EGM. The baby presented fever secondary to hemolytic disease. He was not immunocompromised and did not have a history of operation and severe basic diseases.

The features of this case: fever was the typical clinical manifestation and there was no significant abnormality in the nervous system. Enterococcus meningitis usually presents fever, headache, consciousness disturbance, seizures, and meningeal stimulation signs. Some severe cases may even appear shock, coma, focal neurological deficits, and so on. In this case, fever was the only clinical symptom without consciousness disturbance, seizures, and neck stiffness. It indicated that neurological signs might not be typical in neonates. Risk factors: The neonate diagnosed with EGM had hemolytic disease and his immune system was not well developed yet. Thus, both undeveloped immune function and hemolytic disease could be the risk factors of EMG. By now, the baby in this case was the youngest with EGM among the reported cases in the world.

Ampicillin and penicillin, which kill the bacteria by inhibiting the cell wall, are considered to be the standard antibiotics to resist enterococcus infection. In clinical practice, we usually choose ampicillin and aminoglycoside for enterococcus meningitis in adults. Sometimes patients are allergic to penicillin or present drug resistance, and then sugar peptide antibiotic, such as vancomycin, can be used. Recently, the resistant treatment of enterococcus meningitis faces the new challenges with the vancomycin-resistant enterococcus increasing: multidrug-resistant enterococcus strains arise frequently and the drugs cannot achieve effective concentration in the CSF. Vancomycin is commonly found to be resistant to enterococcus in malignant tumor, immunosuppression, renal insufficiency, and a long course treatment of broad-spectrum antibiotics. While *E gallinarum* features a natural resistance to sugar peptide.[4,6] The patients in previously reported cases of *E gallinarum* were all sensitive to ampicillin, whether resistant to vancomycin or sensitive to vancomycin. CSF cultures and drug-sensitive test in this case of *E gallinarum* were different. The baby was resistant to ampicillin but was sensitive to vancomycin. But the vancomycin appeared ineffective when it was given by intravenous drip for 4 days. Recently, the Food and Drug Administration of the United State has put forward that linezolid quinupristin and dalfopristin synercid can be applied to treat enterococcus infection which present resistant to vancomycin. Linezolid is the best antibiotic to treat enterococcus meningitis due to its good CSF permeability.[7] In this case, CSF cultures and drug-sensitive test of this case showed resistance to ampicillin but sensitivity to vancomycin, but

Table 1

EGM reported around world.

Reference	Age, year	Sex	Potential predisposing	Clinical presentation	Vancomycin	Treatment	Prognosis
8	53	M	Alcohol abuse	Fever, confusion, and neck stiffness	Resistance	IV Ampicillin combined with gentamicin for 3 weeks	Recovery
9	64	M	VP shunt	Fever and lethargy	Sensitive	IV Ampicillin combined with gentamicin for 3 weeks	Recovery
10	51	F	Lumbar drainage of CSF	Fever and headache	Resistance	IV Ampicillin combined with rifampin for 3 weeks	Recovery
3	57	M	VP shunt and rheumatoid arthritis	Fever and neck stiffness	Sensitive	IV Teicoplanin for 4 weeks and interrupt VP shunt	Recovery
10	12	M	Astrocytoma neurosurgery and VP shunt	Fever and drowsiness	Sensitive	IV Ampicillin for 8 weeks	Recovery
4	53	F	Cerebral hemorrhage and neurosurgery	Fever, headache, neck stiffness, and confusion	Sensitive	IV Linezolid for 3 weeks	Recovery
Present report	9 days old	M	Immunocompromised and hemolytic disease	Fever	Sensitive	IV Linezolid for 3 weeks	Recovery

CSF = cerebrospinal fluid, EGM = *Enterococcus gallinarum* meningitis, F = female, IV = intravenous, M = male, VP = ventriculoperitoneal.

vancomycin treatment was not effective, so intravenous linezolid was used instead. Although we were unable to detect drug concentration in CSF, the reaction to linezolid was good. Routine blood test, liver, and kidney functions were normal. The treatment duration in the 6 reported cases of EGM was about 3 weeks, so we thought that the duration of treatment in our case was adequate. The baby was discharged from hospital after 2-week treatment duration, and meningitis relapsed 10 days later. The secondary treatment was extended to 3 weeks. Then the baby was recovered. In conclusion, the treatment duration of EGM would be recommended to be at least 3 weeks.

EGM is relatively rare. Therefore, there is no detailed evaluation about its prognosis at present. The prognosis of the 6 reported patients is optimistic and the clinical symptoms are significantly improved. This case reminds us that EGM may occur in the neonate. Sometimes fever may be the unique typical manifestation, and the effective antibiotics and adequate duration are important. Linezolid is a better choice for treatment, especially for vancomycin-resistant patients.

References

[1] Sood S, Malhotra M, Das BK, et al. Enterococcal infections & antimicrobial resistance. Indian J Med Res 2008;128:111–21.
[2] Murray BE, Arias CA. Mandell GL, Bennett JE, Dolin R. Enterococcus species, Streptococcus bovis group, and Leuconostoc species. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases 7th ed.Churchill Livingstone, New York:2009;2643–53.
[3] Takayama Y, Sunakawa K, Akahoshi T. Meningitis caused by Enterococcus gallinarum in patients with ventriculoperitoneal shunts. J Infect Chemother 2003;9:348–50.
[4] Khan FY, Elshafi SS. Enterococcus gallinarum meningitis: a case report and literature review. J Infect Dev Ctries 2011;3:231–4.
[5] Antonello VS, Zenkner Fde M, Frana J, et al. Enterococcus gallinarum meningitis in an immunocompetent host: a case report. Rev Inst Med Trop Sao Paulo 2010;52:111–2.
[6] Werner G, Klare I, Spencker FB, et al. Intrahospital dissemination of quinupristin/dalfopristinand vancomycin-resistant Enterococcus faecium in a paediatric ward of a German hospital. J Antimicrob Chemother 2003;52:113–5.
[7] Knoll BM, Hellmann M, Kotton CN. Vancomycin-resistant Enterococcus faecium meningitis in adults: case series and review of the literature. Scand J Infect Dis 2012;19:34–7.