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Success of linezolid therapy for postneurosurgical ventriculitis due to vancomycin-resistant Enterococcus faecium: case report and literature review

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Abstract

Background: Vancomycin-resistant Enterococcus faecium ventriculitis is one of the most severe events in postneurosurgical intracranial infections. There are no guidelines recommending an appropriate treatment before.

Case presentation: This case presents a successful linezolid treatment for post-neurosurgical vancomycin-resistant Enterococcus faecium ventriculitis of a 24-year-old man in the department of neurosurgery, Beijing Tiantan Hospital.

Conclusions: Linezolid should be considered as one of the important methods for the treatment of post-neurosurgical intracranial infections caused by vancomycin-resistant Enterococcus.

Keywords: Vancomycin-resistant Enterococcus (VRE), Linezolid (LZD), Neurosurgery

Background

Hospital acquired infection is a tough medical problem existing in many medical treatments. The most common causes are surgical-site-related, catheter-related, and ventilator-associated infections. Some of them may lead to severe results. Neurosurgical site infection often appears as meningitis or ventriculitis, which are considered critical infectious diseases and may lead to the death of the patient. Nosocomially acquired intracranial infections may be caused by a wide array of microorganisms, including staphylococci, enterococci, Gram-negative bacilli and yeasts. However the pathogen such as vancomycin-resistant Enterococcus (VRE) is very rare in intracranial infections. We report a successful case of linezolid treatment for post-neurosurgical vancomycin-resistant Enterococcus faecium ventriculitis.

Case presentation

A 24-year-old man who had presented with diplopia, headache, right side myasthenia and bucking symptoms, was admitted to Beijing Tiantan Hospital for treatment. The MRI revealed a suprasellar cistern tumor. Then he underwent right frontotemporal-orbitozygomatic approach craniotomy for the suprasellar cistern tumor resection. The pathology of tumor was notochordoma. One week after the operation, the CSF leakage appeared. So the patient underwent the second operation to repair the CSF leakage and also got the lumbar cistern drainage. After the surgical intervention, the patient developed a middle-grade fever and altered consciousness. The white blood cell count rose up, so the antimicrobial treatment was initialized with Ceftazidime, Piperacillin and Sulbactam. There is no sign of infection improvement. The body temperature of the patient kept between 38 °C to 39 °C. And the white blood cell count kept between 12×10^9/L and 18×10^9/L. The conscious state of the patient worsened day by day. Twenty days later, the patient developed acute hydrocephalus and brain hernia. The lateral ventricular puncture external drainage was performed immediately. It helped the patient to recover form coma. However the ventriculitis appeared. The cerebrospinal fluid (CSF) obtained from lateral ventricular

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Table 1 Susceptibility results of the pathogen vancomycin-resistant Enterococcus (VRE) faecium

Antimicrobials	MIC
Ampicillin	R(>8)
Gent.Synergy	R(>500)
Imipenem	N/R
Levofloxacin	R(>4)
Linezolid	S(2)
Oxacillin	>2
Penicillin	R(>8)
Tazobae	>8
Rifampin	R(>2)
Strep.Synergy	S(≤1000)
Synercid	S(0.5)
Amox/k Clav	>4/2
Trimeth/Sulfa	>2/38
Tetracycline	S(≤4)
Vancomycin	R(>16)
Chloramphenicol	S(≤8)
Clindammycin	>2
Cefazolin	>16
Ciprofloxacin	R(>2)
Erythromycin	R(>4)
Nitrofurantoin	≤32
Gentamicin	>8

MIC minimum inhibitory concentration(μg/ml), *R* resistant, *S* sensitive, *I* intermediate

puncture external drainage was yellow, turbidity and flocculent. And the white blood cell count of CSF rose up to more than 2000/μL. The antimicrobial treatment changed to amikacin, meropenem and vancomycin for ten days. Later the vancomycin-resistant Enterococcus (VRE) faecium was isolated from the CSF culture. It was resistant to vancomycin and imipenem, but sensitive to linezolid (LZD). Thus linezolid was administrated intravenously 600 mg q12h for half a month. It resulted in a resolution of the ventriculitis and a negative CSF culture. The following occipital ventriculoperitoneal shunt procedure resulted in a cure Figs. 1, 2, 3 and 4 (Table 1).

Discussion

Nosocomial infections are important medical problems in neurosurgical patients. Among the nosocomial infections, meningitis and ventriculitis are fearful infections and can lead to severe complications even death. The reported incidence of postoperative meningitis is quite variable (0.5 – 8 %) [1–5]. The incidence of ventriculitis is even lower.

Post-neurosurgical intracranial infections are mostly caused by a wide array of microorganisms. It is reported that the most common organisms causing meningitis are non-fermentative Gram-negative bacteria (NFGNB) (27.3 %), followed by Pseudomonas aeruginosa (15.6 %) and Klebsiella species (12.6 %). A study of 18092 patients who underwent neurosurgical procedures at the department of neurosurgery, National Institute of Mental Health and Neurological Sciences, Bangalore, India during 2001 to 2007, showed that 415 patients developed infection such as meningitis. Only 9 patients of them developed to enterococcus meningitis [6]. Vancomycin-resistant Enterococcus (VRE) ventriculitis occurs extremely rare. So far there are no guidelines recommending an appropriate treatment.

Linezolid (LZD) is the first licensed member of the oxazolidinone class of antibiotics. It has good activity against almost all Gram-positive pathogens, including multidrug-resistant organisms such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE) faecium [7]. The unique mechanism

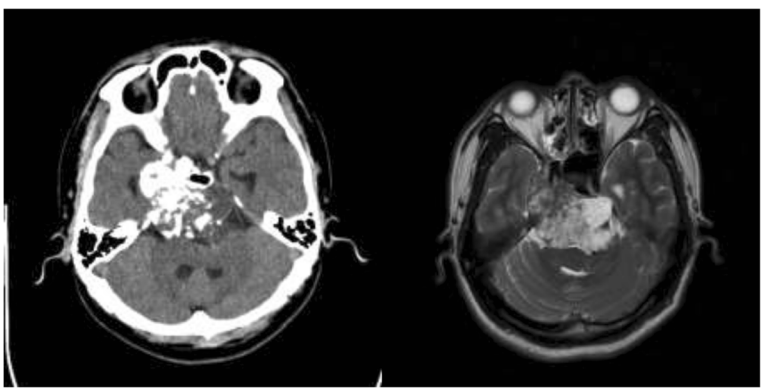

Fig. 1 Preoperative CT and MRI without contrast of the brain reveals a suprasellar cistern tumor

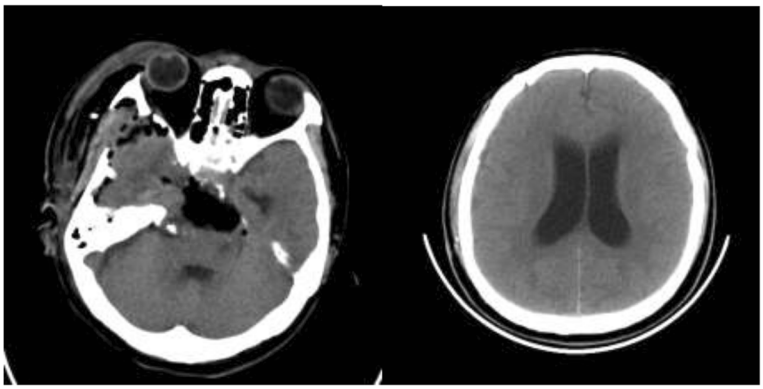

Fig. 2 Postoperative CT reveals the tumor removal but hydrocephalus 20 days after the second operation

of linezolid, that involves inhibition of bacterial protein synthesis at a very early stage of the process, makes cross-resistance between linezolid and other classes of antibacterial agents unlikely [8]. Excellent tissue penetration and great oral bioavailability are notable properties of linezolid. Thus it allows sequential intravenous-to-oral administration without changing the drug or dosage regimen. It is approved in Europe and the USA for the treatment of nosocomial pneumonia, skin and soft tissue infections; and in the USA vancomycin-resistant Enterococcus (VRE) faecium and methicillin-resistant Staphylococcus aureus (MRSA) infections [9]. Linezolid is reported to have good penetration into the CNS [10]. A study in Japan showed the penetration of LZD into the CSF was 58.9 % of the peak value and 133 % of the trough value of serum concentrations following intravenous administration. And the penetration of LZD into the CSF was 82.9 % of the peak value and 145.6 % of the trough value of serum concentrations following oral administration [11]. For patients with a range of serious Gram-positive infections, including those caused by suspected or proven multidrug-resistant pathogens such as VRE or MRSA, linezolid can be an effective and generally well tolerated therapeutic option. In spite of this, gastrointestinal adverse effects are relatively common with linezolid and also associated with thrombocytopenia and myelosuppression [7]. Thus if the adverse effects occur, the doses and treatment period should be reduced.

In this case, the pathogen caused ventriculitis of the patient was vancomycin-resistant Enterococcus (VRE) faecium. It was resistant to many antimicrobials but sensitive to LZD. LZD administrated intravenously 600 mg q12h for half a month, followed by lumbar cistern drainage and VP shunt, led to an excellent outcome. Post-neurosurgical intracranial infections are critical severe events. The appropriate use of antibiotics is a key point. The antibiotics should be sensitive to pathogens and have good penetration into the CNS. The appropriate neurosurgical intervention is also very important, such as lateral ventricular puncture external

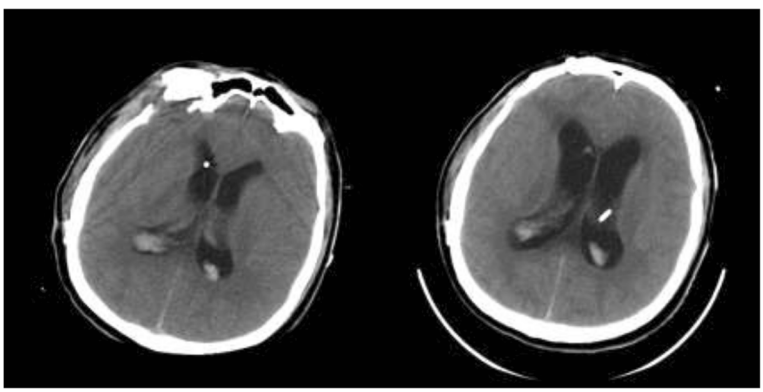

Fig. 3 Postoperative CT reveals the appearance of ventriculitis and the performance of lateral ventricular puncture external drainage

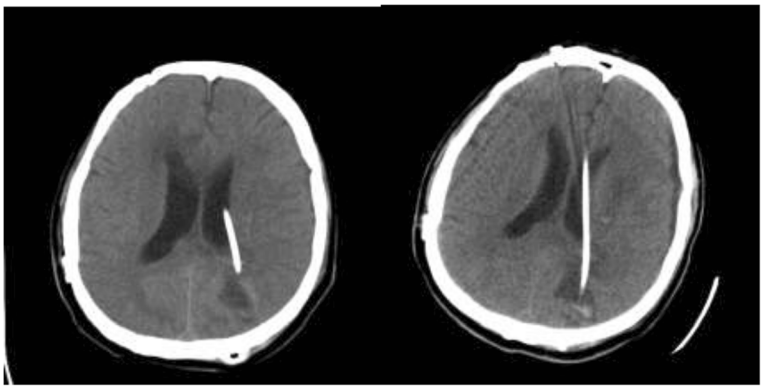

Fig. 4 Postoperative CT reveals the resolution of the ventriculitis and hydrocephalus, after the use of linezolid and the ventriculoperitoneal shunt procedure

drainage, lumbar cistern drainage, and VP shunt. Multiple methods led to the cure of post-neurosurgical vancomycin-resistant Enterococcus faecium ventriculitis in this case.

Conclusion

LZD should be considered as one of the important methods for the treatment of post-neurosurgical intracranial infections caused by vancomycin-resistant Enterococcus.

Abbreviations

CNS: central nervous system; CSF: cerebrospinal fluid; LZD: linezolid; MRSA: methicillin-resistant Staphylococcus aureus; NFGNB: non-fermentative Gram-negative bacteria; VP: ventriculoperitoneal; VRE: vancomycin-resistant Enterococcus.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

JT and DLL contributed with JJQ to write the report. JJQ and JT contributed in clinical treatment of the case. JJQ contributed in drafting the manuscript. JT and DLL contributed in revising the manuscript. All authors read and approved the final manuscript.

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