Treatment of intracranial infection caused by methicillin-resistant *Staphylococcus epidermidis* with linezolid following poor outcome of vancomycin therapy: A case report and literature review

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Case report

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Abstract

Background: To investigate the efficacy of linezolid in the treatment of intracranial infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) or methicillin-resistant coagulase-negative *Staphylococcus* (MRCoNS).

Case presentation: The patient at our hospital was diagnosed with methicillin-resistant *Staphylococcus epidermidis* (MRSE) intracranial infection, which was resistant to oxacillin and sensitive to vancomycin (MIC = 2 μg/mL) and linezolid (MIC = 4 μg/mL). Vancomycin was replaced with linezolid after 36 days of treatment due to poor outcome, and the patient was eventually cured. Further, a total of 23 cases of intracranial MRSA/MRCoNS infections were reported, of which 1 case with MRSA had a vancomycin MIC = 1 μg/mL, while the remaining 22 cases had vancomycin MICs greater than 1 μg/mL, with MIC = 1.5 μg/mL in 1 case, MIC = 2 μg/mL in 19 cases and MIC = 4 μg/mL in 2 cases. The linezolid-containing regimen was used after drug susceptibility results or if the initial treatment failed, leading to recovery in 19 patients, microbial clearance in 3 patients (of which 2 patients died of comorbidities and 1 patient died of *Pseudomonas aeruginosa* infection), and treatment failure in 1 case.

Conclusion: The PK/PD parameter for evaluating the efficacy of vancomycin is AUC/MIC ≥ 400 (assuming a vancomycin MIC_{BMD} of 1 μg/mL), and trough concentration should not be used as a substitute for AUC/MIC. For optimal management, vancomycin dosing should be based on AUC-guided dosing and monitoring. When the vancomycin MIC of MRSA/MRCoNS is > 1 μg/mL, the target AUC/MIC cannot be achieved. In such cases, linezolid can be used with good therapeutic effects.

Background

In hospitalized patients, the integrity of the blood-brain barrier can be disrupted by several invasive procedures, such as craniotomy, the placement of internal or external ventricular catheters, lumbar puncture, and intrathecal infusions. In such situations, specific microorganisms can invade the central nervous system through the blood-brain barrier, leading to health care-associated meningitis or ventriculitis (HCAMV) [1]. HCAMV cases are caused by Gram-positive cocci, particularly coagulase-negative staphylococci (CoNS; specifically, *Staphylococcus epidermidis*). Infectious Diseases Society of America (IDSA) guidelines recommend vancomycin combined with anti-*Pseudomonas* β-lactam drugs, such as cefepime, ceftazidime, or meropenem as an empirical treatment for HCAMV. However, when the vancomycin Minimum Inhibitory Concentration (MIC of methicillin-resistant *Staphylococcus aureus* (MRSA) or methicillin-resistant coagulase-negative *Staphylococcus* (MRCoNS) is greater than or equal to 1 μg/mL, linezolid, daptomycin, or compound sulfamethoxazole should be considered instead [2]. Here, we report a patient with intracranial *Staphylococcus epidermidis* infection who recovered after vancomycin was replaced by linezolid due to poor outcome. Meanwhile, we searched and screened the literature, and further analysed and summarized the cases of intracranial MRSA/MRCoNS infections treated with linezolid.

Case Report

Clinical data at admission

A 67-year-old male patient was admitted to our hospital on March 20, 2020 with a complaint of sudden disturbance of consciousness. The symptoms began six hours before admission, and included the inability to move the right limbs, irritability, and vomiting several times with no obvious cause. A head computed tomography (CT) performed at the local hospital showed left thalamic haemorrhage with intraventricular extension. After symptomatic and supportive treatments, the condition showed no significant improvement, and the blood pressure was not adequately controlled. Then, the patient was transferred to our hospital urgently. An emergency head CT scan showed: (1) left basal ganglia haemorrhage with intraventricular extension, (2) bilateral lacunar infarctions at basal ganglia and senile brain degeneration, and (3) mild bilateral inflammation of ethmoid sinuses. An emergency lung CT scan showed chronic bronchitis-emphysema, pulmonary bullae, and mild chronic inflammation of both lungs. The patient had a 9-year history of bipolar disorder with long-term use of lithium carbonate, and a 6-year-old fracture fixation of the right upper limb. Physical examination at admission showed a body temperature of 36.7 °C, a pulse of 100 bpm, a respiratory rate of 21 breaths per minute, and a blood pressure of 156/92 mm Hg. The patient was in a light coma and showed no response to instructions or questions. Rough respiratory sounds were detected in both lungs, and no moist rale was detected in either of the lower lungs. Neurological examination showed eye opening and vocalization with strong pricking, binocular gaze to the left side, and pupils equal in size with a diameter of 3 mm, round, and reactive to light. No rigidity was detected in the neck and the patient could not cooperate in muscle strength examination. Voluntary movements of the left limbs were observed while no movement was observed in the right limbs. The patient could not cooperate during the examination of muscle tone or tendon reflexes. A positive Babinski sign was observed on the right side but negative on the left side, while a positive Kernig sign was present bilaterally.

Clinical data after treatment

After admission, symptomatic treatments were provided, including haemostasis, dehydration to decrease intracranial pressure, neurotrophic treatment, blood pressure control, and fluid infusion. Bedside bilateral drill, craniotomy and ventricular drainage were performed, and urokinase was injected into bilateral ventricular drainage catheters. Bronchoscopy-guided nasotracheal intubation was performed. A repeat CT scan on March 21 showed that the right ventricular hematoma mostly resolved, and therefore the right ventricular drainage catheter was removed.

On March 23, the patient was still in a light coma, and moist rales in both lower lungs increased, along with an elevated white blood cell (WBC) count (15.36×10^9/L) and an elevated C-reactive protein (CRP) level (59.21 mg/L). Pulmonary infection was diagnosed, and intravenous infusion of

piperacillin-tazobactam (4.5 g every 8 h) was used as an anti-infection treatment. A repeat head CT scan on March 25 showed a significant decrease in the volume of intraventricular hematoma. In order to avoid infection after long-term retention, the drainage catheter of the left ventricle was removed.

On March 30 (d10), the patient developed fever and was in the twilight state of consciousness with aggravation of neck rigidity. The WBC count increased to 17.17×10^9/L, and the first routine and biochemical tests of cerebrospinal fluid (CSF) showed significant increases in cell count and protein level (see Figure 1 for details), leading to a diagnosis of possible intracranial bacterial infection. Piperacillin-tazobactam was discontinued, and the anti-infective therapy of intravenous infusion of vancomycin (1 g every 12 h) combined with ceftriaxone (2 g every 12 h) was administered with lumbar cistern drainage performed concurrently.

The vancomycin trough serum concentration on April 3 was 18.3 μg/mL. On April 8, the patient still had fever with aggravated neck rigidity, accompanied by cough and sputum expectoration. Therefore, the combined anti-infective treatment was considered ineffective, and ceftriaxone was discontinued. A combination of vancomycin with continuous 2-hour intravenous infusion of meropenem (2 g every 8 h) was used.

On April 12 (d23), the patient was in the twilight state of consciousness with no fever. The volume of lumbar cisternal drainage was 150 ml with unobstructed CSF drainage, and the drainage fluid was light yellow and turbid. Repeat blood routine and CRP tests showed decreased WBC count and CRP, and repeat CSF routine and biochemical tests showed that cell count and protein level decreased significantly compared with previous results (Figure 1). On April 18, the results of the first two CSF cultures revealed the presence of *Staphylococcus epidermidis*, which was resistant to oxacillin and sensitive to vancomycin (MIC = 2 μg/mL) and linezolid (MIC = 4 μg/mL). The current anti-infective therapy was deemed effective, and the treatment of vancomycin combined with meropenem continued.

On April 27 (d38), patient's neck rigidity improved, and a repeat CSF examination showed that cell count and protein level further decreased. The lumbar cisternal drainage catheter was removed. On April 29, the CSF metagenomic sequencing revealed *Staphylococcus epidermidis* (read count 1,541), *Propionibacterium acnes* (read count 116) and *Moraxella osloensis* (read count 14), and the treatment of vancomycin combined with meropenem continued.

On May 6 (d47), the patient developed fever again, with a maximum body temperature of 38.4 °C. A repeat CSF examination showed turbid CSF with elevated WBC count, increased proportion of multinucleated cells, and elevated protein level compared with previous tests, leading to the conclusion that the infection aggravated again. The CSF concentration of vancomycin was 5.0 μg/mL. The anti-infective regimen was adjusted to 0.6 g linezolid every 12 h combined with 2 g ceftazidime every 8 h.

On May 10, the patient's liver function test showed 528 U/L ALT and 323 U/L AST. Considering possible linezolid-induced liver injury, linezolid was discontinued and reduced glutathione and bicyclol were given for liver protection. On May 11 (d52), the patient had no fever and showed improved neck rigidity. The results of CSF routine and biochemical tests showed significant improvement, and *Staphylococcus epidermidis* was isolated from the CSF culture. On May 12, given the isolation of *Staphylococcus epidermidis* from several CSF cultures and the poor outcome of vancomycin treatment, anti-infective treatment with linezolid was resumed, combined with entecavir (0.5 mg once a day p.o.) for anti-HBV (hepatitis B virus) treatment. Liver-protective drugs were continued with close monitoring of liver function. A repeat blood biochemical test on May 16 showed 58 U/L aspartate aminotransferase and 125 U/L alanine aminotransferase. On May 24 (d64), routine repeat CSF and biochemical tests showed normal results (Figure 1). On May 25, repeat head and lung CT scans showed left thalamic post-haemorrhagic encephalomalacia, while the rest were similar to previous results.

On May 26, the patient was in the twilight state of consciousness. After tracheotomy, the patient exhibited smooth spontaneous breathing and was supported by liquid diet. The patient had no fever, and there was a slight improvement of neck rigidity. The antibacterial drugs, including linezolid and ceftazidime, were discontinued, while nutritional, supportive, and symptomatic treatments continued. On June 1, the patient regained consciousness and was transferred to the Department of Rehabilitation Medicine for comprehensive rehabilitation. On June 28, the recovery was satisfactory and the patient was discharged from the hospital. The treatment regimens and CSF cell counts during hospitalization in the Department of Neurosurgery are shown in Figure 1.

Literature Review

A search in PubMed, CNKI, Wanfang, and VIP databases using the terms "Linezolid", "Meningitis", "Intracranial infection", and "*Staphylococcus*" was conducted for articles published from the dates the databases were established to June 2020. Inclusion criteria: (1) Clinical data were relatively complete, and linezolid was used to treat cases of intracranial MRSA/MRCoNS infection. (2) Vancomycin MIC value of *Staphylococcus* was recorded in the article. Exclusion criteria: reviews, articles with incomplete clinical data, and duplicate publications.

General information

A total of 7 articles were included with 23 cases reported, all written in English. No relevant Chinese case report that met the inclusion criteria was retrieved (Table 1). Among the 23 patients, 12 were male and 11 were female. Among them, 2 were children and 21 were adults, with ages ranging from 22 days to 80 years.

Treatment and prognosis

Among the 23 cases, 14 were caused by MRSA, 8 by MRCoNS, and 1 by VISA. One patient was initially treated with linezolid due to an allergy to vancomycin. Linezolid was not chosen as the initial treatment for the remaining 22 patients, but they were switched to linezolid when drug sensitivity results were obtained or the initial treatments were not effective. For 19 cases, regimens containing vancomycin were initially selected, of which 1 case had a vancomycin MIC = 1.5 μg/mL of MRSA/MRCoNS, 16 cases had an MIC = 2 μg/mL, and 2 cases had an MIC = 4 μg/mL. After switching to regimens containing linezolid due to the poor outcome of vancomycin treatment, 16 patients fully recovered, 2 patients achieved microbial clearance and then later died of comorbidities, and treatment failed in 1 patient. Among the 23 patients, 21 were treated with linezolid alone for MRSA/MRCoNS, and 2 patients were treated with linezolid combined with daptomycin and rifampicin, and linezolid combined with rifampicin, respectively, both of whom were cured. Fifteen of the 23 case studies provided the linezolid MIC of MRSA/MRCoNS, with an MIC = 1 μg/mL in 12 cases and an MIC = 4, 1.5, and 0.25 μg/mL in each of the remaining cases. All of the 15 patients were cured.

Table 1 Clinical characteristics of 23 patients with intracranial infection treated with linezolid

Patient No.	Age	Gender	CSF leukocytes;	Previous treatment	Pathogen	MIC (mg/L) Vancomycin/linezolid	Treatment and duration	Outcomes
1[3]	62 years	Male	NA	Linezolid	MRSA	1/4	Linezolid +daptomycin+ rifampicin 3 weeks	cured
2[4]	77 years	Male	NA	vancomycin□ ampicillin/sulbactam	VISA	4/NA	Linezolid (11d-27d)□ Moxifloxacin (28d-51d)	cured
3[5]	43 years	Female	NA	vancomycin	MRCoNS	4/1.5	Linezolid + rifampicin 12 weeks	cured
4[6]	80 years	Male	>1×10^9/L	Ceftizoxime, vancomycin	MRSA	2/NA	Linezolid (600 mg×2), 28 days; piperacillin/ tazobactam (4.5 g ×3) after 5 days of linezolid, lasting 3 weeks	Microbiologically cured, but died 3 months later due to gastric bleeding
5[6]	72 years	Female	>1×10^9/L	Ceftizoxime, ceftazidime, vancomycin	MRSA	2/NA	Linezolid (600 mg×2), 21 days	cured
6[6]	36 years	Male	0.25×10^9/L	Ceftizoxime, meropenem	MRSA	2/NA	Linezolid (600 mg×2), 21 days	Microbiologically cured, but died due to intracranial haematoma 2 months later
7[6]	69 years	Male	>1×10^9/L	Ceftizoxime, vancomycin	MRSA	2/NA	Linezolid (600 mg×2), 10 days	Microbiological failure; died despite addition of daptomycin on day 6
8[6]	65 years	Female	0.3×10^9/L	Ceftizoxime, imipenem, vancomycin	MRSA	2/NA	Linezolid (600 mg×2), 21 days	Microbiologically cured, but died 1 month later due to *Pseudomonas aeruginosa* meningitis
9[6]	34 years	Female	0.7×10^9/L	Ceftizoxime, meropenem	MRCoNS	2/NA	Linezolid (600 mg×2), 21 days	Microbiologically cured; survived
10[6]	28 years	Male	0.35×10^9/L	Ceftizoxime	MRCoNS	2/NA	Linezolid (600 mg×2), 21 days	Microbiologically cured; survived
11[7]	34 years	Male	16.32×10^9/L	Cefatriaxone□ vancomycin□ Levofloxacin	MRSA	1.5/0.25	Linezolid+ Levofloxacin□ 59 days	cured
12[8]	22 days	Female	0.18×10^9/L	ampicillin□ cefotaxime□ vancomycin	MRCoNS	2/1	Linezolid□40 days	cured
13[8]	11 months	Female	0.11×10^9/L	vancomycin	MRCoNS	2/1	Linezolid□57 days	cured
14[9]	51 years	Female	0.23×10^9/L	vancomycin□ cefotaxime	MRCoNS	2/1	Linezolid (600 mg×2), 14 days	cured
15[9]	26 years	Male	0.156×10^9/L	vancomycin□ cefotaxime	MRCoNS	2/1	Linezolid (600 mg×2), 14 day□	cured

							ceftazidime (2 g×3)＋10 days	
16[9]	23 years	Male	0.36×10^9/L	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 14 days	cured
17[9]	38 years	Female	0.29×10^9/L	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 14 days＋ colistin (3 MUI×3)＋15 days	cured
18[9]	47 years	Male	0.41×10^9/L	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 14 days	cured
19[9]	58 years	Female	0.189×10^9/L	vancomycin＋ cefotaxime	MRCoNS	2/1	Linezolid (600 mg×2), 14 days	cured
20[9]	49 years	Female	0.258×10^9/L	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 14 days	cured
21[9]	67 years	Male	NA	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 28 days	cured
22[9]	71 years	Male	NA	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 42 days	cured
23[9]	58 years	Female	8.1×10^9/L	vancomycin＋ cefotaxime	MRSA	2/1	Linezolid (600 mg×2), 14 days	cured

Discussion And Conclusions

Evaluation of the efficacy of vancomycin

The currently recognised key PK/PD parameter for evaluating the efficacy of vancomycin is AUC/MIC ≥ 400 (assuming a vancomycin MIC_{BMD} of 1 μg/mL)[10]. Previous studies and the 2009 Guidelines on Therapeutic Monitoring of Vancomycin developed by the Infectious Diseases Society of America (IDSA) recommended trough concentration value as an alternative indicator to AUC/MIC. For complicated infections, it is recommended that the vancomycin trough serum concentration should be maintained at 15–20 μg/mL[11]. However, with the accumulation of more clinical practice experience, the updated 2020 IDSA guidelines stated that the accuracy and reliability of trough concentration values could be affected by different PK parameters[10]. Therefore, the 2020 version of the guidelines recommends AUC-guided dosing and monitoring as a basis for optimal management of vancomycin, especially for serious MRSA infections. *For patients with suspected or diagnosed serious MRSA infections, it is recommended to target an AUC/MIC ratio of 400 to 600 (assuming a vancomycin MIC of 1 mg/L) to achieve clinical efficacy while improving patient safety. Trough concentration of 15–20* μ*g/mL is no longer recommended as a target value alone. In the case reported by our hospital, the vancomycin trough serum concentration* was 18.3 μg/mL, within the range of 15–20 μg/mL, and *the vancomycin concentration in CSF* was 5.0 μg/mL. The plasma AUC was 250 h•μg/mL, and the AUC/MIC ratio was 125 (MIC = 2 μg/mL), unable to reach the target AUC/MIC.

Treatment of intracranial MRSA/MRCoNS infections with linezolid

There were a few case reports on treatment of intracranial MRSA/MRCoNS infections with linezolid. The vancomycin MIC values of *Staphylococcus* recorded in cases identified through searching of Chinese and English literature are shown in Table 1. For the treatment of intracranial MRSA/MRCoNS infections, both the guidelines developed by the European Society of Clinical Microbiology and Infectious Diseases and the IDSA[2, 12] recommend vancomycin as a first-line treatment. However, if the MRSA/MRCoNS has a vancomycin MIC greater than or equal to 1 μg/mL, linezolid, daptomycin, or compound sulfamethoxazole should be considered [1]. Linezolid has been successfully used in many patients with infections caused by cerebrospinal fluid shunt procedures [13-15]. The case reported here involved hospital-acquired intracranial infection due to ventricular drainage, and the patient underwent 36 days of treatment with vancomycin with poor outcome before being switched to linezolid treatment, which led to the eventual full recovery.

The physiochemical characteristics of drugs (such as molecular weight, hydrophilicity, and plasma protein binding rate), the pathophysiology of the peripheral disorders of central nervous system (such as blood-brain inflammation and blood-brain barrier), the PK/PD parameters of the antibacterial drugs (time-dependence or concentration-dependence), and the sensitivity of the bacteria to the drugs should all be considered in the selection of antibacterial drugs for the central nervous system [16]. The molecular weight of linezolid is 337.35, which is much smaller than vancomycin and

teicoplanin, and its level of plasma protein binding is 31%. After oral intake of 600 mg, the steady-state peak serum concentration (C_{max}) of linezolid is 15–27 μg/mL with a high tissue concentration [17]. The CSF/plasma AUC ratio of linezolid is 0.5 to 0.9 when there is no inflammation of the meninges, and 0.7 when there is inflammation of the meninges[16]. The concentration of linezolid in CSF can exceed the MIC value of Gram-positive bacteria that cause intracranial infections. Although linezolid is a bacteriostatic antibiotic, there are several case reports of its use in the management of severe Gram-positive bacterial infection, where antibiotic bactericidal activity might be necessary, such as meningitis and endocarditis [6].

The linezolid MIC of MRSA/MRCoNS was reported in 15 cases, of which one case of MRSA had a linezolid MIC of 4 μg/mL. The patient was treated with linezolid combined with daptomycin and rifampicin and was cured. One case of MRCoNS had a linezolid MIC of 1.5 μg/mL, and the patient was cured by the combined use of linezolid and rifampicin. The remaining cases of MRSA/MRCoNS all had linezolid MIC values less than or equal to 1 μg/mL, and all patients were cured after treatment with linezolid monotherapy. In the case reported at our hospital, the linezolid MIC of *Staphylococcus epidermidis* was 4 μg/mL, and the patient was eventually cured after treatment with linezolid monotherapy. Linezolid is a time-dependent antibacterial drug, and the AUC/MIC and $\%T_{>MIC}$ can be used as PK/PD parameters to determine its efficacy [18]. In the study of PK/PD of linezolid in plasma/CSF by Monte Carlo simulation conducted by Xiaofei Wu et al. [19] linezolid was routinely administered at a dose of 0.6 g every 12 h. When $AUC_{0\sim24h}/AUC \geq 59.1$ was applied as a parameter, the probability of target attainment (PTA) for linezolid achieving the PK/PD index in plasma was greater than or equal to 90 % for pathogens with a MIC of ≤ 2 μg/mL, whereas the PTA was greater than or equal to 90 % in CSF with a MIC of ≤ 1 μg/mL. When $\%T_{>MIC} \geq 40\%$ was applied as a parameter, the PTA of linezolid in plasma/CSF was excellent when the MIC was ≤ 4 μg/mL. In the study by Beer R et al. [20] when the linezolid MICs of the pathogen were 2 μg/mL and 4 μg/mL, the $\%T_{>MIC}$ in CSF were 99.8% and 57.2%, respectively. Therefore, the conventional dose of linezolid can achieve good therapeutic effects when the linezolid MIC of the pathogen is ≤ 2 μg/mL. When the linezolid MIC of the pathogen is 4 μg/mL or the patient is critically ill, it may be necessary to increase the dose, dosing frequency, or the duration of intravenous drip to improve the therapeutic effects. Monitoring drug concentration will facilitate the adjustment of dosing to achieve the best treatment effects [19]. In addition, combination therapy may help to control infections and eradicate pathogens in time. In the study by Theodoros Kelesidis et al. [2], the triple combination of linezolid, daptomycin, and rifampicin had synergistic bactericidal effects in vitro. This regimen may be attempted for salvage treatment. Moreover, the combination of linezolid with rifampicin and the combination of linezolid with vancomycin also revealed synergistic effects in vitro, with case reports on successful clinical applications[21]. However, combination therapies do not always get favourable outcomes. Therefore, further studies are necessary to verify the efficacy of the combination treatment strategy.

Correlation between linezolid and liver injury

Hepatitis B surface antigen, hepatitis B e antibody and hepatitis B core antibody were all positive in the patient, with positive HBV DNA (95×10^3 IU/mL), leading to the diagnosis of HBeAg-negative chronic hepatitis B. Transaminases were elevated in the patient before the use of linezolid. Linezolid treatment was started on May 6 and had been only used for 4 days by May 10 when a progressive increase in transaminases was observed. The possibility of drug-induced liver injury caused by linezolid could not be ruled out. However, previous studies showed that drug-induced liver injury (DILI) with fulminant liver failure and lactic acidosis were probably related to prolonged use of linezolid [22]. In our case, the Roussel Uclaf Causality Assessment Method (RUCAM) yielded a score of 0. Moreover, the liver function gradually improved with subsequent use of linezolid and hepatoprotective treatment. Therefore, linezolid was not considered to correlate with liver injury in this case.

Conclusion

The PK/PD parameter for evaluating the efficacy of vancomycin is AUC/MIC ≥ 400, and trough concentration should not be used as a substitute for AUC/MIC. For optimal management, vancomycin dosing should be based on AUC-guided dosing and monitoring. *In patients with serious MRSA infections, the recommended AUC/MIC ratio is 400 to 600 mg*h/L.*

When the vancomycin MIC of MRSA/MRCoNS is greater than 1 μg/mL, the target AUC/MIC cannot be achieved. In such cases, linezolid can be used to obtain good therapeutic effects. The conventional dose of linezolid can achieve good therapeutic effects when the linezolid MIC of the pathogen is ≤ 2 μg/mL. When the linezolid MIC of the pathogen is 4 μg/mL or patients are critically ill, it may be necessary to increase the dose, dosing frequency, or the duration of intravenous drip to improve the therapeutic effects. Monitoring the drug concentration will facilitate the adjustment of dosing to achieve the best treatment effects. In addition, combination therapy may help to control infections and eradicate pathogens in time, but further studies are necessary to confirm the efficacy of combination treatment strategies.

Declarations

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Availability of data and materials

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Authors' contributions

ZQL and XPY was in charge of case reviewing and preparation of the manuscript. ZQL and SMC collected clinic opinions regarding on this case and drafted the manuscript. LMH and SFW participated in its coordination and revised the manuscript. All authors read and approved the final manuscript. Ethics approval and consent to participate. The study was approved by the Ethics Committee of First hospital of Quanzhou, Fujian, China.

Consent for publication

Written informed consent was obtained from the next of kin of the patient for publication of this Case report and accompanying images.

Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Abbreviations

MRSA: methicillin-resistant *Staphylococcus aureus;* MRCoNS: methicillin-resistant coagulase-negative *Staphylococcus;* MRSE: methicillin-resistant *Staphylococcus epidermidis;* AUC: area under the curve; HCAMV: health care-associated meningitis or ventriculitis; IDSA: Infectious Diseases Society of America; MIC: Minimum Inhibitory Concentration.

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Figures

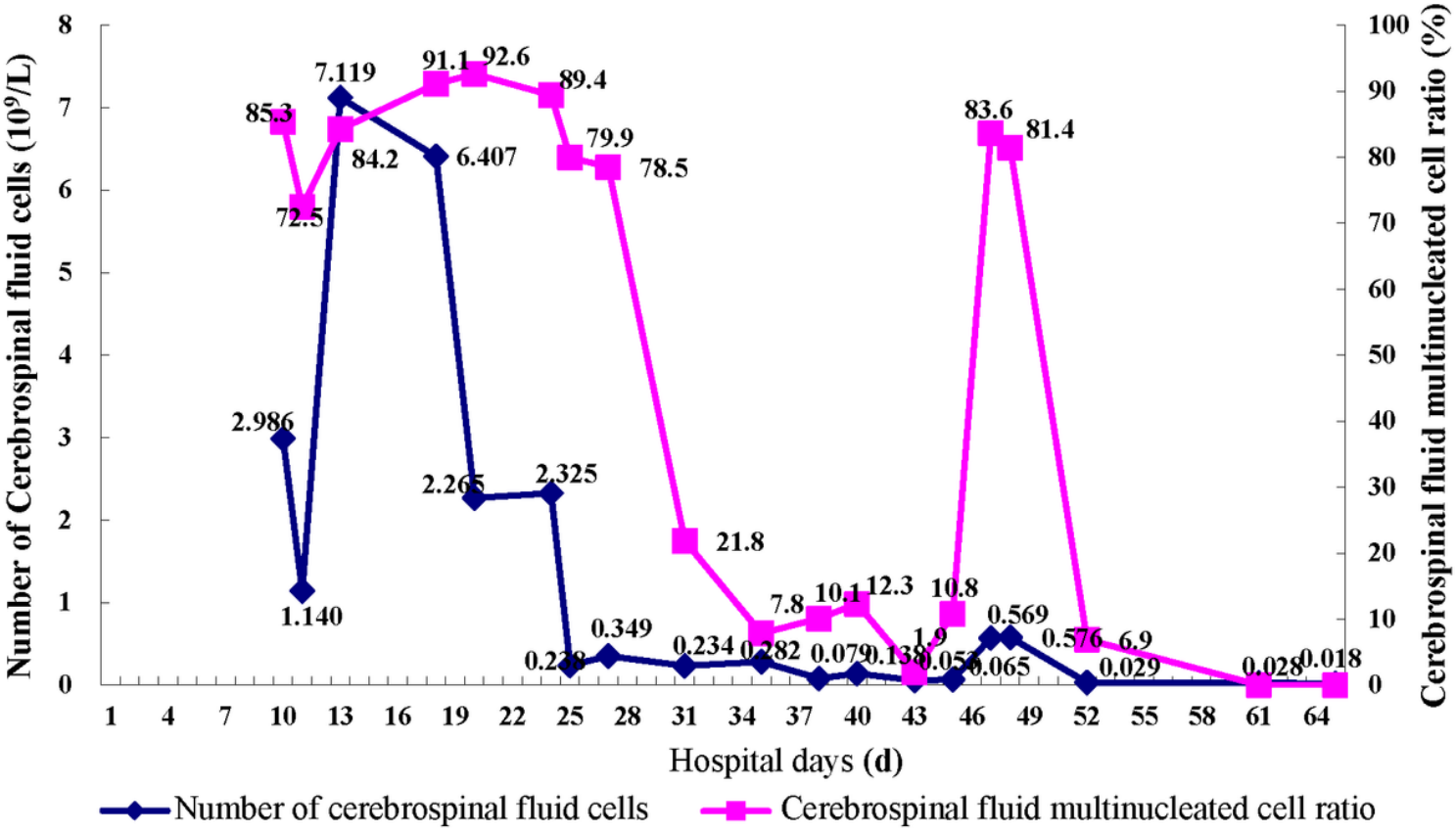

Figure 1

Treatment regimens and CSF cell counts TZP: piperacillin-tazobactam, VAN: vancomycin, CRO：ceftriaxone, MEM: meropenem, LZD: linezolid (discontinued from May 10 to May 11), CAZ: ceftazidime