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CASE REPORT

Purulent Meningitis Due to *Porphyromonas endodontalis, Bacteroides heparinolyticus, Prevotella pleuritidis* and *Streptococcus constellatus* from Oral and Maxillofacial Space Infection: A Case Report

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Background: Purulent meningitis caused by polymicrobial oral anaerobes represents a rare but life-threatening clinical challenge, with *Porphyromonas endodontalis, Bacteroides heparinolyticus, Prevotella pleuritidis*, and *Streptococcus constellatus* being pfastidious organisms. Traditional diagnostic methods often fail to identify these fastidious organisms, leading to delayed or inappropriate therapy.

Case Presentation: We report a rare case of purulent meningitis resulting from a polymicrobial infection involving *Porphyromonas endodontalis, Bacteroides heparinolyticus, Prevotella pleuritidis*, and *Streptococcus constellatus* in a 76-year-old male patient who presented with a 40-day history of left facial pain. This case represents the first documented instance of these four oral anaerobes concurrently causing an infection of the central nervous system.

Conclusion: To the best of our knowledge, this case represents the first documented evidence of polymicrobial purulent meningitis caused by oral anaerobes, specifically *Porphyromonas endodontalis, Bacteroides heparinolyticus, Prevotella pleuritidis*, and S*treptococcus constellatus*. Our findings not only provide direct evidence for the oral-central nervous system (CNS) infection pathway but also validate that the valuable approach based on metagenomic next-generation sequencing (mNGS) offers significant clinical insights for diagnostic and therapeutic strategies.

Keywords: purulent meningitis, *Porphyromonas endodontalis*, *Bacteroides heparinolyticus*, prevotellapleuritidis, *Streptococcus constellatus*, oral and maxillofacial space infections, case report

Introduction

Purulent meningitis is an inflammation of the cerebrospinal membranes caused by a purulent bacterial infection, representing one of the common diseases of the central nervous system.[1] Clinical symptoms typically include fever, chills, signs of meningeal irritation, increased intracranial pressure, impaired consciousness, and seizures. Notably, purulent meningitis is associated with a high risk of mortality and long-term disability.Oral and maxillofacial space infection,[2] commonly referred to as oral and maxillofacial cellulitis, is an acute, diffuse, suppurative inflammation that arises in the loose connective tissues situated between the jaws, muscles, cervical membranes, and skin. This condition is marked by a significant prevalence of infections involving both intrinsically resistant organisms and acquired drug-resistant bacteria, a high incidence of severe infections, and an elevated risk of mortality.

The aforementioned diseases are prevalent in neurology and oral and maxillofacial surgery, respectively. However, purulent meningitis resulting from oral and maxillofacial space infections originating from oral sources, specifically odontogenic infections, is clinically rare and has not been extensively documented in the literature.[3–8] In this report, we

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present a successful diagnosis and treatment of purulent meningitis caused by a variety of anaerobic bacteria from oral sources, predominantly including *Porphyromonas endodontalis, Bacteroides heparinolyticus,Prevotellapleuritidis* and *Streptococcus constellatus*, in the context of an oral and maxillofacial interstitial infection. Traditional microbiological methods, such as culture, often fail to identify fastidious and anaerobic bacteria, particularly in patients who have undergone prior empirical antibiotic therapy. Metagenomic next-generation sequencing (mNGS) is a powerful, unbiased detection technique that facilitates high-throughput sequencing of nucleic acids (DNA and/or RNA) from all microorganisms present in a clinical sample simultaneously, without necessitating a prior hypothesis regarding a specific pathogen. This capability renders mNGS particularly valuable for identifying difficult-to-culture organisms, rare pathogens, and complex polymicrobial infections, such as the case presented here, thereby potentially overcoming the limitations of traditional diagnostics and informing targeted antimicrobial therapy.Our aim is to contribute valuable diagnostic and therapeutic insights regarding this uncommon condition, further highlighting the utility of mNGS in such challenging scenarios.

Case Presentation

The patient is a 76-year-old man who was admitted to the hospital primarily due to "left facial pain for 40 days, aggravated for 6 days." Initially, 40 days prior, the patient experienced left facial pain of unclear origin, which was intermittent, dull, and tolerable. Over time, this pain evolved into a persistent, sharp discomfort that prevented him from opening his mouth, resulting in a constant state of distress without relief. The patient self-administered oral painkillers intermittently but ultimately sought medical attention, accompanied by family members, due to the intolerable nature of the pain. During the outpatient visit, an MRI of the trigeminal nerve revealed a close relationship between the left trigeminal nerve and adjacent small blood vessels. Consequently, the outpatient physician admitted the patient to the hospital with a diagnosis of "Trigeminal neuralgia".The patient denied having chronic diseases, including hypertension, type 2 diabetes mellitus, coronary heart disease, cerebrovascular disease, psychiatric disorders, asthma, and a history of hepatitis, tuberculosis, malaria and also reported no history of surgery, trauma, drug or food allergies, family history of chronic conditions, as well as no history of smoking or alcohol consumption.

Upon admission, the patient's blood glucose level was recorded at 4.9 mmol/L, with blood pressure at 100/67 mmHg, a respiratory rate of 20 breaths per minute, and pulse oximetry showing 92%. The body temperature was 37.5°C. Auscultation revealed slightly coarse respiratory sounds in both lungs, but no distinct dry or wet rales were noted. The heart rate remained stable, and no abnormal pathologic murmurs were detected. The patient exhibited intermittent drowsiness, yet maintained clear speech and provided tangential responses, indicating generally normal higher nervous function. Examination revealed symmetrical bilateral ophthalmoplegia, with pupils equal in size, approximately 3 mm in diameter, and both direct and indirect light reflexes were intact. Eye movements were normal in all directions, and no nystagmus was observed. The bilateral frontal lines and nasolabial grooves were symmetrical. The tongue appeared centered, while the left temporal, parotid, and inferotemporal regions exhibited slight swelling, with fluctuating sensation upon touch, and significant pressure and pain. The patient could open the mouth to approximately one finger's width, accompanied by facial pain during this action. Limb muscle strength was assessed at grade 5, and muscle tone was within normal limits. Symmetrical bilateral pinprick nociception and tendon reflexes were noted. Both the finger-nose and heel-knee-tibia tests yielded negative results, meningeal irritation signs were absent, and no pathological signs were elicited.

The test results obtained on the day of admission indicated a blood leukocyte count of 20.8 x 10^9/L, with a neutrophil ratio of 88.8% and a neutrophil count of 18.45 x 10^9/L. The C-reactive protein (CRP) level was measured at 144.17 mg/L, while calcitonin was found to be 0.63 ng/mL. Albumin levels were at 25.8g/L, glycosylated hemoglobin was 6.3%, and D-dimer was recorded at 0.95μg/mL. The potassium level was noted to be low at 3.01mmol/L. No abnormalities were detected in myocardial injury markers, myoenzyme profiles, liver function tests, lipid levels, or nail function assessments.

Facial enhancement CT revealed swelling in the left side of the facial mandibular branch, particularly in the pterygoid region, characterized by scattered small non-enhanced low-density shadows and blurred surrounding fat interstitials, suggestive of infectious lesions (Figure 1). Lung CT findings indicated pulmonary emphysema and scattered fibrous foci. Whole abdomen CT showed pancreatic fat substitution, renal cysts, and signs of an enlarged prostate. Cranial imaging

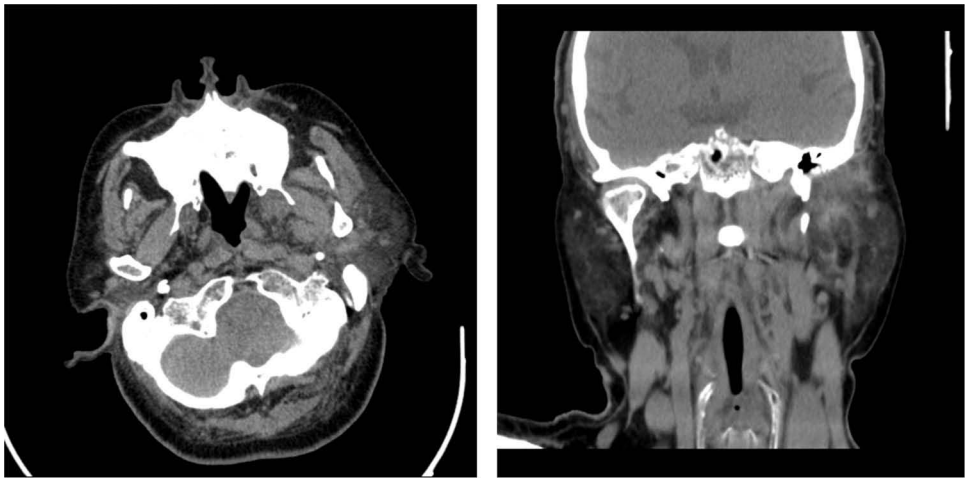

Figure 1 Facial enhancement CT.

suggested abnormal signals in the cerebral white matter along with cerebral atrophy. Abdominal ultrasound confirmed the presence of simple renal cysts, whereas cardiac ultrasound indicated mild aortic and mitral regurgitation.Carotid vascular ultrasound indicated the presence of carotid atherosclerosis with plaque formation. Due to the patient's intermittent drowsiness and hypothermia, a lumbar puncture was subsequently performed. The cerebrospinal fluid (CSF) exhibited a "rice soup" appearance (Figure 2A) and its biochemistry revealed: glucose 2.00mmol/L, chloride 125.0mmol/L, adenosine deaminase 0.98U/L, and a protein concentration of 2.43g/L (Figure 2C). Routine analysis of the CSF showed a positive qualitative result for PAN protein (+++), a red blood cell count of 50 x 10^6/L, a white blood cell count of 7915 x 10^6/L (Figure 2B), and a pressure measurement of 280 mm water column. Given the significant abnormalities in

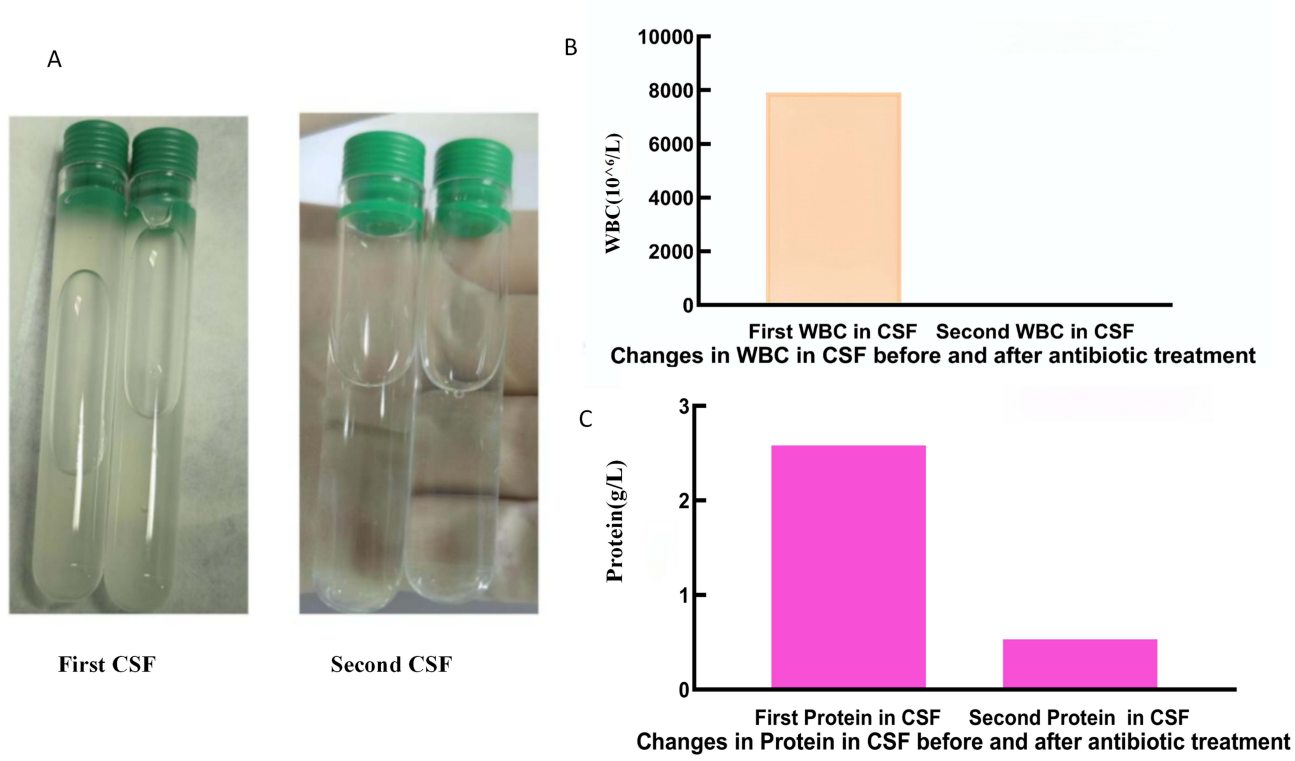

Figure 2 Appearance and test results of cerebrospinal fluid. (**A**) Appearance of CSF obtained via lumbar puncture; (**B**) Outline findings in CSF; (**C**) Biochemical findings in CSF.

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the CSF and the high likelihood of purulent meningitis, a cerebrospinal fluid pathogen metagenomic next-generation sequencing (mNGS) test was promptly conducted. The results, received two days later, identified *Porphyromonas endodontalis, Bacteroides heparinolyticus*, and *Prevotella pleuritidis*, strongly suggesting a mixed infection involving multiple anaerobes. Five days later, the blood culture returned positive for *Streptococcus constellatus*.

On the day of admission, the antibiotic regimen selected was meropenem 2g every 8 hours. The patient continued to experience intermittent fever, with a maximum temperature of 39.4 °C, and the level of consciousness deteriorated from a shallow to a moderate coma. Considering the cerebrospinal fluid mNGS results, which indicated a mixed infection caused by anaerobic Gram-negative bacilli of oral origin, the treatment was adjusted by adding Metronidazole Sodium Chloride Injection 0.5g every 12 hours to the original meropenem regimen. Following this adjustment, the patient's body temperature showed a tendency to decline, although a low-grade fever persisted. Blood cultures suggested the presence of Streptococcus constellatus subspecies. To further enhance the antimicrobial effect, linezolid tablets 600mg were added orally twice daily, in conjunction with the existing meropenem and metronidazole regimen (Figure 3). After two weeks of this combined anti-infective treatment, the patient's body temperature returned to the normal range, consciousness improved to a clear state, and the patient was able to respond appropriately. Neurological function also appeared to normalize. Cerebrospinal fluid analysis revealed the following biochemistry: glucose 2.40mmol/L, chloride 129.0mmol/L, protein quantification 0.59mmol/L (Figure 2C). The cerebrospinal fluid routine showed a colorless and transparent appearance, with a red blood cell count of 10 x 10^6/L, leukocyte count of 37 x 10^6/L (Figure 2B), and a positive result for Pan protein qualitatively.Subsequent review of the facial enhancement CT scan revealed that the infectious lesion in the left mandibular branch-pterygoid region had resolved. Additionally, the left facial swelling had subsided, was no longer painful, and the patient was able to open his mouth normally without any impact on his eating. Consequently, the patient was discharged from the hospital with an excellent clinical outcome.

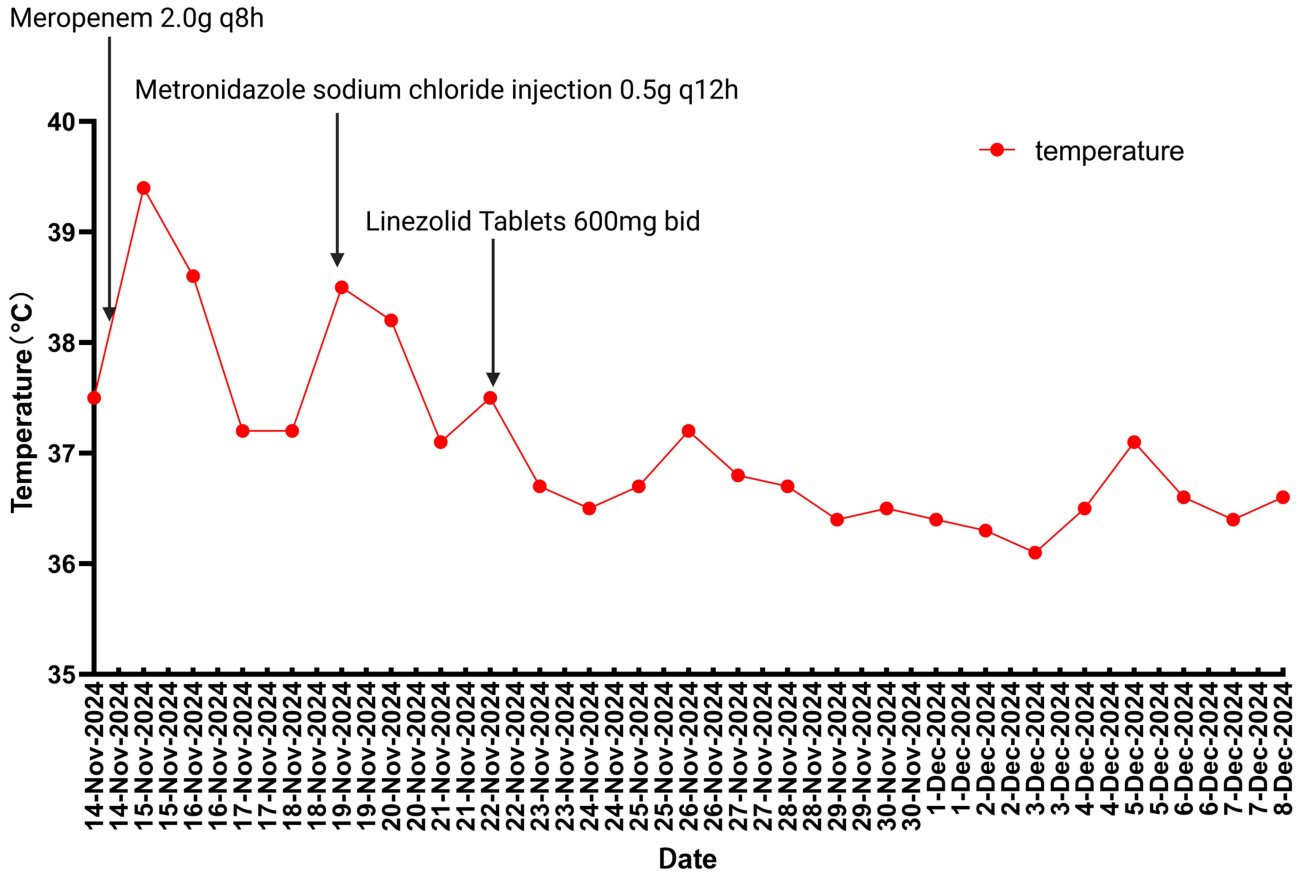

Figure 3 Temperature changes and antibiotic regimen adjustments during treatment.(the black arrow indicates the antibiotic regimen corresponding to a specific body temperature.).

Discussion

Purulent meningitis is an intracranial infectious disease characterized by high rates of disability and mortality, along with severe clinical manifestations and a poor prognosis.[9–11] This type of infection typically breaches the protective barrier of the blood-brain barrier and tends to occur when the body's immune system is compromised.[12] Common clinical manifestations include fever, chills, altered consciousness, limb convulsions, and headache.Purulent meningitis is primarily attributed to two main categories of causative factors: endogenous and exogenous. Endogenous routes of infection primarily involve bloodstream infections, such as those secondary to bacteremia. In contrast, exogenous factors encompass intracranial infections that arise as a result of neurosurgical procedures or require surgical intervention.[13,14] This includes meningitis caused by retrograde bacterial infection following neurosurgery, particularly in cases involving intracranial pus, ventriculo-abdominal shunts, or lumbar pool drainage.

Oral and maxillofacial space infections(OMSI) are among the most common infectious diseases affecting the oral and maxillofacial region. These infections can be categorized based on anatomical structures into several distinct types: occlusal space, pterygomandibular space, infratemporal space, temporal space, submandibular space, parapharyngeal space, buccal space, and floor-of-mouth space infections. Clinical manifestations of OMSI encompass both local and systemic symptoms. Local symptoms may include acute skin redness, swelling, pain, elevated skin temperature, dysphagia, restricted mouth opening, depressed edema, and twitching. Systemic symptoms can manifest as chills, fever, headache, and generalized fatigue and malaise.

The cerebrospinal fluid (CSF) exhibited a "rice soup" appearance, and its biochemistry was consistent with purulent meningitis, necessitating immediate empirical meropenem therapy. Given the limitations of traditional culture methods in identifying fastidious or pre-treated organisms, we simultaneously employed cerebrospinal fluid metagenomic next-generation sequencing (mNGS). This unbiased method enables comprehensive pathogen detection directly from clinical samples, proving crucial for guiding timely and precise antibiotic adjustments in complex, culture-negative infections such as this one.

The follow-up history indicates that the patient has experienced prolonged left facial pain, and examination reveals significant swelling on the left side of the face, suggesting the possibility of a local abscess. This raises concerns regarding a soft tissue infection in the oral and maxillofacial region. Additionally, the patient's family reported that the patient has never brushed their teeth, indicating extremely poor oral hygiene. Consequently, it is highly probable that the causative organisms of the patient's septic meningitis include anaerobic bacteria originating from the oral cavity. Although cerebrospinal fluid culture yielded negative results,the subsequent cerebrospinal fluid metagenomic next-generation sequencing (mNGS) results identified three Gram-negative bacilli with high relative abundance and sequence counts:*Porphyromonas endodontalis,Bacteroides heparinolyticus*,and *Prevotellapleuritidis*.Additionally, a total of background flora, including *Streptococcus constellatus*, were also reported.Metagenomic next-generation sequencing (mNGS) of cerebrospinal fluid (CSF) was conducted utilizing shotgun sequencing to analyze all DNA present in the sample. Total DNA was extracted from the CSF, and sequencing was performed on the Illumina high-throughput sequencing platform. Bioinformatic analysis was executed using a microbial-specific database to accurately identify microbial sequences.(The testing company is HEIMER medicine).A review of the literature indicates that Porphyromonas endodontalis,[15] a Gram-negative bacterium, is an endodontic pathogen closely associated with both primary and secondary root canal infections. *Bacteroides heparinolyticus*,[16,17] a Gram-negative anaerobic bacillus, is part of the normal flora found in the oral, respiratory, intestinal, and genitourinary tracts of humans and animals. This conditionally pathogenic bacterium is known to cause abscesses and bacteremia, and it has been primarily isolated from cat and dog bite wounds, with additional case reports documenting its isolation from patients suffering from periodontitis.*Prevotella pleuritidis*[18] is a gram-negative anaerobic bacillus that has been isolated from pleural fluid and is known to cause lung and liver abscesses. Notably, large quantities of *Prevotella pleuropneumoniae* are frequently found in the oral cavities of heavy smokers and in the saliva of patients with early-onset rheumatoid arthritis. Furthermore, an elevated proportion of *Prevotella pleuropneumoniae* has been observed in patients with systemic lupus erythematosus who also have periodontitis.After approximately three days of the meropenem regimen, the patient continued to experience intermittent fever and poor mental status. It was deemed possible that meropenem did not fully cover the sensitive organisms, particularly the three Gram-negative anaerobic bacilli indicated by the cerebrospinal fluid metagenomic next-generation sequencing (mNGS) results.

The pathophysiology of meningitis caused by oral anaerobes and streptococci involves a complex interplay of microbial virulence factors and host immune response. Porphyromonas, Prevotella, and Bacteroides species produce various virulence factors, including proteases, endotoxins, and capsular polysaccharides, which can facilitate tissue invasion, evade host immunity, and potentially disrupt the blood-brain barrier. Streptococcus constellatus, a member of the Streptococcus anginosus group, is known for its pyogenic potential and ability to cause abscesses and bacteremia, which may serve as a precursor to metastatic CNS infection. The proposed mechanisms for CNS invasion include hematogenous spread secondary to bacteremia, as evidenced in our case by the positive blood culture, and direct extension through anatomical channels such as the valveless emissary veins connecting the facial venous plexus to the cavernous sinus. This polymicrobial synergy might exacerbate the inflammatory process, leading to the severe clinical presentation observed.

Given the significant implications of the cerebrospinal fluid mNGS findings, we promptly modified the antibiotic regimen to include meropenem in combination with metronidazole sodium chloride injection to address the potential co-infection. Following the initial adjustment of the antibiotic regimen, the patient maintained a relatively normal temperature for approximately two days; however, fever persisted, reaching up to 38°C.Despite the administration of meropenem in conjunction with metronidazole sodium chloride injection to address co-infections, the patient's fever continued. It is crucial to note that the current antibiotic regimen did not provide comprehensive coverage of the causative organisms. At this juncture, the analysis of the cerebrospinal fluid mNGS results prompted a shift in our diagnostic approach, suggesting that the background flora may also be pathogenic and capable of eliciting clinical symptoms. In this instance, the patient's background flora comprised over ten species, including gram-positive bacteria and various viral genera. However, it remains unclear which specific pathogen or pathogens were primarily responsible for the patient's condition following the second adjustment of the antibiotic regimen.The traditional microbiological culture method of blood culture provided critical information regarding the patient's condition. The blood culture results were positive for *Streptococcus constellatus*, indicating the presence of bacteremia. Given that *Streptococcus constellatus* has been identified in two sets of blood cultures from separate venipuncture sites and as part of the background flora in cerebrospinal fluid mNGS, there is substantial evidence to suggest that the patient experienced a co-infection with *Streptococcus constellatus* in the cerebrospinal fluid. Notably, *Streptococcus constellatus* infections are distinctly different from those caused by the other three oral anaerobes. Consequently, the antimicrobial coverage provided by the combined anti-infective regimen of meropenem and metronidazole sodium chloride injection was inadequate, resulting in poor control of fever and other infection-related symptoms.In response to these findings, we promptly modified the antibiotic regimen to include a combination of meropenem, metronidazole sodium chloride injection, and linezolid tablets for infection management. Following the third adjustment of the antibiotic therapy, the patient's body temperature swiftly returned to the normal range, his mental state gradually improved, and his higher neurological functions approached normalcy. Additionally, markers of inflammation and cerebrospinal fluid showed significant improvement, leading to the patient's discharge after a total hospitalization of 25 days.In our study, the negative cerebrospinal fluid (CSF) culture likely resulted from several factors: (a) Timing of Antimicrobial Administration: The patient received empirical treatment with meropenem immediately upon admission, prior to the lumbar puncture. This early antibiotic intervention may have reduced the bacterial load in the CSF below the detection threshold of traditional culture methods, while the blood culture, collected earlier, remained positive. (b) Sensitivity of Detection Methods: The metagenomic next-generation sequencing (mNGS) of CSF detected multiple anaerobic bacteria (eg,*Porphyromonas endodontalis, Bacteroides heparinolyticus, Prevotella pleuritidis*) and *Streptococcus constellatus*, which were not identified by culture. This underscores the superior sensitivity of mNGS in detecting fastidious or low-abundance pathogens, particularly in patients pretreated with antibiotics. (c) Compartmental Differences: The blood culture isolated *Streptococcus constellatus*, suggesting bacteremia secondary to an oral and maxillofacial infection.However, the CSF may have harbored a mixed anaerobic infection with lower bacterial viability due to the blood-brain barrier and prior antibiotic exposure.

In clinical practice, accurately diagnosing purulent meningitis is often straightforward, with lumbar puncture results serving as a reliable indicator. However, identifying the etiology of purulent meningitis, particularly for rare causes, presents significant challenges.[19,20] This identification is crucial for the timely and appropriate adjustment of antibiotic regimens in the later stages of the disease, and it serves as a key indicator of the quality of diagnosis and treatment. When investigating the disease's cause, special attention should be given to the potential for intracranial purulent meningitis resulting from infections

in the maxillofacial space of oral origin, particularly in patients with oral diseases, poor oral hygiene, or facial soft tissue swelling. Additionally, the possibility of concurrent bacteremia or sepsis must be considered. In such cases, it is important to conduct macro gene sequencing of pathogens during the collection of clinical specimens, such as cerebrospinal fluid or blood, to identify specific infectious agents and inform subsequent antibiotic adjustments. It is also important to note that due to the complexity of the infection, the possibility of infections caused by background microorganisms in metagenomic next-generation sequencing (mNGS) cannot be discounted. A comprehensive assessment should be made based on the clinical condition, potentially in conjunction with traditional diagnostic methods when necessary.

This patient was discharged from the hospital after more than two months of treatment, during which he was misdiagnosed with trigeminal neuralgia on several occasions. His condition was only correctly identified following the onset of fever and altered consciousness, subsequent to a lumbar puncture. Throughout the treatment, the antibiotic regimen was adjusted twice due to a mixed infection involving multiple gram-negative anaerobic bacilli of oral origin and gram-positive bacillus bacteremia. Each modification of the antibiotic therapy was carefully aligned with the clinical symptoms and supported by effective auxiliary examinations. Notably, the emerging technology of metagenomic next-generation sequencing (mNGS) played a crucial role in this process,[21] while traditional microbial culture methods also provided significant assistance. This case underscores the importance of integrating both emerging diagnostic technologies and traditional methods to enhance clinical decision-making.

This case report has several limitations. First, the patient's advanced age and poor baseline oral hygiene, although central to the pathogenesis, may limit the generalizability of our findings to younger, healthier populations. Second, the negative CSF culture likely resulted from the empirical administration of meropenem prior to lumbar puncture, which, while a necessary clinical intervention, undoubtedly affected our ability to isolate and confirm the pathogens using traditional gold-standard methods. Third, the absence of long-term neurological follow-up after discharge restricts our understanding of the patient's complete functional outcome.

Conclusion

This case highlights that severe purulent meningitis can originate from odontogenic sources, particularly in elderly patients with poor oral hygiene.Our findings emphasize the critical importance of preventive strategies, including routine dental care and improved oral hygiene, to mitigate the risk of such severe complications. While diagnostic technologies, such as mNGS, were pivotal in identifying the polymicrobial etiology in this instance, their broader application faces challenges related to cost, accessibility, and interpretation, which must be addressed for wider implementation. The timely and accurate adjustment of antibiotic regimens, guided by advanced diagnostics alongside clinical findings, remains paramount for achieving a favorable outcome. The findings from this case primarily illuminate the diagnostic and therapeutic approach for similar patient profiles—those with underlying odontogenic infections presenting with neurological sequelae. However, their generalizability to broader populations requires validation through larger, prospective studies. Future research should explicitly focus on validating the proposed oral-CNS infection pathway and systematically assessing the prevalence and clinical impact of polymicrobial CNS infections facilitated by mNGS. Integrating these advanced technologies with conventional methods will be crucial in enhancing clinical decision-making for these complex infections.

Ethics Approval and Consent for Publication

This study has been reviewed and approved by the Research Ethics Committee of Suining Central Hospital. The patient provided informed consent for the publication of clinical details, and written informed consent was obtained for the publication of case details and images. The details of the case can be published without further institutional approval.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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