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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Hepatitis B virus in cerebrospinal fluid of a patient with purulent bacterial meningitis detected by multiplex-PCR: A case report

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Abstract

BACKGROUND

Bacterial meningitis (BM) is a common central nervous system inflammatory disease. BM may cause serious complications, and early diagnosis is essential to improve the prognosis of affected patients.

CASE SUMMARY

A 37-year-old man was hospitalized with purulent meningitis because of worsening headache for 12 h, accompanied by vomiting, fever, and rhinorrhea. Head computed tomography showed a lesion in the left frontal lobe. Infectious disease screening showed positivity for hepatitis B surface antigen, hepatitis B e antigen, and hepatitis B core antigen. Cerebrospinal fluid (CSF) leak was suspected based on clinical history. *Streptococcus pneumoniae* (*S. pneumoniae*) was detected in CSF by metagenomic next-generation sequencing (mNGS) technology, confirming the diagnosis of purulent BM. After treatment, multiplex PCR indicated the presence of hepatitis B virus (HBV) DNA and absence of *S. pneumoniae* DNA in CSF samples.

CONCLUSION

We report a rare case of HBV in the CSF of a patient with purulent BM. Multiplex PCR is more sensitive than mNGS for detecting HBV DNA.

Key Words: Purulent meningitis; *Streptococcus pneumoniae*; Hepatitis B virus; Multiplex PCR; Cerebrospinal fluid; Case report

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Core Tip: The advantages of multiplex PCR are rapid detection and high sensitivity and accuracy. Multiplex PCR can assist in the diagnosis of bacterial and viral meningitis in culture-negative cerebrospinal fluid (CSF). Furthermore, this technique can improve the accuracy of diagnosis of acute bacterial meningitis (BM) in the clinical setting in culture-positive or culture-negative CSF. We report a rare case of hepatitis B virus (HBV) in the CSF of a patient with purulent BM and demonstrate that multiplex PCR is more sensitive than metagenomic next-generation sequencing for detecting HBV DNA.

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INTRODUCTION

Bacterial meningitis (BM) is a common central nervous system (CNS) inflammatory disease[1] that usually affects infants and immunocompromised adults[2,3]. BM can cause headache, nausea, fever, altered mental status, and sudden death[4] and is diagnosed by cerebrospinal fluid (CSF) examination. Most meningitis patients survive; however, one-fifth to one-third of survivors, especially newborns and children, have long-term neurological sequelae[5]. BM can be caused by different bacterial pathogens, and several bacterial species have become more prevalent in the past few decades, including *Streptococcus pneumoniae* (*S. pneumoniae*)[6], *Haemophilus influenzae*[7], and *Neisseria meningitidis*[8]. Gram-positive *S. pneumoniae* is the main causative agent of BM in many developing countries[9]. Although the mechanism by which *S. pneumoniae* crosses the blood-brain barrier (BBB) is incompletely understood, bacterial adhesion to the vascular endothelium is a crucial event in meningitis progression[10]. Therefore, timely diagnosis and treatment of BM are imperative because of the possibility of severe CNS complications[11].

The gold standard test for detecting BM is CSF bacterial culture[12]. Nonetheless, this method has limitations, including low sensitivity and delayed microbial growth, affecting clinical decision-making. Consequently, other methods are necessary for the diagnosis of meningitis. Metagenomic next-generation sequencing (mNGS) is widely used to detect pathogen nucleic acids in clinical samples[13]. Furthermore, multiplex PCR is fast and highly accurate and sensitive[14]. The early detection and diagnosis of BM are fundamental to improve long-term prognosis in affected patients. In the present case, CSF samples were analyzed by mNGS and multiplex PCR, and our patient had BM and co-infection with hepatitis B virus (HBV).

CASE PRESENTATION

Chief complaints

On 15 December 2020, a 37-year-old man was admitted to the hospital with purulent BM associated with worsening headache for 12 h and altered consciousness for 7 h.

History of present illness

Twelve hours before admission, the patient had a persistent headache without obvious cause, accompanied by nausea, vomiting, fever, and rhinorrhea. His body temperature was 37.8 °C.

History of past illness

Medical history showed that the patient had fractured the skull and ribs in a car accident 15 years prior. And he was diagnosed with purulent BM accompanied by rhinorrhea and CSF leak 5 years prior.

Personal and family history

The patient had a free previous personal and family history.

Physical examination

The patient was hospitalized at Huairou Hospital (Beijing, China) 4 h later. Head computed tomography (CT) examination showed a lesion in the left frontal lobe. Routine blood examination showed a white blood cell count $\geq 10.02 \times 10^9/L$, neutrophil count $\geq 89.10\%$, and procalcitonin ≥ 1.62 ng/mL. The results of liver and renal function, coagulation test, blood ammonia, and blood gas analysis were unremarkable.

Laboratory examinations

The results of infectious disease screening indicated positivity for hepatitis B surface antigen (HBsAg) (250 IU/mL), hepatitis B e antigen (HBeAg) (211.40 S/CO), and hepatitis B core antigen (HBcAg) (1.2 S/CO), confirming the diagnosis of purulent BM.

CSF samples were collected by lumbar puncture[15]. *S. pneumoniae* was detected using mNGS, confirming the diagnosis of purulent BM. Bacterial infection was controlled with vancomycin and meropenem. On January 14, multiplex PCR indicated the presence of HBV DNA and absence of *S. pneumoniae* DNA in CSF samples.

Imaging examinations

CT scanning indicated that intracranial hemorrhage secondary to intracranial infection was observed, accompanied by hearing disorders (Figure 1).

FINAL DIAGNOSIS

The patient was diagnosed with purulent BM and HBV detected in CSF.

TREATMENT

Symptoms worsened, and the patient presented altered consciousness and restlessness. He was given ceftriaxone, acyclovir, diazepam, and dexamethasone to reduce cerebral edema; however, there was no clinical improvement. The patient was transferred to Xuanwu Hospital (Beijing, China). At the emergency department, his body temperature was 39.1 °C, and hospitalization was recommended.

OUTCOME AND FOLLOW-UP

The patient was discharged from the hospital when clinical symptoms disappeared and CSF test returned to normal status. And a liver specialist treatment was recommended after discharge.

DISCUSSION

In this case, the detection of *S. pneumoniae* in CSF samples by mNGS confirmed the diagnosis of purulent BM. Infectious disease screening indicated positivity for HBsAg, HBeAg, and HBcAg. After treatment, multiplex PCR indicated the presence of HBV DNA and absence of *S. pneumoniae* DNA in CSF samples, demonstrating the high sensitivity of this molecular technique.

Twelve hours before hospitalization, the patient had worsening headache, altered consciousness, rhinorrhea, then intracranial hemorrhage secondary to intracranial infection accompanied by hearing disorders, and was diagnosed with purulent BM. Medical history showed that the patient had fractured the skull in a car accident and was diagnosed with purulent BM 5 years prior. *S. pneumoniae* was detected in the CSF by mNGS, confirming the diagnosis of purulent BM.

S. pneumoniae is one of the most common human pathogens and the causative agent of meningitis and other diseases[16]. Our findings are supported by a previous study, wherein the risk of late-onset BM was higher in adults with head surgeries[17], and the present patient had fractured the skull before. HBV was not detected in the CSF by



Figure 1 Computed tomography scanning results (intracranial hemorrhage secondary to intracranial infection).

mNGS, consistent with the literature. mNGS has high sensitivity and specificity for detecting *S. pneumoniae* but is less sensitive than RT-PCR for the diagnosis of encephalitis[18].

After antibiotic treatment, multiplex PCR results showed positivity for HBV DNA and negativity for *S. pneumoniae* DNA in the CSF. In this respect, it was reported that HBsAg and HBV viral load were differentially detected in the CSF and blood[19]. Additionally, HBV was detected in the CSF of patients with *S. pneumoniae* infections, demonstrating that HBV can cross the BBB. However, whether HBV can cause more severe complications is unknown.

The advantages of multiplex PCR are rapid detection and high sensitivity and accuracy[20]. Albuquerque *et al*[14] have revealed that multiplex PCR can assist in the diagnosis of bacterial and viral meningitis in culture-negative CSF. Furthermore, this technique can improve the accuracy of diagnosis of acute BM in the clinical setting in culture-positive or culture-negative CSF.

CONCLUSION

We report a rare case of HBV in the CSF of a patient with purulent BM and demonstrate that multiplex PCR is more sensitive than mNGS for detecting HBV DNA.

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