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LETTER TO THE EDITOR

Evaluating the Impact of Rapid Multiplex PCR Testing on Meningitis and Encephalitis Diagnosis: a Retrospective Analysis

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SUMMARY

Background: **Meningitis and encephalitis are life-threatening neurological emergencies requiring prompt diagnosis and treatment. Traditional diagnostic methods often lack the speed and sensitivity needed for rapid clinical decision-making. This study evaluates the effectiveness of rapid multiplex PCR testing in diagnosing meningitis and encephalitis.**
Methods: **Between March 28, 2022, and May 31, 2024, we analyzed cerebrospinal fluid collected from a cohort of patients aged 24 to 87 at Asia University Hospital. These specimens were analyzed using the FilmArray Meningitis/Encephalitis (ME) Panel.**
Results: **The study included 19 patients who underwent FilmArray ME panel testing. Of these, 2 (10.5%) tested positive, while 17 (89.5%) tested negative. Among the positive specimens, herpes simplex virus-1 was detected in one patient, and Varicella zoster virus in the other.**
Conclusions: **This study underscores the clinical value of the FilmArray ME panel as a rapid and reliable tool for diagnosing meningitis and encephalitis. Multiplex PCR significantly improves diagnostic accuracy and reduces time to diagnosis, facilitating faster clinical intervention and improved patient outcomes.**
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KEYWORDS

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TO THE EDITOR

Meningitis and encephalitis are severe inflammatory conditions of the central nervous system, often caused by infectious agents such as bacteria, viruses, and fungi. These diseases can have significant functional and vital implications, impacting patient health and outcomes. Besides the direct costs associated with hospitalization, these infections also incur substantial indirect costs due to the loss of the patient's contribution to society [1,2]. Prompt and accurate identification of the causative agent is crucial for effective treatment and reducing morbidity and mortality. Conventional diagnostic methods, including culture and serology, are often time-consuming and may lack sensitivity. In recent years, rapid

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multiplex PCR testing has emerged as a promising tool for the simultaneous detection of multiple pathogens with high sensitivity and specificity. This study evaluates the effectiveness of rapid multiplex PCR testing in diagnosing meningitis and encephalitis.

The FilmArray Meningitis/Encephalitis (ME) Panel (BioFire Diagnostics®) is an FDA-cleared, multiplex PCR-based assay designed for the rapid and comprehensive detection of 14 common pathogens responsible for central nervous system infections. This panel detects six bacterial pathogens, seven viral pathogens, and one fungal pathogen. The FilmArray system streamlines sample preparation, amplification, detection, and analysis into a unified automated process. The procedure involves loading a small volume of CSF into the FilmArray pouch, which is then inserted into the instrument. The system carries out nucleic acid extraction and reverse transcription for RNA viruses, PCR amplification, and detection of amplified products using a combination of nested multiplex PCR and high-resolution melt curve analysis. The average turnaround time for multiplex PCR was 1 hour, significantly shorter than the 48 - 72 hours required for conventional methods. This rapid turnaround allowed for timely clinical decision-making and intervention. A previous study demonstrated that the FilmArray ME Panel is a highly sensitive and specific test for diagnosing meningitis and encephalitis. Utilizing this comprehensive and rapid test is expected to result in enhanced patient outcomes and more effective antimicrobial stewardship [3].

This study aimed to assess the prevalence and distribution of viral and bacterial pathogens in cerebrospinal fluid (CSF). We performed a retrospective analysis of CSF specimens collected from patients admitted to Asia University Hospital from March 28, 2022, to May 31, 2024. These specimens, obtained from 19 patients aged 24 to 87 (11 males [57.9%] and 8 females [42.1%]), were analyzed using the FilmArray ME Panel. Of the 19 patients, 2 (10.5%) tested positive and 17 (89.5%) tested negative. The positive specimens detected herpes simplex virus-1 (HSV-1) in one patient and varicella zoster virus (VZV) in the other.

We present two cases diagnosed using the FilmArray ME Panel for CSF analysis. The first case involves a 69-year-old male patient with respiratory failure who tested positive for HSV-1, enabling timely antiviral treatment. His CSF analysis revealed an RBC count of 17/μL, a WBC count of 31/μL with a differential of 31.8% lymphocytes and 68.2% monocytes, and an elevated CSF lactate level of 36.7 mg/dL (normal range: 10 - 22 mg/dL). Biochemical analysis showed a glucose level of 73 mg/dL (normal range: 40 - 70 mg/dL), an LDH level of 54 U/L, a microprotein level of 94 mg/dL (normal range: 15 - 45 mg/dL), and a microalbumin level of 44.45 mg/dL (normal range: 10 - 30 mg/dL). These findings suggest an inflammatory response within the central nervous system.

The second case involves a 73-year-old female patient with end-stage renal disease (ESRD) and an altered state of consciousness who tested positive for VZV. An abnormal EEG was noted. Her biochemical analysis indicated a glucose level of 455 mg/dL (normal range: 70 - 100 mg/dL) and a HbA1c level of 10.2% (normal range: 4 - 6%). Her CSF analysis showed a glucose level of 100 mg/dL (normal range: 40 - 70 mg/dL) and a microprotein level of 122 mg/dL (normal range: 15 - 45 mg/dL). This case represents meningitis combined with a VZV infection.

HSV-1 is the primary cause of sporadic encephalitis globally, with an incidence of 2 to 4 cases per 1,000,000 individuals [4]. Without timely antiviral treatment, the mortality rate can reach 70%, and the morbidity rate can be as high as 50% [5]. In Taiwan, Le SH et al. assessed the performance of the BioFire® ME Panel in 42 patients with clinically suspected CNS infections. They reported an overall positivity rate of 14.3% and observed perfect agreement in the detection of HSV, VZV, and Streptococcus agalactiae across conventional PCR, bacterial culture, the BioFire® ME Panel, and multiplex RT-PCR results [6]. Recently, Clague M et al. demonstrated that the implementation of the BioFire® ME Panel reduced the time needed to obtain CSF HSV-1 PCR results and shortened the duration of intravenous acyclovir treatment [7]. These improvements in testing and treatment times may decrease hospital treatment costs and reduce the unnecessary use of antiviral medications. Previous studies have also shown that implementing the BioFire® ME Panel results in a shorter duration of acyclovir treatment [8-10].

VZV can lead to various CNS conditions, with meningitis and meningoencephalitis being the primary complications [11,12]. Prompt intravenous antiviral treatment for VZV meningitis and meningoencephalitis is crucial and is associated with better outcomes [13]. VZV meningitis can develop in immunocompetent individuals without any preceding symptoms. Rapid molecular testing with the FilmArray can significantly aid antimicrobial stewardship by enabling early and accurate diagnosis, thus preventing the unnecessary use of antibiotics [13]. From the evidence presented, the BioFire® ME Panel is a highly effective tool for rapidly diagnosing CNS infections, reducing treatment times, and improving clinical outcomes.

Our study underscores the clinical advantages of rapid multiplex PCR testing in the management of meningitis and encephalitis. The enhanced diagnostic accuracy and expedited results facilitate prompt and appropriate treatment, ultimately improving patient outcomes and reducing the risk of complications. While our findings are based on a single-center retrospective analysis, they highlight the potential for broader implementation of rapid multiplex PCR testing in clinical practice. We recommend that further multicenter prospective studies be conducted to validate these findings and assess the cost-effectiveness of rapid multiplex PCR testing. Such studies could provide a stronger evidence base for integrating this technology into standard diagnostic protocols for meningitis and encephalitis.

In conclusion, rapid multiplex PCR testing represents a valuable addition to the diagnostic arsenal for meningitis and encephalitis, offering superior sensitivity, specificity, and turnaround time compared to conventional methods. We believe that its adoption in clinical settings can lead to more timely and accurate diagnoses, facilitating early targeted therapy and better patient outcomes.

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Declaration of Interest:
There are no conflicts of interest associated with this paper.

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