



CONTRIBUTION OF MOLECULAR BIOLOGY IN THE ETIOLOGICAL DIAGNOSIS OF INFECTIOUS MENINGITIS

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ABSTRACT Infectious meningitis is a potentially fatal condition that requires prompt and accurate diagnosis. Traditional methods such as bacterial culture often have limitations in detecting all possible pathogens. This study aims to evaluate the contribution of the FilmArray® Meningitis/Encephalitis (M/E) multiplex PCR panel in diagnosing infectious meningitis by comparing its performance with conventional culture methods. A total of 115 cerebrospinal fluid (CSF) samples were analyzed over a three-year period, with the FilmArray® panel detecting pathogens in 22.6% of the samples, highlighting its efficacy in rapid and comprehensive pathogen detection. Our results suggest that the FilmArray® panel can be a valuable complement to conventional microbiological techniques in the diagnostic workflow for infectious meningitis.

KEYWORDS : Infectious meningitis, PCR multiplex, FilmArray panel, Pathogen detection, Cerebrospinal fluid (CSF)

INTRODUCTION

Infectious meningitis remains a serious, potentially fatal condition requiring early and accurate diagnosis to guide effective treatment. Conventional diagnostic methods, such as bacterial culture and microscopy, may be slow, and sometimes fail to detect all pathogens, particularly viruses. Molecular biology techniques, including multiplex PCR panels, offer rapid and reliable alternatives. The FilmArray® Meningitis/Encephalitis panel is a promising tool that can detect multiple pathogens simultaneously from cerebrospinal fluid (CSF) in a short time frame. This study evaluates the diagnostic value of the FilmArray® panel in comparison to traditional culture methods for infectious meningitis.

MATERIALS AND METHODS

Study Design

This was a retrospective descriptive study conducted at the Avicenna Military Hospital in Marrakech, Morocco, from January 2018 to December 2020. The study involved 115 cerebrospinal fluid samples, collected from patients clinically suspected of having infectious meningitis. These samples were analyzed using both conventional microbiological techniques and the FilmArray® Meningitis/Encephalitis (M/E) multiplex PCR panel.

Inclusion Criteria

- Patients with suspected infectious meningitis who underwent both traditional bacteriological studies and FilmArray® M/E PCR testing on CSF during the study period.

Exclusion Criteria

- Redundant samples.
- Invalid FilmArray® results.
- CSF samples processed by conventional methods only.

Testing Methods

- **Conventional Microbiological Methods:** Cultures were performed on all samples using standard microbiological techniques to identify bacterial, viral, and fungal pathogens.
- **FilmArray® M/E Panel:** This multiplex PCR panel was used to detect 14 pathogens (bacterial, viral, and fungal) directly from CSF samples.

RESULTS

Epidemiological Characteristics of Meningitis Cases

1. Distribution of Samples by Requesting Departments:

- **Emergency Department:** 36
- **Intensive Care Unit (ICU):** 30
- **Internal Medicine:** 18
- **Neurology:** 13
- **Neurosurgery:** 8

Diagnostic Performance of the FilmArray® M/E Panel

1. **Overall Positivity Rate:** Among the 115 samples tested, the FilmArray® M/E panel detected at least one pathogen in 26 samples, resulting in an overall positivity rate of 22.6%.
2. **Co-Infections:**
 - 25 samples had a single infection.
 - 1 sample exhibited a co-infection.
3. **Pathogens Detected by the FilmArray® Panel:** A total of 27 pathogens were detected, with enteroviruses being the most commonly identified. Other pathogens included Cytomegalovirus, Herpes Simplex Virus, Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis, among others.

Pathogens Detected by Conventional Culture

1. **Overall Positivity Rate:** Conventional culture methods detected 6 pathogens, resulting in a positivity rate of 5.2%. The most frequently detected pathogen was Streptococcus pneumoniae, which accounted for 50% of the bacterial isolates.

Antibiotic Sensitivity Testing:

Antibiotic sensitivity testing was performed on all bacterial isolates, providing essential information for guiding appropriate antimicrobial therapy.

FilmArray® Results in Culture-Negative Samples:

The FilmArray® panel diagnosed 23 cases of infectious meningitis where the conventional culture results were negative, highlighting its ability to identify pathogens that were not detected by culture.

Turnaround Time:

The median turnaround time for results from the FilmArray® M/E panel was 5 hours, significantly faster than conventional culture methods.

DISCUSSION

Performance of the FilmArray® M/E Panel

The FilmArray® M/E panel is an automated multiplex PCR system capable of detecting and identifying 14 pathogens (bacterial, viral, and fungal) in approximately one hour from as little as 200 µl of CSF. In our study, the FilmArray® panel had a positivity rate of 22.6%, which is notably higher than the 5.2% positivity rate observed with conventional culture methods. This demonstrates the superior sensitivity of the FilmArray® system, particularly in detecting viruses and fastidious pathogens.

The ability of the FilmArray® panel to identify pathogens in culture-negative samples underscores the advantage of molecular methods over traditional cultures, which can be time-consuming and may miss some pathogens.

Advantages of the FilmArray® M/E Panel

1. **Rapid Diagnostic Results:** The FilmArray® panel provides results in approximately 1 hour, which is crucial for the timely initiation of appropriate treatment in critically ill patients.
2. **Rationalization of Antimicrobial Therapy:** Rapid pathogen identification allows for targeted antimicrobial therapy, potentially reducing the unnecessary use of broad-spectrum antibiotics and lowering the risk of antimicrobial resistance.
3. **Reduction in Hospitalization Duration:** Early and accurate pathogen identification can lead to earlier discharge, thus reducing the overall length of hospitalization and healthcare costs.

Limitations

1. **High Cost:** The FilmArray® panel is relatively expensive, which may limit its widespread use in resource-limited settings. However, its potential to improve diagnosis and reduce unnecessary treatments could offset the initial costs in some settings.
2. **Detection Limitations:** The FilmArray® panel detects a limited number of pathogens, and certain less common pathogens may not be included in the panel. Additionally, antibiotic susceptibility testing is not part of the PCR process and must still be done separately.
3. **Need for Supplementary Testing:** While the FilmArray® panel is a valuable diagnostic tool, it should be used as a complement to traditional microbiological methods, including antibiotic susceptibility testing, to ensure comprehensive patient management.

CONCLUSION

The FilmArray® Meningitis/Encephalitis panel is a rapid, simple, and reliable tool for diagnosing infectious meningitis. Its superior sensitivity and faster turnaround time compared to conventional methods make it a valuable addition to the diagnostic workflow. However, molecular tests should be used in conjunction with traditional microbiological methods, especially to guide antibiotic therapy and to detect pathogens not covered by the panel.