Enhancing Pathogen Identification Using a Comprehensive PCR System in Adult and Pediatric patients with Meningitis and a negative Gram stain

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Abstract

Background: Meningitis with a negative CSF Gram stain represents a diagnostic and therapeutic challenge, as the majority of the causative organisms are unknown. Novel and fast molecular techniques may increase the detection of the etiological agents. Methods: Patients admitted to the 4 hospitals in Houston, TX between Nov. 2008 – Mar. 2014 with community-acquired meningitis (fever, headache, vomiting, photophobia, stiff neck, focal neurological symptoms, CSF cell count > 5 cells/mm³ and a negative CSF Gram stain were eligible. Residual patient CSF underwent additional testing by a research only version of the FilmArray™ Meningitis / Encephalitis panel (FA ME, BioFire Diagnostics, LLC). The panel requires 200 µL CSF and simultaneously tests for 6 bacteria (S. pneumoniae, N. meningitidis, S. agalactiae, H. influenzae, L. monocytogenes, E. coli K1), 8 viruses (Herpes simplex types 1, 2, 6, E. coli, EBV, Enterovirus, Parvovirus, Varicella zoster virus (VZV) and 2 fungi (Cryptococcus neoformans and C. albicans). Results: Of the 149 patients enrolled, 48 (32.2%) had residual CSF (38 adults, 10 children < age 18) available for FA ME testing. Pathogens were identified in 14 (29.2%) of 48 samples by standard evaluation and 15 (31.2%) by FA ME. Among FA ME results, viral pathogens were most common (EBV 8, HSV2 3, VZV (3), HSV1 (1), enterovirus (1), followed by bacterial [S. pneumoniae] and fungal [C. neoformans] (1)). Co-detections were present in 6 patients (12.5%): EBV was present in all 6) along with VZV (2); HSV1 (1), HSV2 (1), C. neoformans (1), and S. pneumoniae (1). In 8 (16.6%) patients, FA ME identified pathogens not previously identified. Standard evaluations identified pathogens in 5 (15.2%) of 33 FA ME negative samples [West Nile Virus (WNV) 4, Histoplasma capsulatum (1)]. Conclusion: Testing with the FA ME panel resulted in pathogen detections not previously recognized and for which treatment is recommended. The FA ME panel did not detect, however, some pathogens identified by standard techniques; assays for WNV and Histoplasma are not contained on the panel. Rapid, comprehensive testing for the most common pathogens causing meningitis will aid in the diagnosis and treatment of patients with negative CSF Gram stains.

Methods

Background

The capacity to rapidly identify the organisms is critical for the accurate diagnosis and treatment. Standard techniques require several days for initial identification of a pathogenic organism, and some organisms are not recognized using the standard techniques. The use of a comprehensive Polymerase chain reaction (PCR) system have expanded the range of pathogens that can be identified in clinical laboratories.

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Results

| Test | Cx | CSF | Blood | FAME | FilmArray | MLB-DOS | VB | VE | NA | ME | Meningitis/Encephalitis panel
|------|----|-----|------|------|----------|-------|---|---|---|---|-------------------
|      |    |     |      |      |          |       |   |   |   |   |                  |
|      |    |     |      |      |          |       |   |   |   |   |                  |

Conclusions

- Testing with the FA ME panel resulted in pathogen detections not previously recognized and for which treatment is recommended.
- Rapid, comprehensive testing for the most common pathogens causing meningitis will aid in the diagnosis and treatment of patients with negative CSF Gram stains.

This poster contains information regarding assays that have not been cleared by the FDA for in vitro diagnostic use.

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