Implementation of a Rapid Molecular Meningitis Panel

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TEAM, DRIVEN TO MAKE A DIFFERENCE

Background

Infection of the meninges (meningitis) or of the brain (encephalitis) is associated with high mortality and morbidity rates. Acute bacterial meningitis is a rare, but potentially fatal disease where symptoms can appear suddenly and escalate quickly to brain damage, hearing and/or speech loss, blindness, and death. Rapid initial diagnosis and treatment is critical, particularly for bacterial infections. Viral meningitis is more common, but typically mild and non-lethal. The ability to provide a more comprehensive diagnostic laboratory test with faster turnaround time (TAT) could potentially improve outcomes by directing more specific therapy in patients with meningitis or encephalitis (ME) and prevent unnecessary prophylactic treatment for patients without disease. In addition, faster, in-house, test could allow better management of patients with suspected ME and perhaps rule out unneeded therapy, and eliminate adverse reactions associated with unnecessary therapy.

Project Goal and Implementation Plan

To add a molecular test to detect viral, bacterial, and yeast organisms that cause ME in lieu of sending this testing to a reference laboratory. This will reduce time from specimen receipt to result to less than 3 hours. We required both positive and negative results be immediately called to providers. Testing was discussed before implementation with ED/ER staff and Pediatric staff members so they would know this test would take priority and that all results would be called immediately. Our goal was for patients to be treated faster if therapy was needed and to not treat patients who did not have infectious ME. These results could also help determine if patients needed to be admitted or could be safely discharged. Admission would depend on clinical assessment but the molecular test results, if provided quickly, could provide valuable information in the overall assessment of the patient.

BioFire FilmArray Molecular Meningitis Panel

Bacteria:	Sensitivity	Specificity
Escherichia coli K1	100%	99.90%
Haemophilus influenzae	100%	99.90%
Listeria monocytogenes	*	100%
Neisseria meningitidis (encapsulated)	*	100%
Streptococcus agalactiae	*	99.90%
Streptococcus pneumoniae	100%	99.20%
Viruses:		
Cytomegalovirus	100%	99.80%
Enterovirus	95.70%	99.50%
Herpes simplex virus 1	100%	99.90%
Herpes simplex virus 2	100%	99.90%
Human herpesvirus 6	85.70%	99.70%
Human parechovirus	100%	99.80%
Varicella zoster virus	100%	99.80%
Yeast:		
Cryptococcus neoformans/gattii	100%	99.70%

* Calculation based on 4 or fewer positive results. A total of 1,560 CSF samples analyzed.

Table 1: Biofire FilmArray Meningitis/Encephalitis (ME) Panel , Package Insert, dated June 2017, Table 9.

Improvement Process

Our team chose a rapid molecular test that detects 14 of the most common pathogens responsible for community acquired ME which includes viruses, bacteria and yeast. (Table 1)

While this test will not detect all organisms that cause ME, it detects over 95% of the organisms that cause ME in the United States. This test allowed for better workflow since preparation, amplification, detection, and analysis is in one automated system with a run time of approximately 1 hour, with only 2 minutes of hands-on time. We collected the TAT on all cases since implementation to collect a year of data. We worked with clinical staff regarding implementation, with focus on Pediatrics and ED/ER. Our laboratory performed the test 24 hours per day, 365 days per year with results called as soon as testing was completed. Both positive and negative results were called to allow for better patient management.

The team used a combination of PDSA methodology and other tools such as spaghetti diagrams to remove process waste between the receiving and reporting milestones. Physical steps were reduced from 48 steps to 18 steps on average after careful consideration was given to selection of the appropriate location of the system. Although recent staff satisfaction results are pending, it is perceived that workflow improvements will indicate a higher level of engagement.

Results and Outcomes

Testing started in June 2016 and data was collected until end of May 2017 and 223 tests completed with an average time from receipt of specimen to final result of 2 hours and 8 minutes. This was well below our goal of 3 hours. A chart review of all tested patients showed 67 patients had been deferred from admission when ME was ruled out with a negative test result and appropriate clinical assessment. (See Figure 1)

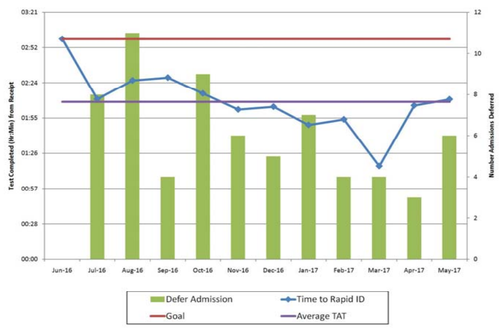

Figure 1: Average time from specimen receipt to result called to provider with a goal of less than 3 hours. Time tended to get faster as technologists got used to the new workflow.

Out of the 67 patients deferred, 17 were positive for viral meningitis (7 Enterovirus, 7 Human parechovirus, 1 Human herpesvirus 6, and 2 Herpes simplex virus 2). These infections were considered mild and self limiting and thus did not require admission. The remaining 50 were all negative for pathogens and thus ME was ruled out. (Table 2)

Pathogens Detected Summary Table

Bacteria:	Detected	Admitted	Deferred
Escherichia coli K1	2	2	0
Haemophilus influenzae	2	2	0
Streptococcus agalactiae	2	2	0
Streptococcus pneumoniae	1	1	0
Bacteria Total	**7**	**7**	**0**
Viruses:			
Cytomegalovirus	1	1	0
Enterovirus	12	5	7
Herpes simplex virus 1	1	1	0
Herpes simplex virus 2	7	5	2
Human herpesvirus 6	4	3	1
Human parechovirus	9	2	7
Varicella zoster virus	3	3	0
Virus Total	**37**	**20**	**17**
Yeast:			
Cryptococcus neoformans/gattii	2	2	0
Yeast Total	**2**	**2**	**0**
Total Pathogens Detected	**46**	**29**	**17**

Table 2: Pathogens detected during the first year and those that were deferred from admission due to low virulence or mild symptoms.

Length of stay (LOS) for all patients tested for ME was 6.0 days ranging from 2 to 25 days. Patient's with positive ME results, LOS averaged 4.5 days which was 1.5 days less (25% reduction) than the average for all patients tested.

Of 37 positive viral ME cases, 20 were admitted, 17 of those received antiviral medication while the remaining 3 did not require therapy. None of the remaining 17 deferred positive patients received antiviral therapy. Most were positive for either Enterovirus or Human parechovirus . Both produce very mild symptoms, are rarely fatal unless the patient is immune compromised, and usually resolve over 3 to 5 days without therapy.

We had 3 suspected yeast ME cases, 2 were positive with the molecular panel and one was negative. The negative molecular ME panel case was Cryptococcal antigen positive but culture negative. This was thought to be a false positive antigen test. This shows that older antigen testing is not always correct. Of the two that were molecular ME test positive for yeast , both were admitted, treated, and all cultures grew. These two cases resulted in the longest admission times. We had 6 bacterial molecular panel positive ME patients. Five were admitted and all 6 received appropriate antibiotic therapy. One patient that was not admitted and was co-infected with Enterovirus. We believe the cause of the meningitis was Enterovirus, as the bacterial culture was negative.

None of the 152 negative molecular ME panel patients received therapy for suspected ME and 106 were admitted for other medical reasons.

In a retrospective look at 2015, we found the positive test rate was 10% for reference lab testing for ME which is below the 20.6% positive rate of molecular testing. Our positivity rate for the new molecular ME is more than double that of reference lab testing, enabling faster and more accurate diagnosis.

Cost of Molecular

A summary of the cost for this new testing compared to similar send out testing is seen in the Table 3 below. The total cost for this testing in the first year of operation was $93,600.00. By comparison, if we shipped out testing for full viral panels (not as inclusive as our panel) and also performed bacterial antigen testing in house, the cost would be $127,556.00, which is $33,956.00 more than in house testing. The savings in the first year is reduced by the initial instrumentation cost . In subsequent years the savings per year is estimated to be $78,956.00. Labor was not considered since the labor to set up and complete the newer molecular panel is similar to the labor associated with shipping to a reference laboratory. Culture costs were also not included since fungal and bacterial cultures were also ordered on most patients, before and after implementation.

Costing Summary Table

		Cost	Number	Total Cost
First Year of Operation	Instrument	$45,000.00	1	$45,000.00
	Reagents	$200.00	223	$44,600.00
	QC/Controls	$200.00	20	$4,000.00
		$45,400.00		**$93,600.00**
	Ship Out Viral Panel	$560.00	223	$124,880.00
	Antigen Testing	$12.00	223	$2,676.00
		$572.00		**$127,556.00**
	Reduction of Cost/ Ship Out			**$33,956.00**
Subsequent Years				
	Reagents	$200.00	223	$44,600.00
	QC/Controls	$200.00	20	$4,000.00
		$400.00		**$48,600.00**
	Reduction of Cost/ Ship Out			**$78,956.00**

Table 3: Cost of testing compared to ship out testing laboratory panels.

Conclusion

Rapid molecular testing of CSF specimens in patients with suspected ME resulted in faster and more accurate diagnosis and more appropriate therapy. The results have reduced the use of unnecessary antibiotics, antifungals, and antivirals in patients who do not have infectious ME while allowing faster and more specific therapy in those with positive results.