Plasma Metagenomic Next Generation Sequencing Assay for Identifying Pathogens: A Retrospective Review of Test Utilization in a Large Children's Hospital

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BACKGROUND

Rapid and sensitive diagnostic methods can reduce the use of broad-spectrum antibiotics with timely diagnosis. Until recently, most rapid methods have focused on single or limited panel pathogen identification by PCR. Newer tests that utilize cell-free plasma DNA metagenomic next generation sequencing (mNGS) technology to identify over a thousand pathogens are promising. However, it is unclear if mNGS offers additional diagnostic value, improves sensitivity, or reduces time to detection when testing is completed in the same time frame (i.e. concurrently) as conventional testing. Understanding where in the diagnostic workup these costly tests add value is important to diagnostic stewardship initiatives.

PURPOSE

The goal of this study was to assess the diagnostic value of mNGS by Karius from Redwood, CA in a pediatric patient population as compared to conventional microbiological methods.

METHODS

- Retrospective chart review of all patients with mNGS testing as part of clinical care at Texas Children's Hospital (TCH) from 4/1/2019-6/30/2019 was performed
- Details about mNGS were recorded: results, specimen collection time, result time in the electronic medical record (EMR), and turnaround time (TAT)
- The same information was obtained for conventional testing (culture, serology, PCR, and histopathology) performed 1 week before and after mNGS testing
- Positive and negative agreement between mNGS and conventional testing was assessed
- Electronic records of patients with discordant results were reviewed to determine whether antimicrobials were added or changed based on the discordant mNGS result

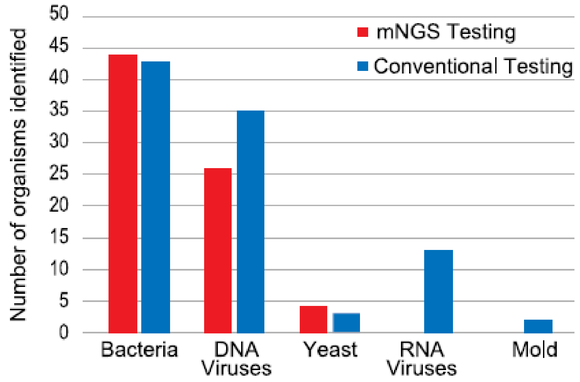

Figure 1: Number of different types of organisms identified by mNGS and conventional testing
Note: mNGS does not identify RNA viruses

		Conventional Testing +	Conventional Testing -
mNGS	+	22	10
	-	14	14
		36 (total +ve)	24 (total –ve)
		Positive Agreement: 61% (22/36) Negative Agreement: 58% (14/24)	

Table 1. Positive and negative agreement between mNGS and conventional testing

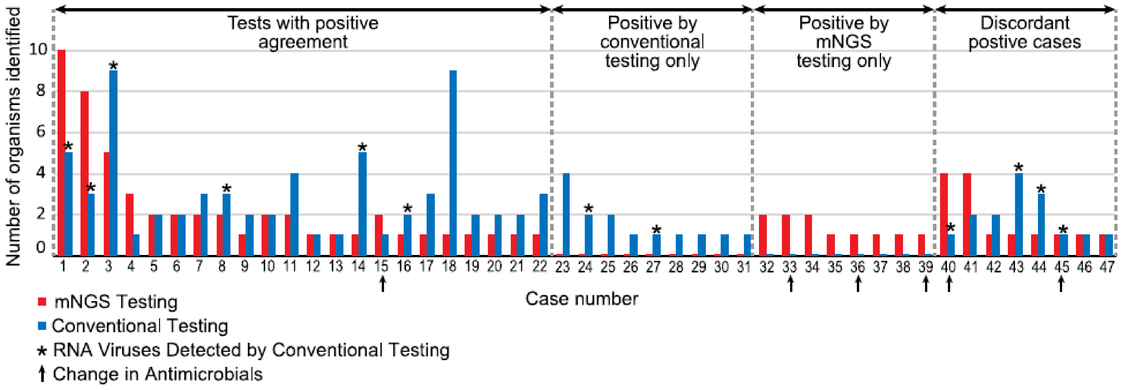

Figure 2: Number of organisms per patient identified by conventional testing and mNGS

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RESULTS

- Majority were immunosuppressed (62%). Primary indication for testing was to evaluate lesions (e.g. lung nodule) seen on imaging (40%)
- For concordant results, conventional tests were collected 1.6 (CI 0.3, 2.9) days earlier than mNGS and results were reported 3.5 (CI 1.8, 5.2) days earlier for conventional testing compared to mNGS
- In 73% of patients with concordant results, the organism identification was known by conventional testing prior to the mNGS result and in 45% of cases the organism identification was known prior to mNGS collection
- Turnaround time was shorter for conventional testing than for mNGS (1.8 versus 4.0 days, p = 0.0001)
- In 26% of cases in which mNGS identified a unique organism antimicrobials were changed

CONCLUSION

mNGS did not add diagnostic value by improving overall sensitivity or shortening turnaround time. This underscores the importance of implementing lab stewardship to optimize the diagnostic utility of mNGS for each patient. Conventional testing should be prioritized and mNGS should be used in well-defined clinical scenarios.

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