Performance of Next Generation Sequencing in Isolating a Pathogen in Pediatric Osteoarticular Infections

Nanda Ramchandar, MD, MPH,[1*] Jessica Burns, MD, MPH,[2] Andrew Pennock,[2] MD, Christopher Cannavino, MD,[1*] Lauge Farnaes, MD, PHD[3*]

[1]University of California, San Diego, Pediatric Infectious Disease, San Diego, USA, [2]University of California, San Diego, Pediatric Orthopedics, San Diego, USA, [3]Rady Children's Institute for Genom

*Dr. Cannavino and Dr. Farnaes contributed equally to the manuscript as senior authors

Nanda Ramchandar,
nramchandar@rchsd.org,
858 576 1700, ext 5331

Introduction

- Osteoarticular infections are often encountered in the pediatric population.

- Therapy is guided by isolation of a putative organism, however, operative cultures are often negative.

- Next generation sequencing (NGS) allows for more sensitive sampling of body compartments generally considered sterile.

- We sought to evaluate the utility of NGS in comparison to culture in detecting a pathogenic organism in acute osteomyelitis and septic arthritis in children.

Methods

- This was a single-site study to evaluate the utility of NGS (IDbyDNA, Salt Lake City, UT) in comparison to culture in detecting a pathogenic organism in acute osteomyelitis and septic arthritis in children.

- Eligible patients were all patients with osteomyelitis or septic arthritis admitted from July 2019 through July 2020.

- We excluded any patients with bone or joint surgery within 30 days prior to admission.

- Operative samples were chosen at the surgeon's discretion (joint aspirate, synovium, or bone) based on operative findings.

Results

- We enrolled 42 subjects. NGS of the operative samples identified a pathogen in 26 (61.9%) patients versus 19 (45.2%) by culture.

- Operative culture missed the diagnosis in 10 cases, though PCR identified the organism in 6 of those cases (5 were cases in which *Kingella kingae* was identified).

- In 4 subjects, NGS identified a putative organism where standard care testing (either PCR or culture) was negative.
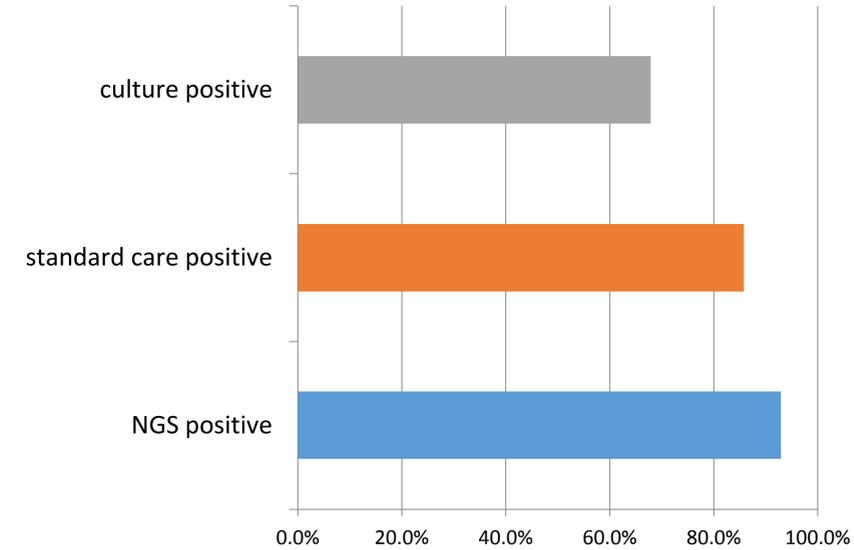
- NGS was falsely positive in 1 subject and falsely negative for one other subject.

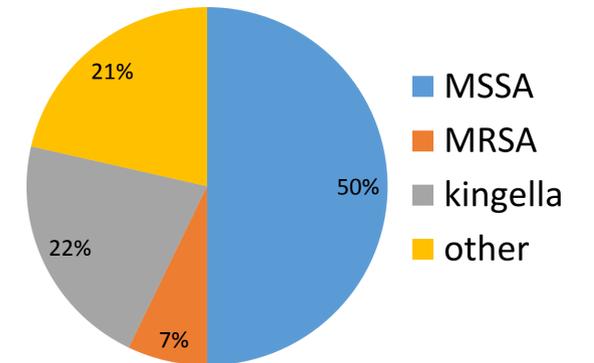|	All	organism isolated	no organism isolated	p value
n (%)	42	28 (66.7)	14 (33.3)	
average age, years (SD)	9.1 (5.7)	9.7 (6.5)	7.9 (3.9)	0.34
hispanic, n (%)	13 (31.0)	6.0 (21.4)	7 (50.0)	0.08
duration of symptoms if <1 week, n (%)	29 (69.1)	17 (60.7)	12 (85.7)	0.2
Length of hospitalization, days (median, IQR)	4.5 (3.0-6.0)	5.0 (4-6.3)	3.5 (3.0-4.8)	
Average admission CRP mg/dL (SD)	6.7 (7.7)	7.8 (8.5)	4.6 (5.6)	0.2
Average admission ESR mm/hr (SD)	39.6 (20.0)	39.5 (21.0)	39.7 (18.6)	1.0
osteomyelitis n (%)	24 (57)	17 (60.7)	7.0 (50.0)	0.5
septic arthritis n (%)	17 (40.5)	11 (39.3)	6.0 (42.9)	1.0
both (osteomyelitis and septic arthritis) n (%)	2.0 (4.8)	0.0 (0.0)	2.0 (14.3)	0.1
positive blood culture, n (%)	3.0 (7.1)	3.0 (10.7)	0.0 (0.0)	0.5
subperiosteal abscess, n (%)	8.0 (19.1)	7.0 (25.0)	1.0 (7.1)	0.2
received antibiotics prior to surgery, n (%)	33 (78.6)	22 (78.6)	11 (78.6)	1.0

Clinical Characteristics

Percent of all subjects in whom a putative organism was detected.

Percent by organism of subjects with positive result by any detection method. "Other" includes *Escherichia coli, Enterobacter cloacae, Brevundimonas vesicularis, Borrelia burgdorferi* , and *Neisseria gonoerrhea*

	All			Bone			Joint		
	% positive	Sensitivity (95% CI,)	Specificity (95% CI,)	% positive	Sensitivity (95% CI,)	Specificity (95% CI,)	% positive	Sensitivity (95% CI,)	Specificity (95% CI,)
NGS (operative sample)	61.9	0.93 (0.77-0.99)	0.93 (0.66-0.99)	66.7	0.94 (0.71-0.99)	1.0 (0.40-1.0)	50.0	.91 (0.59-0.99)	0.90 (0.55-0.99)
Culture	45.2	0.66 (0.46-0.82)	0.85 (0.55-0.98)	61.9	0.76 (0.50-0.93)	1.0 (0.40-1.0)	25.0	0.45 (0.167-0.77)	0.80 (0.44-0.97)
Standard care	57.1	0.86 (0.67-0.96)	0.86 (0.57-0.98)	76.2	0.82 (0.57-0.96)	1.0 (0.40-1.0)	50.0	.91 (0.59-0.99)	0.80 (0.44-0.97)

Comparison of sensitivity and specificity of Next generation sequencing (NGS) versus culture and standard care (PCR or culture)

Conclusions

In this single site prospective study of pediatric osteoarticular infections, we demonstrate improved sensitivity and specificity of NGS testing when compared to standard culture.

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