

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

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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.

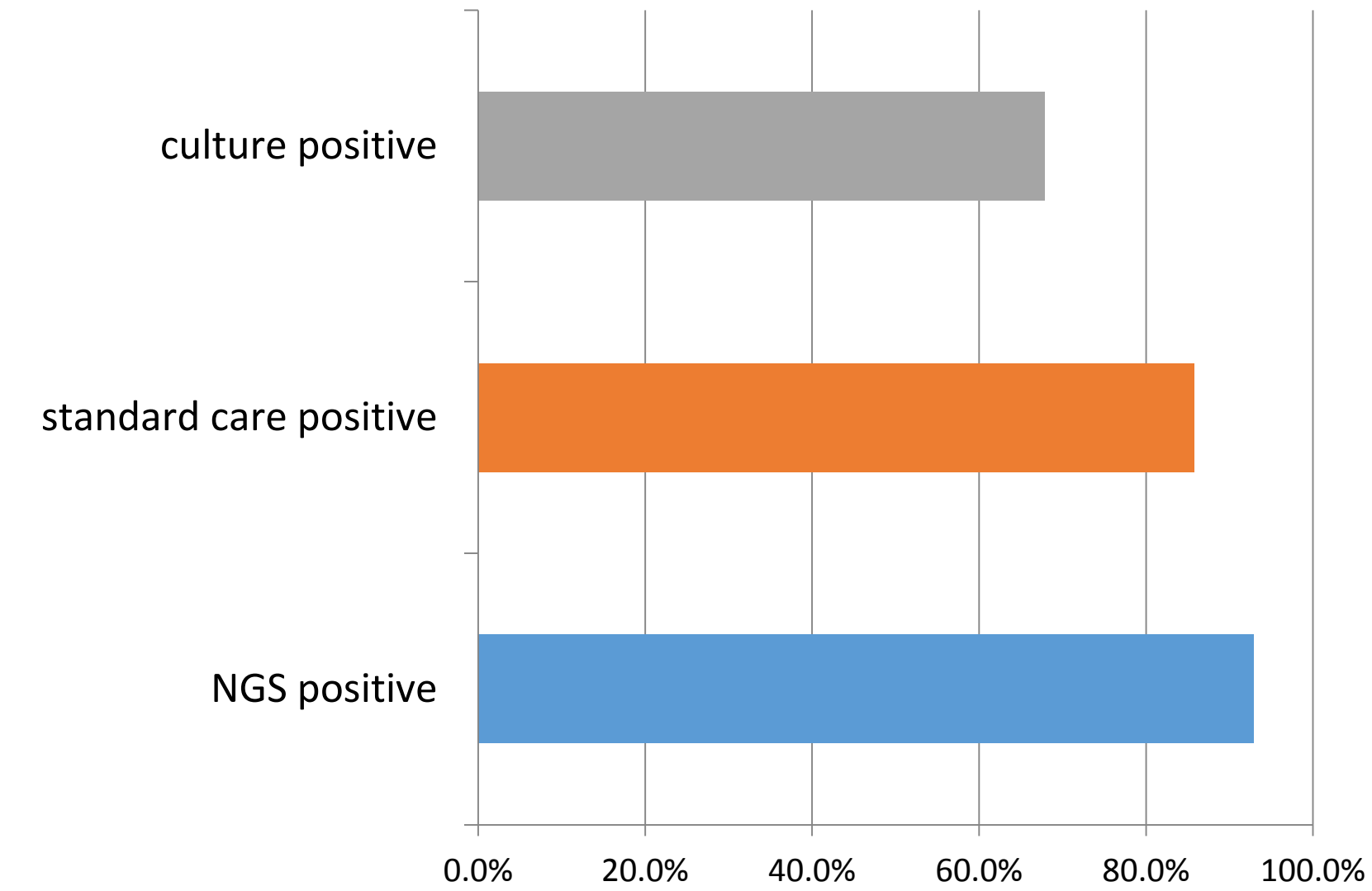
- NGS was falsely positive in 1 subject and falsely negative for one other subject.

	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

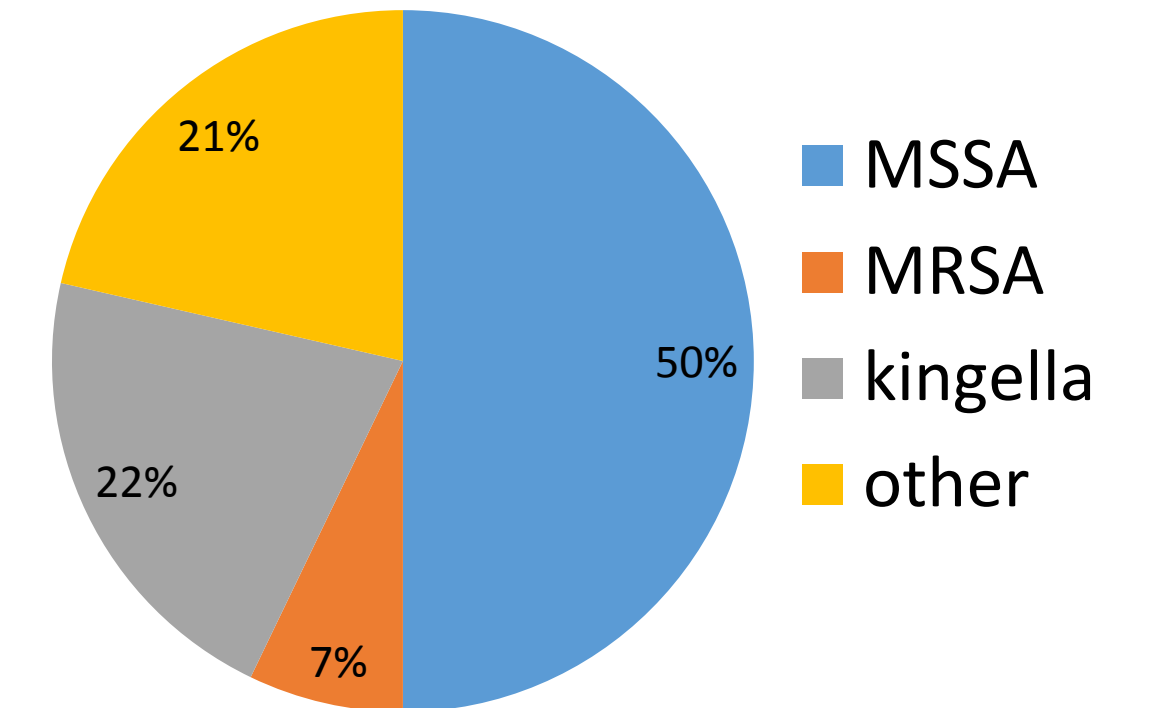
Clinical Characteristics

	All		Bone		Joint	
	% 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)
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)
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)

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



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 gonorrhoea*

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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