1834. Incremental Diagnostic Value of 16S Ribosomal RNA Gene Polymerase Chain Reaction/Sanger Sequencing in Clinical Practice

Sarwat Khalil, MD[1]; Madiha Fida, MD[1]; Douglas W. Challener, MD[1]; Omar Abu Saleh, MBBS[1]; Muhammad R. Sohail, MD[2]; Joshua Yang, MLS (ASCP)[1]; Bobbi Pritt, MD[1]; Audrey Schuetz, MD[1]; Robin Patel, MD[1] and Robin Patel, MD[1]; [1]Mayo Clinic, Rochester, Minnesota; [2]Mayo Clinic College of Medicine, Rochester, Minnesota

Session: 183. Innovative Diagnostics
Friday, October 4, 2019: 2:45 PM

Background. Polymerase chain reaction (PCR)/sequencing targeting the 16S ribosomal RNA (rRNA) gene to detect bacteria in normally sterile tissues and fluids has become increasingly popular in clinical medicine. This culture-independent technique can detect bacteria that are nonviable or difficult to cultivate using conventional methods. The clinical value of this type of testing is not well defined. We aimed to assess the diagnostic value of 16S rRNA PCR/Sanger sequencing as a clinical diagnostic assay at Mayo Clinic.

Methods. This is an interim analysis of the first 173 of 478 patients who had 16S rRNA PCR/Sanger sequencing done on sterile tissues or fluids at our institution from April, 2017 to November, 2018 as part of routine clinical practice. Medical records are being retrospectively reviewed, with results compared with those of culture.

Results. We reviewed 207 specimens from 173 patients (musculoskeletal 79%, cardiovascular 7%, central nervous system 4%, other 9%) that underwent 16S rRNA PCR/Sanger sequencing by clinical request (Table 1). In 90% of these specimens, the test was pre-planned rather than added-on. Nine specimens were excluded from analysis, as cultures were not performed. Overall concordance of culture with PCR/sequencing was 81% (160/197; $P < 0.0001$). Of 44 culture-positive specimens, PCR detected the same bacterium in 21 (48%) (Table 2). 45% (20/44) of those with positive cultures and 46% of those with positive PCR/sequencing results had received prior antimicrobial therapy (Table 3). PCR was negative in 139/144 specimens that were culture-negative (97%). PCR/sequencing was helpful in detecting a putative bacterial pathogen in 4 patients with negative cultures (Table 4).

Conclusion. Overall, 16S rRNA PCR/Sanger sequencing improved diagnostic yield compared with culture in a minority of cases. The described assay is limited by its inability to detect polymicrobial infections, a technical limitation that could possibly be addressed using massive parallel sequencing. Careful selection of cases and a save and add-on approach may be more cost-effective than upfront testing, although this was requested in a minority of cases.

Table 1. Characteristics of specimens

	Prior Antibiotic Therapy		Gram Stain		Culture	
	Yes	No	Positive	Negative	Positive	Negative
Positive PCR/Sequencing N=26	12	14	9	17	21	5
Negative PCR N=162	49	113	5	157	23	139
Fisher's Exact Test	p = 0.1186		p = 0.0001		p = 0.0001	

10 specimens were not included in this table because 6 had DNA detected without identification and 4 had PCR inhibitors

Table 2. Specimens with same bacterium detected by both PCR and culture

Clinical Syndrome	Specimen Tested	Bacterium Detected by PCR/Sanger Sequencing	Bacterium Detected in Culture	Gram Stain	Prior Antibiotic Therapy
PJI	Periprosthetic joint tissue	*Staphylococcus* species	*Staphylococcus aureus*	GPC	Yes
PJI	Periprosthetic joint tissue	*Staphylococcus* species	*Staphylococcus capitis*	Negative	Yes
PJI	Periprosthetic joint tissue	*Streptococcus* species	*Streptococcus mitis* group	GPC	No
PJI	Periprosthetic joint tissue	*Staphylococcus* species	*Staphylococcus epidermidis*	GPC	No
PJI	Synovial fluid	*Streptococcus agalactiae*	*Streptococcus agalactiae*	GPC	Yes
PJI	Synovial fluid	*Streptococcus agalactiae*	*Streptococcus agalactiae*	Negative	Yes
PJI	Synovial fluid	*Staphylococcus* species	*Staphylococcus aureus*	Negative	Yes
PJI	Synovial fluid	*Klebsiella* species	*Klebsiella pneumoniae*	Negative	No
PJI	Synovial fluid	*Staphylococcus* species	*Staphylococcus epidermidis*	GPC	No
PJI	Synovial fluid	*Streptococcus mitis* group	*Streptococcus mitis* group	Negative	No
PJI	Synovial fluid	*Corynebacterium* species	*Corynebacterium striatum*	Negative	No
PJI	Synovial fluid	*Corynebacterium* species	*Corynebacterium striatum*	Negative	No
PJI	Abscess fluid	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*	Negative	Yes
Native Joint Infection	Synovial fluid	*Staphylococcus* species	*Staphylococcus aureus*	GPC	No
Native Joint Infection	Synovial fluid	*Streptococcus agalactiae*	*Streptococcus agalactiae*	GPC	Yes
Native Joint Infection	Synovial fluid	*Staphylococcus* species	*Staphylococcus aureus*	GPC	Yes
Osteomyelitis	Bone	*Streptococcus anginosus* group	*Streptococcus anginosus* group	--	No
Osteomyelitis	Bone	*Staphylococcus* species	*Staphylococcus aureus*	--	No
Osteomyelitis	Bone	*Fusibacterium* species	*Fusibacterium* species	--	No
RP infection	Paraspinal tissue	*Finegoldia magna*	*Finegoldia magna*	Negative	No
RP infection	RP tissue	*Finegoldia magna*	*Finegoldia magna*	Negative	No

PJI, Prosthetic joint infection; GPC, Gram positive cocci; RP, Retroperitoneal

Table 3. Bacterium identified by PCR/sequencing or isolated in culture in relationship to antibiotic therapy prior to testing

	Prior Antibiotic Therapy	
	Yes	No
Positive PCR/Sequencing (N=26)	12	14
Positive Culture (N=44)	20	24

Table 4. Characteristics of specimens with positive PCR/sequencing and negative cultures

Infectious Syndrome	Source	Bacterium Detected by PCR/Sanger Sequencing	Bacterium Detected in Culture	Impact on Clinical Care	Prior Antimicrobial therapy
Frontal Epidural Abscess	Paranasal sinus	*Haemophilus* species	Negative	No	Yes
Retroperitoneal Infection	Retroperitoneal tissue	*Pseudomonas* species	Negative	Yes	No
Aortic Graft Infection	Aortic graft	*Streptococcus agalactiae*	Negative	Yes	Yes
Prosthetic Joint Infection	Periprosthetic joint tissue	*Streptococcus* species	Negative	Yes	No

Disclosures. Robin Patel, MD, ASM and IDSA: Other Financial or Material Support, Travel reimbursement, editor's stipends; CD Diagnostics, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, ContraFect, TenNor Therapeutics Limited, Shionogi: Grant/Research Support; Curetis, Specific Technologies, NextGen Diagnostics, PathoQuest, Qvella: Consultant; NBME, Up-to-Date, the Infectious Diseases Board Review Course: Honorarium recipient, Other Financial or Material Support; Patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued: Other Financial or Material Support, Patents.

1835. High Burden of Invasive Staphylococcus aureus Disease Among Native Americans on the White Mountain Apache Tribal Lands

Catherine Sutcliffe, PhD, ScM[1]; Lindsay Grant, PhD, MPH[1]; Angelina Reid, Lab Technician[2]; Grace K. Douglass, MPH[1]; Laura B. Brown, MD[1]; Kamellia Kellywood[1]; Robert Weatherholtz, BS[3]; Robin Hubler, MS[4]; Alvaro Quintana, MD, MSc[5]; Ryan M. Close, MD, MPH[6]; James McAuley, MD, MPH[6]; Mathuram Santosham, MD, MPH[7]; Katherine O'Brien, MD, MPH[3] and Laura Hammitt, MD[3] [1]Johns Hopkins Bloomberg School of Public Health/Center for American Indian Health, Baltimore, Maryland; [2]Johns Hopkins Center for American Indian Health, Whiteriver, Arizona; [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; [4]Pfizer, Collegeville, Pennsylvania; [5]Pfizer Inc., Collegeville, Pennsylvania; [6]Indian Health Service, Whiteriver, Arizona; [7]Johns Hopkins Bloomberg School of Public Health, Baltim, Baltimore, Maryland

Session: 185. *Staph aureus*: New Perspectives on an Old Foe
Friday, October 4, 2019: 1:45 PM

Background. Native Americans in the southwestern United States (US) have a higher risk of many infectious diseases than the general US population. The objective of this study was to determine the burden of invasive Staphylococcus aureus disease among Native Americans on the White Mountain Apache (WMA) Tribal lands.

Methods. Prospective population and laboratory-based surveillance for invasive *S. aureus* infections was conducted from May 2016 through April 2018. A case was defined as a Native American individual living on or around the WMA Tribal lands with S. aureus isolated from a normally sterile site. Incidence rates were calculated using the Indian Health Service User Population as the denominator. Age-standardized incidence rates were calculated by direct standardization methods using US Census data from 2015 as the reference.

Results. Fifty-three cases were identified (Year 1: 24; Year 2: 29). Most cases were adults (90.6%; median age: 47.4 years) and had ≥1 underlying medical condition (86.8%), of which the most common were obesity (50.0%) and diabetes (50.0%). 26.4% of cases were categorized as community acquired. Most infections were methicillin-resistant (MRSA; 75.5%). 88.7% of cases were hospitalized, 7.5% required amputation, and 7.7% died within 30 days of the initial culture. The overall incidence of invasive S. aureus was 156.3 per 100,000 persons (95% confidence interval [CI]: 119.4, 204.5) with no significant difference in the incidence by year (Year 1: 141.5; Year 2: 171.1; incidence rate ratio: 1.21; 95% CI: 0.70, 2.08). The overall incidence of invasive MRSA was 118.0 per 100,000 persons (95% CI: 86.5, 160.8) with no significant difference by year (Year 1: 106.1; Year 2: 129.8; incidence rate ratio: 1.22; 95% CI: 0.66, 2.28). The incidence of invasive S. aureus and MRSA increased with age and was highest among individuals 50–64 years of age. The overall age-adjusted incidence of invasive MRSA was 138.2 per 100,000 persons (Year 1: 125.2; Year 2: 150.9, for comparison US 2015 general population: 18.8 per 100,000 persons).

Conclusion. The WMA community has one of the highest reported incidence rates globally of invasive MRSA. Interventions are urgently needed in this community to reduce the morbidity and mortality associated with these infections.

Disclosures. **All Authors:** No reported Disclosures.