Novel Technique to Expeditiously Identify Pathogenic Organisms in Antibiotic Treated Osteomyelitis

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Introduction

Bone biopsy is considered the reference standard in the diagnosis of osteomyelitis(OM).(1) However, bone biopsy lacks a standardized definition and the statistical reliability of both microbiological and pathological examination of bone biopsy has been shown to have significant variability. Howard et al. reported sensitivity and specificity as 87% and 93% respectively for bone biopsy.(2)

Meyr et al. reported pathologist agreement below the level of a reference standard for bone biopsy based OM and highlighted the need for a more comprehensive diagnostic protocol.(3) In addition, targeted antibiotic therapy for OM can be complicated by factors including the length of time needed to identify pathogenic organisms by traditional bone biopsy cultures and ongoing antibiotic therapy at the time of bone biopsy.

Purpose

The purpose of this study is to describe a novel technique which quickly identifies pathogenic organisms in osteomyelitis through use of a DNA probe ASSAY testing on BMA. We suggest that this method, which is already utilized in rapid identification of pathogenic organisms in blood cultures, can further be utilized in the rapid identification of pathogenic organisms for patients with suspected osteomyelitis. This may expedite targeted antibiotic therapy and have a subsequent effect on decreasing hospital length of stay and costs.

Methods

Case series consisting of 4 individuals (3 males, 1female) with an average age of 51. All patients presented to the hospital in the year 2019 with concern for osteomyelitis.

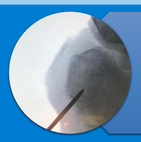
DNA ASSAY identifies the following bacterial species.(4)

Species
Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus lugdunensis
Streptococcus anginosus Group
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
Enterococcus faecalis
Enterococcus faecium
Genus
Staphylococcus spp.
Streptococcus spp.
Listeria spp.
Resistance
mecA (methicillin)*
vanA (vancomycin)**
vanB (vancomycin)**

Species
*Escherichia coli**
Klebsiella oxytoca
Klebsiella pneumoniae
Pseudomonas aeruginosa
Genus
Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Proteus spp.
Resistance
CTX-M (ESBL)
IMP (carbapenemase)
KPC (carbapenemase)
NDM (carbapenemase)
OXA (carbapenemase)
VIM (carbapenemase)

The blood culture DNA probe ASSAY is a qualitative in-vitro diagnostic test for the detection and identification of potentially pathogenic bacteria and is FDA approved and validated for use directly from blood culture bottles.(4)

Procedure



STEP ONE

Patient taken to the OR for fluoroscopic guided procedure

STEP TWO

Aspirate 20ccs of BMA with Jamshidi needle, send in blood culture bottles

STEP THREE

Obtain bone specimen for aerobic/anaerobic cultures and pathology for histologic evaluation

STEP FOUR

BMA incubated in automated system and under positive microbial growth obtain gram stain

STEP FIVE

Gram positive DNA probe testing. Subculture for susceptibility testing

Results

	DNA Probe ASSAY BMA Aerobic	DNA Probe ASSAY BMA Anaerobic	Bone Biopsy Pathology	Bone Biopsy Aerobic Cultures	Bone Biopsy Anaerobic Cultures
Patient 1 Calcaneus	**STAPHY-LOCOCCUS EPIDER-MIDIS**	No growth	Negative OM	No growth	No growth
Patient 2 Calcaneus	No growth	No growth	**Chronic OM**	No growth	No growth
Patient 3 Tibia	No growth	No growth	Negative OM	**STAPHY-LOCOCCUS COAGULASE NEGATIVE**	No growth
Patient 4 Calcaneus	**MICRO-COCCUS LUTEUS**	No growth	Negative OM	No growth	No growth

Patient 1 on BMA DNA ASSAY showed Staphylococcus Epidermidis. Susceptibilities showed resistance to erythromycin and oxacillin. Patient 2 bone biopsy sent to pathology resulted chronic OM. Patient 3 traditional culture showed Staphylococcus coagulase negative. Patient 4 on BMA DNA ASSAY showed Micrococcus Luteus.

Discussion

According to a study by Bates et al., false positive blood cultures often lead to unnecessary antibiotic use, increased hospital costs and length of stay.(5) In a study by Walker et al, bacteremia was retrospectively reviewed prior to and after implementation of DNA probe ASSAY system. They reported organism identification was achieved more quickly post DNA probe ASSAY implementation(mean 10.9 vs. 37.9 hr, $p<0.001$). Length of ICU stay and 30-day mortality was significantly lower in the post implementation group ($p<0.05$).(6) While conventional microbiological methods for bone biopsy may require 2 to 4 days to produce bacterial identification and susceptibility results, DNA probe test provides results within 2.5 hours of culture positivity.(4) With faster time to organism identification, physicians can rapidly implement targeted antibiotic therapy. Not only does this automated bench-top process decrease the time to results but it can also provide results that may not be obtainable due to yields needed for traditional bone culture protocols. We believe that this novel technique of detecting osteomyelitis is not only faster but may also produce a more accurate result.

Proposed Protocol

Emergency department patient presentation suspicious for osteomyelitis

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Primary and secondary patient evaluation, indicated imaging and lab work

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Bedside percutaneous fluoroscopic guided bone marrow aspiration under sedation or local anesthesia

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DNA ASSAY analysis of BMA with other indicated testing

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Rapid identification of pathogenic organism

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Faster time to targeted antibiotic therapy, Decreased length of hospital stay, Decreased health care costs

As DNA probe ASSAY systems are already in use at several hospitals for blood cultures, this technique to identify pathogenic organisms in osteomyelitis can be easily implemented. We propose that individuals that present to an emergency department for suspected osteomyelitis of a long bone can have a percutaneous extraction of BMA and sent for our proposed diagnostic protocol. We believe this protocol will correlate directly with quick and accurate targeted antibiotic therapy, improved treatment results, shorter length of stay, and decreased health care costs.

Conclusion

Bone marrow aspirate sent for DNA ASSAY testing can quickly obtain positive results for pathogen targeted antibiotic therapy. This protocol may also reduce the existing diagnostic variability present with current bone biopsy techniques. Our proposed novel technique warrants consideration to expeditiously identify pathogenic organisms in osteomyelitis. We suggest that BMA DNA probe ASSAY testing could be performed in conjunction with other clinical and laboratory findings to aid in the diagnosis of osteomyelitis. Results should not be used as the sole basis for diagnosis, treatment or patient management decisions. Randomized controlled studies in larger sample sizes should be performed to further evaluate and develop new standardized protocol using DNA probe ASSAY testing in diagnosis of OM and identification of pathogenic organisms.

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