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ASM Microbe 2019 Abstract Summary

Karius® Test for Culture-Negative Endocarditis

Poster Session CIV01—Clinical Studies of Adult Infectious Diseases
Sunday | June 23 | 11:00 AM–1:00 PM

Poster CIV-150

Detection of *Bartonella* Species in Culture-Negative Endocarditis Using the Karius Test, a Plasma Next-Generation Sequencing Test for Pathogen Detection

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Study Design

Karius Test results from two patients with culture-negative endocarditis (CNE) were analyzed in the context of the clinical scenario and surgical as well as antimicrobial treatment. The quantities of pathogen detected were reported as Molecules of microbial cell-free DNA fragments Per Microliter of plasma (MPM) and the values were used for monitoring response to treatment.

Results

1. **Case 1**—Young adult male with a history of bicuspid aortic valve and valve repair presented with CNE and renal failure. Initial infectious workup was unrevealing. The Karius Test detected *Bartonella henselae* at 20,804 MPM. Repeat testing following surgical and antimicrobial treatment showed a reduction in *B. henselae* signal to 5 MPM.

2. **Case 2**—Young adult male with pulmonary/mitral valve stenosis and a history of balloon valvuloplasty presented with CNE and renal failure. The Karius Test detected *Bartonella vinsonii* at 64 MPM. The organism is typically transmitted through contact with canines. Repeat testing after surgical and antimicrobial treatment showed the signal for *B. vinsonii* was no longer detectable.

In both cases, the rapid turnaround time of the Karius Test led to targeted antimicrobial treatment. Subsequent results from other microbiological tests were consistent with the Karius Test results.

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CIV – 150

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Background

Background: *Bartonella* species are fastidious Gram-negative bacteria that can cause culture-negative endocarditis (CNE), lymphadenitis, visceral abscesses and fever of unknown origin. Diagnosis frequently requires sampling of infected tissue and identification by culture or specialized stains is difficult. Serology can be unreliable, with long turnaround times and detection limited to *B. henselae* and *B. quintana*. Furthermore, clinical presentation is non-specific, and may require simultaneous testing for multiple potential etiologies.

Methods: The Karius Test (KT) (Redwood City, CA) is a Next-Generation Sequencing (NGS) assay that detects microbial cell-free DNA (cfDNA) in plasma. After cfDNA is extracted and NGS performed, human sequences are removed and remaining sequences are aligned to a curated pathogen database of > 1000 organisms. Organisms present above a statistical threshold are reported and quantified in DNA molecules per microliter (MPM).

Results: The KT was used to identify *Bartonella* species in two patients with CNE. The KT identified *B. henselae* (20,804 MPM) in a 20-year-old male with a history of bicuspid aortic valve and valve repair who presented with CNE and renal failure. Initial infectious workup was unrevealing. Ultimately the patient was found to have elevated IgG for *B. henselae, B. quintana, Legionella,* and *Coxiella burnetii*, with *B. henselae* positive PCR from blood and aortic valve tissue. A second patient, a 21-year-old male with pulmonary/mitral valve stenosis and a history of balloon valvuloplasty, presented with CNE and renal failure. The KT identified *B. vinsonii* (64 MPM) which is typically transmitted through contact with canines. The patient had positive serology for *C. burnetii* but indeterminate serology for *B. henselae*/*quintana*. After surgical intervention, *B. vinsonii* was identified by 16S sequencing of the mitral valve tissue. In both cases rapid diagnosis led to targeted treatment with doxycycline/rifampin. Patients had serial sampling to assess the cfDNA signal in response to antibiotic treatment and surgical resection. In the first patient the *B. henselae* cfDNA signal decreased from 20,804 MPM to 5 MPM (residual disease could not be fully surgically debrided); in the second patient the *B. vinsonii* cfDNA signal decreased from 64 MPM to undetectable levels.

The Karius® Test

- The Karius NGS test identifies microbial cfDNA in plasma from bacteria, DNA viruses, yeasts, mold, and protozoa
- Next day results* are reported from a single blood draw processed at CAP-accredited and CLIA-licensed laboratory

*About 80% of specimens received by 8:30 AM (PT) Monday through Saturday are reported the next day.

Case #1

20yo male with bicuspid aortic valve status post valve repair who presented with culture negative endocarditis and renal failure/glomerulonephritis.

Echocardiogram: severe aortic valve dysfunction including dysplastic prolapsed aortic valve with mild stenosis.

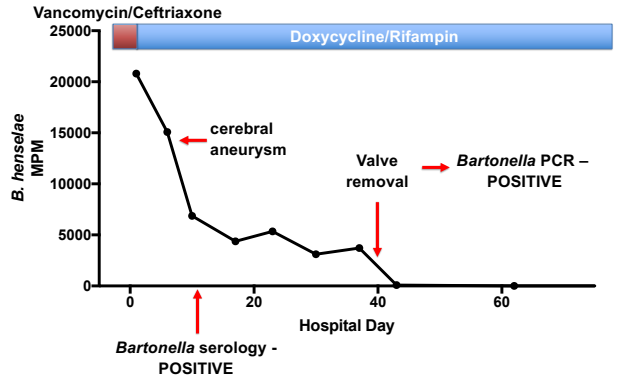
***Bartonella* testing**
- IgG Positive
- Bartonella PCR (blood) Positive
- Bartonella PCR (aortic valve) Positive

Initial Karius Test Report

TEST RESULTS

MICROORGANISM NAME	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Bartonella henselae	20,804	< 10

Serial, Quantitative Karius Test Results



Case #2

21yo male with pulmonary stenosis, mitral valve stenosis status post conduit placement and balloon valvuloplasty who presented with subacute endocarditis and renal failure/glomerulonephritis.

Echocardiogram: abnormal thickening of the mitral valve with mitral stenosis, regurgitation, and moderately dilated left atrium and pulmonary veins.

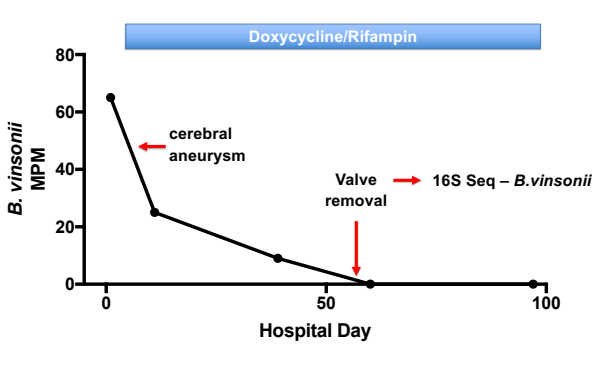
***Bartonella* testing**
- Serology *Bartonella henselae/Bartonella quintana* indeterminate
- Mitral valve tissue demonstrated *Bartonella vinsonii* by 16S PCR testing.

Initial Karius Test Report

TEST RESULTS

MICROORGANISM NAME	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Bartonella vinsonii	64	< 10

Serial, Quantitative Karius Test Results



Conclusions

- Plasma microbial cell-free DNA NGS is a rapid, non-invasive means of identifying a spectrum of *Bartonella* species implicated in CNE.
- Quantitative, serial testing can be used to monitor response to therapy.
- Microbial cfDNA sequencing can be a useful tool in the management of endocarditis.

REFERENCES
1. Blauwkamp TA et al. Analytical and Clinical Validation of a Microbial Cell-Free DNA Sequencing Test for Infectious Disease. Nature Microbiology 2019 April, 4(4):663-674.
2. Shah, Fowler et al. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis Using the Karius Plasma Next Generation Sequencing Test. IDWeek 2018.
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