Challenge M233-5

November 2023

Blood: *Cardiobacterium hominis*

HISTORY

A simulated blood culture sample collected from a 68 year old male in-patient with suspected endocarditis was sent to category A laboratories.

Participants were expected to isolate and report *Cardiobacterium hominis.*

CMPT QA/QC/STATISTICS

All simulated blood samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of *Cardiobacterium hominis*.

The samples are assessed for homogeneity and stability using in-house quality control methods and random selection of samples before and during production, and post sample delivery. The number of random samples selected is 15% of the total production batch.

The challenge sample lot was confirmed to be homogeneous and stable for 12 days.

Organism identification was confirmed by a reference laboratory.

All challenge components have in-house assigned values based on the most clinically appropriate result; the most clinically appropriate result is determined by expert committee evaluation. No further statistical analysis is performed on the results beyond that described under "Suitability for grading."

SURVEY RESULTS

Reference laboratories: 11/12 (92%) labs reported *Cardiobacterium hominis*, 1 lab reported the organism failed to grow for identification, 1 lab indicated it does not normally process this type of sample

Participants: 30/46 (65%) participants reported *Cardiobacterium hominis*, 11 labs reported gram negative bacilli and referred sample for ID (Table 1)

MAIN EDUCATIONAL POINTS from M233-5

1. *Cardiobacterium hominis* is an uncommon but important cause of bacterial endocarditis. It grows well enough from routine blood cultures without extended incubation and rapid identification is important for appropriate clinical therapy.
2. *C. hominis* is readily differentiated from other HACEK group genera/species. The Gram smear is distinctive (slender Gram-negative bacilli, often in a rosette like formation), and modern identification methods (e.g. MALDI-ToF and rapid ID systems) perform well.
3. Accurate antimicrobial susceptibility testing can be problematic due to slower growth, but this micro-organism is susceptible to a wide selection of agents (see below), so that testing is less essential.

Suitability for Grading

A challenge is considered suitable for grading if agreement is reached by 80 percent of selected reference group and at least 50 percent of the participants.

Organism identification was correctly performed by at least 80 percent of reference laboratories and greater than 50 percent of all laboratories and was thus, determined to be suitable for grading.

Grading

Maximum grade: 4

Reporting *Cardiobacterium hominis* was graded 4 as was gram negative bacilli referred for further identification.

Table 1. Identification results

Reported	Total	Grade
Cardiobacterium hominis ± presumptive ± refer	30	4
Batonnets gram négatif, (ex *Cardiobacterium, Leptotrichia, Simonsiella, Streptobacillus*), refer	1	4
gram negative bacilli/bacillus/rods, refer ± suggestive of HACEK group of organisms ± fastidious ± facultative	11	4
Eikenella corrodens, probable, refer	1	0
Micrococcus luteus	1	0
Staphylococcus aureus	1	0
Staphylococcus epidermidis (Coagulase-Neg Staphylococcus)	1	0
Failed to grow for Identification	1	Ungraded
no report	1	0
shipping delay, no report	1	ungraded
refer/sample not normally processed	5	ungraded
Total	**54**	

COMMENTS ON RESULTS

This challenge was performed well by the majority of laboratories. In addition, a large proportion of laboratories utilized MALDI -ToF for identification. This rapid identification from a clinical specimen is important because although uncommon, *C. hominis* is an important cause of bacterial endocarditis.

Most patients with infective endocarditis are likely to be managed in tertiary care facilities and their laboratories usually have such automated identification systems available. It was noteworthy that 3 laboratories reported a gram positive isolate. They should carefully examine their Gram staining reagents and methodology.

Laboratories using MALDI-ToF should ensure that they have validated their system with known isolates of *C. hominis* before accepting test results with isolates from clinical specimens.

ISOLATION AND IDENTIFICATION

Cardiobacterium hominis, a fastidious, gram negative bacillus belonging to the HACEK group (*Haemophilus parainfluenzae, Aggregatibacter aphrophilus* and *Actinobacillus actinomycetemcomitans, C. hominis, Eikenella corrodens* and *Kingella* species), is a cause of infective endocarditis. These species generally grow reasonably well from blood cultures but on occasion, culture positivity may be delayed.[1]

The *Cardiobacterium* genus consists of facultatively anaerobic, nonmotile, gram negative rods with two species, *C. hominis* and *C. valvarum*. *Cardiobacterium* spp. are pleomorphic on blood agar. *C. hominis* stains irregularly and appears as straight, gram negative rods in short chains, pairs, or rosettes, sometimes with bulbous ends; occasionally, filaments are formed. On chocolate agar, this morphology is less distinct than on blood agar.

Cardiobacterium species grow best in an atmosphere of 5% CO_2 and increased humidity for initial growth on blood agar. Cardiobacterium species have most often been isolated from blood. They may be slow growing, but extended culture of blood samples may not be required beyond 5 days. The newer blood culture systems appear to allow adequate growth of these species.

Colonies of *Cardiobacterium* species attain a diameter of approximately 1mm after 48h at 37°C on blood agar; they are circular, smooth, and opaque and may pit the agar.[2] Isolates are indole and oxidase positive, although the reactions may be weak. These and characteristic sugar fermentation distinguish *C. hominis* from other slow-growing, gram negative bacilli

ANTIMICROBIAL SUSCEPTIBILITY

Cardiobacterium hominis and *C. valvarum* are susceptible to many antimicrobials, including penicillin. β-lactamase production is rare, and its effect can be neutralized by clavulanic acid.[2] Standard treatment for infective endocarditis with these organisms is ceftriaxone or ampicillin, or an alternative of a fluroquinolone.6

CLINICAL RELEVANCE

The normal habitat of *Cardiobacterium* species is the human oral cavity and nasopharynx but possibly also the gastrointestinal and urogenital tracts.

Disease caused by both *Cardiobacterium* species is mainly HACEK endocarditis; on rare occasions, *C. hominis* has been isolated from other body sites. Most reported *C. valvarum* endocarditis cases were of odontogenic origin, related to periodontal diseases.[2]

HACEK endocarditis accounts for 1–3% of all infective endocarditis; it mostly affects patients with underlying heart disease or prosthetic valves, and is characterized by an insidious course, with a mean diagnosis delay of 1–3 months.

Cardiobacterium spp. are the third most common agents responsible for HACEK endocarditis, accounting for 13–27% of all HACEK endocarditis.[3]

Main predisposing factors are pre-existing heart disease (60%) and poor dentition/previous dental procedure (58%), while infective endocarditis preferentially occurs in patients with native valves (65–80%).[4, 5]

Aortic (30–49%) and mitral (45–50%) valves are most commonly involved.[4,5] Surgical cardiac replacement is performed in 40% of patients, and the overall outcome is favourable in most cases (87–89%).[3-5]

REFERENCES

1. Asai N, Sakanashi D, Suematsu H, et al. Infective endocarditis caused by *Cardiobacterium hominis* endocarditis: a case report and review of the literature. J Infect Chemother. 2019;25:626-629.

2. Zbinden R, von Graevenitz A. *Aggregatibacter, Capnocytophaga, Eikenella, Kingella, Pasteurella*, and other fastidious or rarely encountered gram-negative rods. In Carrol KC et. al., ed. Manual of Clinical Microbiology. Vol 1. 10th ed. Washington, DC: ASM;2019:656.

3. Revest M, Egmann G, Cattoir V, Tattevin P. HACEK endocarditis: state-of-the-art. Expert Rev Anti Infect Ther. 2016;14:523-530.

4. Chambers ST, Murdoch D, Morris A, et al. HACEK infective endocarditis: characteristics and outcomes from a large, multinational cohort. PLoS One. 2013;8:e63181.

5. Das M, Badley AD, Cockerill FR, et al. Infective endocarditis caused by HACEK microorganisms. Annual Review of Medicine. 1997;48:25-33.

6. Baddour LM, Wilson WR, Bayer AS, et al. Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals From the American Heart Association. *Circulation*. 2015;132(15):1435-1486. doi:10.1161/CIR.0000000000000296