Cardiobacterium hominis endocarditis: A case report and review of the literature

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The present case report describes the clinical course of a patient who presented with *Cardiobacterium hominis* endocarditis. A review of the literature follows the case presentation. *C hominis*, a fastidious Gram-negative bacillus, is a member of the HACEK group of microorganisms (*Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *C hominis*, *Eikenella corrodens* and *Kingella kingae)*. Endocarditis caused by *C hominis* is uncommon and generally follows a subacute course. Patients may present with constitutional symptoms, symptoms related to valvular destruction or symptoms secondary to embolic events. Diagnosis requires identification of the pathogen from blood or vegetation by either culture or molecular techniques. Blood cultures may require prolonged incubation, highlighting the importance of incubating blood cultures for at least two to three weeks in patients with suspected endocarditis. In the past, *C hominis* was generally sensitive to penicillin. However, reports of beta-lactamase-producing *C hominis* have appeared in the literature over the past decade. The current recommendation for first-line treatment is a third-generation cephalosporin (ceftriaxone) for four weeks (six weeks if a prosthetic valve is in place).

Key Words: Cardiobacterium hominis; *Endocarditis*

L'endocardite à *Cardiobacterium hominis*: Un rapport de cas et une analyse bibliographique

Le présent rapport de cas décrit l'évolution clinique d'un patient qui a consulté en raison d'une endocardite à *Cardiobacterium hominis*. Une analyse bibliographique suit la présentation du cas. Le *C hominis*, un bacille gram négatif pernicieux, fait partie du groupe HACEK de microogranismes (espèces d'*Haemophilus*, *Actinobacillus actinomycetemcomitans*, *C hominis*, *Eikenella corrodens* et *Kingella kingae*). L'endocartite causée par le *C hominis* est peu courante et suit généralement une évolution subaiguë. Les patients peuvent souffrir de symptômes constitutionnels, reliés à la destruction valvulaire ou secondaires à un événement embolique. Pour poser un diagnostic, il faut repérer le pathogène dans le sang ou les végétations au moyen d'une culture ou d'une technique moléculaire. Les analyses sanguines peuvent exiger une incubation prolongée, soulignant l'importance d'incuber les cultures sanguines pendant au moins deux à trois semaines chez les patients atteints d'une endocardite présumée. Par le passé, le *C hominis* était généralement sensible à la pénicilline, mais des cas de *C hominis* producteurs de bétalactamase ont été cités dans les publications depuis dix ans. Le traitement de première ligne actuellement recommandé consiste à administrer une céphalosporine de troisième génération (ceftriaxone) pendant quatre semaines (six semaines en présence d'une prothèse valvulaire).

CASE PRESENTATION

A fifty-six-year-old Caucasian man with no significant past medical history was transferred to the tertiary care Health Sciences Centre (Winnipeg, Manitoba) from a peripheral hospital with new-onset congestive heart failure. The patient reported that he had been feeling 'unwell' for the past several weeks. He had a four-day history of flu-like symptoms, including myalgias, and a two-day history of increasing dyspnea, orthopnea, slight chest pressure and fever. He denied taking any medications. The patient's dental history was not obtained.

Physical examination revealed a middle-aged man in moderate respiratory distress, with a blood pressure of 200/96 mmHg, a heart rate of 153 beats/min, a respiratory rate of 41 breaths/min and an oxygen saturation of 89% on a 15 L nonrebreath mask. The patient was febrile, with a temperature of 38.4°C (taken rectally). Cardiac examination demonstrated a jugular venous pressure at eight vertical centimetres above the sternal angle and a grade III/VI holosystolic murmur consistent with mitral regurgitation. Respiratory examination was significant for decreased air entry and coarse crackles bilaterally. Peripheral stigmata of endocarditis were not observed, with the exception of mild splenomegaly. The remainder of the physical examination was unremarkable.

Laboratory investigations demonstrated a white blood cell count of 29.2×10^9/L (2.33% bands), and a normochromic, normocytic anemia (hemoglobin concentration of 107 g/L). The patient's troponin I value was slightly increased at 0.9 µg/L (reference normal less than 0.2 µg/L). An electrocardiogram demonstrated sinus tachycardia. On chest x-ray, bilateral perihilar infiltrates, worse on the right side, were observed, consistent with asymmetric alveolar edema and possible pneumonia. Blood cultures were sent and empirical antibiotic therapy with cefuroxime and azithromycin was initiated. The patient was transferred to the medical intensive care unit, where he was subsequently intubated for respiratory failure and treated with inotropes for cardiogenic shock.

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TABLE 1
Comparison of *Cardiobacterium hominis* endocarditis with endocarditis caused by other bacteria*

	HACEK†		Typical pathogens		IVDU series
	Current review	Paturel et al (41)	Sandre and Shafran (40)	Pelletier and Petersdorf (39)	Sandre and Shafran (40)
Pathogen(s) in series	*C hominis*	*Actinobacillus actinomycetemcomitans*	*Staphylococcus aureus* (30%), streptococci (43%), enterococci (5%), HACEK† (5%), other (17%)	*S aureus* (29.6%), streptococci (28%), enterococci (9.6%), HACEK† (0.8%), other (32%)	*S aureus* (40%), streptococci (7%), *Pseudomonas aeruginosa* (13%), polymicrobial (27%), other (13%)
General data					
Number of cases of endocarditis in series	67	102	80	125‡	15
Patient age (mean years)	48.5	46.8	49	43	35
Symptom duration	145 days	91 days	29 days	42 days	11 days
Predisposing cardiac condition	76% (44 of 58)	76.5% (78 of 102) (26% [27 of 102] with a prosthetic valve)	55% (no prosthetic valve endocarditis in this series)	72% (12% with prosthetic heart valve)	7%
Symptoms/signs					
Constitutional symptoms	83% (24 of 29)§	66.7% (30 of 45) with weight loss	Chills 51%, arthralgias/myalgias 25%, back pain 14%	Chills 41%, sweats 24%, anorexia 24%, myalgias 12%, arthralgias 12%	Chills 67%, arthralgias/ myalgias 20%, back pain 13%
Fever	81% (46 of 57) as either a symptom or a sign	97.4% (76 of 78) as either a symptom or a sign	90% as symptom, 63% as sign	84% as symptom, 77% as sign	87% as symptom, 54% as sign
Splinter hemorrhages	37.5% (6 of 16)	ND	35%	ND	20%
Splenomegaly	50% (23 of 46)	35.6% (27 of 76)	19%	28%	20%
Clubbing	18.4% (7 of 38)	ND	15%	12%	20%
Petechiae	32.5% (13 of 40)	ND	16%	ND	0%
Murmur	96% (25 of 26)	73% (57 of 78) with a new or altered murmur	95%	89%	93%
Congestive heart failure	38.5% (20 of 52)	27% (21 of 57)	41%	66%	20%
Embolic events	44% (12 of 27)¶	29.5% (23 of 55)	43%	50%	67%
Laboratory abnormalities					
Anemia	78.6% (33 of 42)	88% (59 of 67)	69%	Common	67%
Leukocytosis	25.6% (10 of 39)	45.2% (28 of 62)	ND	ND	ND
Elevated ESR (>20)	93.9% (31 of 33)	98.4% (62 of 63)	88.9% (48 of 54)	Common	88.9% (8 of 9)

*Numbers in parentheses indicate the numbers of patients that could be evaluated; where no parentheses appear, percentages reflect those of the total number of cases in a series. *Data taken from references 1 to 32 and 39 to 41; †A group of microorganisms that includes* Haemophilus *species,* A actinomycetemcomitans, C hominis, Eikenella corrodens *and* Kingella kingae; ‡*Data are from 122 cases for constitutional symptoms and fever as a symptom;* §*Insufficient data to provide percentages for individual symptoms;* ¶*Data taken from reference 1. ESR Erythrocyte sedimentation rate; IVDU Intravenous drug user; ND No data*

An echocardiogram performed one day after admission revealed severe mitral insufficiency. Neither papillary muscle rupture nor vegetations were seen. On the fourth hospital day, the patient was taken to the operating room for mitral valve replacement. During the surgery, extensive destruction of the anterior leaflet of the mitral valve was observed and a diagnosis of endocarditis was entertained. Two holes were observed in the aortic valve (noted to be quadricuspid), which was also replaced. The patient's postoperative course was complicated by cardiac tamponade related to bleeding from sternal wires, necessitating a second operation, and third-degree heart block requiring placement of a pacemaker.

The blood cultures collected on admission were reported as growing Gram-negative bacilli three days after being drawn. At that time, antibiotic treatment was changed to cefotaxime. Ten days after admission, *Cardiobacterium hominis* was identified as the pathogen. Cultures of both valves were negative for bacteria, acid-fast bacilli and fungi. The patient was discharged home after 22 days in hospital and continued therapy with intravenous antibiotics to complete a four-week course. He was asymptomatic at a one-year follow-up visit.

LITERATURE REVIEW

Previous case reports and reviews of *C hominis* endocarditis were obtained by performing a MEDLINE search using the search strategy 'cardiobacterium' AND ('endocarditis' OR 'endocarditis' [Medical Subject Headings]). The search term 'HACEK' was also used to obtain additional case series from

which data on individual cases of C *hominis* endocarditis could be extracted. The references cited in all of the case reports included in the present review were examined for additional cases not indexed on MEDLINE. Only those papers published in the English language were reviewed, although additional cases have been published in French, Hebrew, Spanish, German and Portuguese. The data to follow were primarily obtained from a review published in 1983 (1) and case reports that have appeared in the literature subsequent to that publication (2-32). To date, there have been 67 cases of C *hominis* endocarditis reported in the English-language literature (including the present case) from which individual patient data were extractable (1-32). In many of these cases, data reporting was not complete. Hence, where percentages are calculated in subsequent parts of the present review, the denominator for the total number of cases is always less than 67.

C *hominis* is an uncommon cause of endocarditis. It is a member of the HACEK group of microorganisms (*Haemophilus* species, *Actinobacillus actinomycetemcomitans*, C *hominis*, *Eikenella corrodens* and *Kingella kingae*). A study published in 1990 by Steckelberg et al (33) found this group of bacteria to be responsible for approximately 3% (two of 68) of community-acquired cases of endocarditis and 6% (38 of 629) of cases in a referral population. In a series of patients diagnosed with HACEK endocarditis described by Das et al (34), C *hominis* was the etiological pathogen in 27% (12 of 45) of cases.

C *hominis* was first isolated from patients with endocarditis in 1962 (35). At that time, it was classified as a *Pasteurella*-like organism and was designated group II D (35). Slotnick and Dougherty (36) subsequently proposed the name C *hominis* in 1964. C *hominis* is a constituent of the normal flora (37). In one study (37), C *hominis* was demonstrated to be present in the nose and throat of 68% of healthy individuals. It has also been detected in stool samples by fluorescent antibody analysis (37). Microbiologically, C *hominis* has been described as a fastidious, pleomorphic Gram-negative bacillus (1,36,38). It is a facultative anaerobe and grows best in a humid atmosphere with increased CO_2 tension (1,36,38). C *hominis* produces indole and is oxidase-positive (1,36,38). It ferments glucose, sorbitol, mannose, sucrose and, in most cases, maltose and mannitol (1,36,38). It does not demonstrate urease, catalase, nitrate reductase, phenylalanine deaminase, beta galactosidase, lysine decarboxylase, ornithine decarboxylase or arginine dihydrolase activity (1,36). These characteristics help distinguish it from other members of the HACEK group.

There are several factors thought to predispose patients to C *hominis* endocarditis. Dental work is a potential cause of bacteremia and has been cited as a risk factor leading to infection. Twelve of 27 patients (44%) reviewed by Wormser and Bottone (1) were reported to have had a dental procedure or oral infection before the onset of symptoms. Structural cardiac abnormalities also predispose to infection with C *hominis* and are present in 76% (44 of 58) of case reports in the literature for which data were available (1-32). This percentage is similar to that reported in other case series of endocarditis caused by more typical pathogens (Table 1) (1-32,39-41). Previous valve replacement, previous rheumatic heart disease, previous endocarditis, known ventricular septal defect, known bicuspid aortic valve, congenital aortic valve disease (type not specified), mitral valve prolapse with murmur (type not specified) and dilated cardiomyopathy have all been described as potential predisposing cardiac lesions in cases of C *hominis* endocarditis (2-32). The present patient had a quadricuspid aortic valve, and this may have placed him at risk for this infection. There has been one case report in the literature of bacteremia due to upper gastrointestinal endoscopy as the potential cause of C *hominis* endocarditis (2). Neither intravenous drug use nor infection at another site in the body have been described as risk factors for C *hominis* endocarditis, in contrast with endocarditis caused by other pathogens (eg, *Staphylococcus aureus*) (1-32,39).

Endocarditis caused by C *hominis* has been reported in both men and women (1-32). Case reports have described patients between the ages of 17 and 82 years (mean patient age 48.5 years) (1-32). Most case reports in the literature have described aortic and/or mitral valve involvement (1-32). However, pulmonary valve involvement has been documented (42).

The clinical manifestations of C *hominis* endocarditis are presented in Table 1 and contrasted with those of endocarditis caused by *A actinomycetemcomitans* (another HACEK microorganism) and other more typical bacteria (1-32,39-41). C *hominis* is a pathogen of relatively low virulence (1); as such, patients typically present with a picture of subacute endocarditis, often feeling unwell for a period ranging from weeks to months before a diagnosis is reached (1-32). The patient described in the present report was unwell for several weeks before seeking medical attention. The mean duration of symptoms before diagnosis is 145 days, but the range is extremely variable (from less than one week to more than 11 months) (1-32). This is prolonged relative to endocarditis caused by staphylococci and streptococci (Table 1) (1-32,39-40). Patients will often report constitutional symptoms, including fatigue, lethargy, sweats, chills, myalgias, arthralgias, anorexia and weight loss (1-32). Eighty-three per cent (24 of 29) of cases in the literature have described at least one of these symptoms (2-32). Orthopnea and dyspnea may be a part of the presentation if the valvular lesion has progressed to the point where it is causing heart failure (3,38,43). This was the case with the patient described in the present report. Symptoms of heart failure may develop or progress despite appropriate antibiotic therapy depending on the extent of valvular damage before diagnosis (43).

Physical findings that have been documented in case reports include splinter hemorrhages in 37.5% (six of 16) of cases, clubbing in 18.4% (seven of 38) of cases, splenomegaly in 50% (23 of 46) of cases, petechiae in 32.5% (13 of 40) of cases and signs of congestive heart failure in 38.5% (20 of 52) of cases (1-32). Roth spots have been rarely reported (43). Fever as either a sign or a symptom has been described in 81% (46 of 57) of cases (1-32). A heart murmur has been auscultated at the time of diagnosis in 96% (25 of 26) of patients described in the literature (1-32). None of these physical findings clearly differentiates C *hominis* endocarditis from other more common causes of endocarditis (Table 1) (1-32,39,40).

Laboratory features of C *hominis* endocarditis include mild-to-moderate anemia, reported in 78.6% (33 of 42) of cases (mean hemoglobin level 101 g/L, range 82 g/L to 114 g/L [1-32]), and an elevated erythrocyte sedimentation rate, reported in 93.9% (31 of 33) of cases (mean 73.3 mm/h, range of 25 mm/h to 133 mm/h [1-32]). The frequency of anemia and elevated erythrocyte sedimentation rate observed with C *hominis* endocarditis are again comparable with endocarditis caused by other bacteria (Table 1) (1-32,39-41). Tests for rheumatoid factor and C-reactive protein may also be elevated (1,4-9). An

increased white blood cell count, typically to less than 15×10^9/L, has been documented in 25.6% (10 of 39) of case reports (1-32). A more profound degree of leukocytosis has been infrequently described in cases where the patient was acutely ill on presentation (2). With respect to the present patient, the leukocytosis observed was likely related in part to the stress response associated with acute valve failure. Significant thrombocytopenia (platelet count of 17×10^9/L) has been described in one case report (10), which is thought to be due in part to the production of platelet autoantibodies. Glomerulonephritis has been described in the literature in association with *C hominis* endocarditis (4,42). Hematuria and a rising creatinine level may suggest the development of this complication (42).

Embolic phenomena associated with *C hominis* endocarditis have been reported often (1,5,9,11-14,42,44,45). Forty-four per cent (12 of 27) of patients in the review by Wormser and Bottone (1) had at least one embolic event. Embolism has been responsible for atypical presentations of *C hominis* endocarditis. Wong and Chan (11) described a 28-year-old man who presented with neurological signs and symptoms, including transient vertiginous attacks, intermittent vertical diplopia, slurring of speech, left-sided weakness (face, arm) and left incomplete homonymous hemianopia. Embolization from a valvular vegetation was the presumed cause of these symptoms (11). Francioli et al (12) described a 30-year-old man with *C hominis* endocarditis who presented with bacterial meningitis, thought to be secondary to septic embolization. Mueller et al (9) published a case report of a patient with *C hominis* endocarditis who presented with sudden onset of sharp right calf pain and had a pulseless right foot on examination due to embolic occlusion of the right popliteal artery. Pulmonary embolism has been infrequently reported as a consequence of right-sided valvular infection (42). Mycotic aneurysm formation (cerebral, femoral and visceral) has also been described (1,15,16,44,45). In general, embolic phenomena are no more common with *C hominis* endocarditis than with other types of bacterial endocarditis (Table 1) (1-32,39-41).

Diagnosing endocarditis caused by *C hominis* requires demonstration of this pathogen in blood or vegetation. Blood cultures for *C hominis* may need a prolonged period of incubation. Positive cultures have generally been reported after an incubation time ranging from two to 14 days (1,3,7,8,10, 12-14,17-28); however, it should be noted that in case reports published since January 2002 (including the case described presently), cultures have been positive in less than five days (10,19). Two case reports have recently described the identification of *C hominis* using molecular techniques (9,29). Mueller et al (9) diagnosed *C hominis* endocarditis by broad-range polymerase chain reaction (PCR) amplification of 16s ribosomal RNA in embolic material, followed by single-strand sequencing. Similarly, Nikkari et al (29) used broad-range PCR amplification of 16s ribosomal RNA followed by sequencing of the PCR product to demonstrate the presence of *C hominis* in an aortic valve tissue sample.

Once a diagnosis is made, treatment rests with antibiotic therapy. The majority of *C hominis* isolates previously reported in the literature were sensitive to penicillin (1,2,5-9, 11-14,18,19,21,22,24,25,28,30). Over the past decade, however, there have been two case reports describing endocarditis caused by beta-lactamase-producing *C hominis* (3,20). The isolate described in the first of these two cases (20) was reported to be resistant to cefotaxime in addition to penicillin, although the criteria used to determine resistance were unclear. Treatment of the patient described in this case consisted of vancomycin and rifampin for four weeks, followed by amoxicillin/clavulanate for two weeks (20). The isolate described in the second case report (3) had an elevated minimal inhibitory concentration for both ceftriaxone (1 µg/mL) and vancomycin (8 µg/mL), in addition to penicillin (minimal inhibitory concentration higher than 256 µg/mL) (3). In this case, the patient was treated successfully with ciprofloxacin (3). The current recommendation for first-line treatment of *C hominis* endocarditis is a third-generation cephalosporin such as intravenous ceftriaxone 2 g daily for four weeks (six weeks in the case of prosthetic valve infection) (46). The combination of ampicillin and gentamicin can be considered as an alternative (46). However, as illustrated by the aforementioned two reports (3,20), there is the need to develop consensus guidelines describing appropriate susceptibility testing (media/growth conditions) and interpretive breakpoints to further guide antibiotic selection for individual patients (47). At present, such guidelines do not exist (47). Valve replacement and/or repair may be necessary in the treatment of *C hominis* endocarditis depending on the extent of valvular destruction and the patient's symptoms (1-25,28-31). Surgery has been required in 40% of cases (23 of 57) reported in the literature (1-32). The present patient underwent replacement of both his mitral and aortic valve because of severe symptoms of congestive heart failure. A good clinical outcome has been reported in 90% (55 of 61) of cases reviewed here; however, this may be the result of publication bias (1-32).

CONCLUSION

C hominis is an infrequent cause of endocarditis. Clinically, *C hominis* endocarditis presents similar to other causes of endocarditis, although it generally follows a more prolonged course, with symptoms present for weeks or months before a diagnosis is made. Diagnosis in the past has often required prolonged incubation of blood cultures. While more recent reports have described positive cultures with incubation times of less than five days, the paucity of data regarding time to positive culture would still argue in favour of ensuring that blood cultures are incubated for at least two to three weeks in suspected cases of endocarditis (46). Molecular methods of diagnosing this pathogen have recently been reported and may provide an alternative method of diagnosis in the future. Most isolates of *C hominis* reported in the literature have been sensitive to penicillin. However, there are published cases that exist describing beta-lactamase-producing *C hominis*. Currently, third-generation cephalosporins (such as ceftriaxone) are recommended as first-line therapy.

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REFERENCES

1. Wormser GP, Bottone EJ. *Cardiobacterium hominis*: Review of microbiologic and clinical features. Rev Infect Dis 1983;5:680-91.
2. Pritchard TM, Foust RT, Cantely JR, Leman RB. Prosthetic valve endocarditis due to *Cardiobacterium hominis* occurring after upper gastrointestinal endoscopy. Am J Med 1991;90:516-8.
3. Lu PL, Hsueh PR, Hung CC, Teng LJ, Jang TN, Luh KT. Infective endocarditis complicated with progressive heart failure due to beta-lactamase-producing *Cardiobacterium hominis*. J Clin Microbiol 2000;38:2015-7.

4. Le Moing V, Lacassin F, Delahousse M, et al. Use of corticosteroids in glomerulonephritis related to infective endocarditis: Three cases and review. Clin Infect Dis 1999;28:1057-61.
5. Christen RD. *Cardiobacterium hominis* endocarditis in a patient with a hypersensitivity reaction to penicillin. Successful treatment with partial resection of the posterior mitral valve leaflet and antibiotic therapy with cefazolin. Infection 1990;18:291-3.
6. Lane T, MacGregor RR, Wright D, Hollander J. *Cardiobacterium hominis*: An elusive cause of endocarditis. J Infect 1983;6:75-80.
7. Marques MT, Barreira R, Almeida M, Gil V. *Cardiobacterium hominis* prosthetic valve endocarditis diagnosed in Portugal. Ann Biol Clin (Paris) 1995;53:299-300.
8. DeGuise M, Lalonde G, Girouard Y. *Cardiobacterium hominis* endocarditis. Can J Cardiol 1990;6:461-2.
9. Mueller NJ, Kaplan V, Zbinden R, Altwegg M. Diagnosis of *Cardiobacterium hominis* endocarditis by broad-range PCR from arterio-embolic tissue. Infection 1999;27:278-9.
10. Arnold DM, Smaill F, Warkentin TE, Christjanson L, Walker I. *Cardiobacterium hominis* endocarditis associated with very severe thrombocytopenia and platelet autoantibodies. Am J Hematol 2004;76:373-7.
11. Wong MJ, Chan RM. Atypical presentation of *Cardiobacterium hominis* endocarditis. Can Med Assoc J 1982;127:511-2.
12. Francioli PB, Roussianos D, Glauser MP. *Cardiobacterium hominis* endocarditis manifesting as bacterial meningitis. Arch Intern Med 1983;143:1483-4.
13. Chong Y, Kim TS, Lee SY, Shim WH, Choo BK. *Cardiobacterium hominis* endocarditis – A case report. Yonsei Med J 1985;26:78-81.
14. Maeland A, Teieh AN, Arnesen H, Garborg I. *Cardiobacterium hominis* endocarditis. Eur J Clin Microbiol 1983;2:216-7.
15. Lin BH, Vieco PT. Intracranial mycotic aneurysm in a patient with endocarditis caused by *Cardiobacterium hominis*. Can Assoc Radiol J 1995;46:40-2.
16. Silver SE. Ruptured mycotic aneurysm of the superior mesenteric artery that was due to cardiobacterium endocarditis. Clin Infect Dis 1999;29:1573-4.
17. Taveras JM 3rd, Campo R, Segal N, Urena PE, Lacayo L. Apparent culture-negative endocarditis of the prosthetic valve caused by *Cardiobacterium hominis*. South Med J 1993;86:1439-40.
18. Currie PF, Codispoti M, Mankad PS, Godman MJ. Late aortic homograft valve endocarditis caused by *Cardiobacterium hominis*: A case report and review of the literature. Heart 2000;83:579-81.
19. Apisarnthanarak A, Johnson RM, Braverman AC, Dunne WM, Little JR. *Cardiobacterium hominis* bioprosthetic mitral valve endocarditis presenting as septic arthritis. Diagn Microbiol Infect Dis 2002;42:79-81.
20. Le Quellec A, Bessis D, Perez C, Ciurana AJ. Endocarditis due to beta-lactamase-producing *Cardiobacterium hominis*. Clin Infect Dis 1994;19:994-5.
21. El Khizzi N, Kasab SA, Osoba AO. HACEK group endocarditis at the Riyadh Armed Forces Hospital. J Infect 1997;34:69-74.
22. Meyer DJ, Gerding DN. Favorable prognosis of patients with prosthetic valve endocarditis caused by gram-negative bacilli of the HACEK group. Am J Med 1988;85:104-7.
23. Colebunders R, Mertens A, Mahler C, Parizel G. *Cardiobacterium hominis* endocarditis. Acta Clin Belg 1982;37:158-61.
24. Manso E, Strusi P, Massacci C, Ferrini L. Endocarditis due to *Cardiobacterium hominis*. Boll Ist Sieroter Milan 1987;66:489-90.
25. Kiwan Y, Shuhaiber H, Chungh T. *Cardiobacterium hominis* endocarditis. Report of one case and review of the literature. J Cardiovasc Surg 1989;30:281-3.
26. Zbinden R, Hany A, Luthy R, Conen D, Heinzer I. Antibody response in six HACEK endocarditis cases under therapy. APMIS 1998;106:547-52.
27. Vogt K, Klefisch F, Hahn H, Schmutzler H. Antibacterial efficacy of ciprofloxacin in a case of endocarditis due to *Cardiobacterium hominis*. Zentralbl Bakteriol 1994;281:80-4.
28. Bruun B, Buch J, Kirkegaard E, Bjaeldager P. Endocarditis caused by *Cardiobacterium hominis*. Two case reports. Acta Pathol Microbiol Immunol Scand [B] 1983;91:325-8.
29. Nikkari S, Gotoff R, Bourbeau PP, Brown RE, Kamal NR, Relman DA. Identification of *Cardiobacterium hominis* by broad-range bacterial polymerase chain reaction analysis in a case of culture-negative endocarditis. Arch Intern Med 2002;162:477-9.
30. Jolie A, Gnann JW Jr. *Cardiobacterium hominis* causing late prosthetic valve endocarditis. South Med J 1986;79:1461-2.
31. Robison WJ, Vitelli AS. Infectious endocarditis caused by *Cardiobacterium hominis*. South Med J 1985;78:1020-1.
32. Botha P, Venter M. *Cardiobacterium hominis* as a cause of bacterial endocarditis. S Afr Med J 1996;86:91.
33. Steckelberg JM, Melton LJ 3rd, Ilstrup DM, Rouse MS, Wilson WR. Influence of referral bias on the apparent clinical spectrum of infective endocarditis. Am J Med 1990;88:582-8.
34. Das M, Badley AD, Cockerill FR, Steckelberg JM, Wilson WR. Infective endocarditis caused by HACEK microorganisms. Annu Rev Med 1997;48:25-33.
35. Tucker DN, Slotnick IJ, King EO, Tynes B, Nicholson J, Crevasse L. Endocarditis caused by a *Pasteurella*-like organism; report of four cases. N Engl J Med 1962;267:913-6.
36. Slotnick IJ, Dougherty M. Further characterization of an unclassified group of bacteria causing endocarditis in man: *Cardiobacterium hominis* gen. et sp. n. Antonie Van Leeuwenhoek 1964;30:261-72.
37. Slotnick IJ, Mertz JA, Dougherty M. Fluorescent antibody detection of human occurrence of an unclassified bacterial group causing endocarditis. J Infect Dis 1964;114:503-5.
38. Midgley J, LaPage SP, Jenkins BA, Barrow GI, Roberts ME, Buck AG. *Cardiobacterium hominis* endocarditis. J Med Microbiol 1970;3:91-8.
39. Pelletier LL Jr, Petersdorf RG. Infective endocarditis: A review of 125 cases from the University of Washington Hospitals, 1963-72. Medicine (Baltimore) 1977;56:287-313.
40. Sandre RM, Shafran SD. Infective endocarditis: Review of 135 cases over 9 years. Clin Infect Dis 1996;22:276-86.
41. Paturel L, Casalta JP, Habib G, Nezri M, Raoult D. *Actinobacillus actinomycetemcomitans* endocarditis. Clin Microbiol Infect 2004;10:98-118.
42. Geraci JE, Greipp PR, Wilkowske CJ, Wilson WR, Washington JA 2nd. *Cardiobacterium hominis* endocarditis. Four cases with clinical and laboratory observations. Mayo Clin Proc 1978;53:49-53.
43. Savage DD, Kagan RL, Young NA, Horvath AE. *Cardiobacterium hominis* endocarditis: Description of two patients and characterization of the organism. J Clin Microbiol 1977;5:75-80.
44. Perdue GD, Dorney ER, Ferrier F. Embolomycotic aneurysm associated with bacterial endocarditis due to *Cardiobacterium hominis*. Am Surg 1968;34:901-4.
45. Laguna J, Derby BM, Chase R. *Cardiobacterium hominis* endocarditis with cerebral mycotic aneurysm. Arch Neurol 1975;32:438-9.
46. Wilson WR, Karchmer AW, Dajani AS, et al. Antibiotic treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. American Heart Association. JAMA 1995;274:1706-13.
47. Jorgensen JH. Need for susceptibility testing guidelines for fastidious or less-frequently isolated bacteria. J Clin Microbiol 2004;42:493-6.