CASE REPORT

Gemella endocarditis: a case report and a review of the literature

Dima Youssef[1], Ibrahim Youssef[2], Tariq S. Marroush[3], Mamta Sharma[1]

[1]Division of Infectious Disease, Ascension Saint John Hospital and Medical Center, Detroit, USA, [2]Michigan Medicine, University of Michigan, Ann Arbor, USA, [3]Division of Cardiology, Ascension Saint John Hospital and Medical Center, Detroit, USA

Access this article online

Website: www.avicennajmed.com

DOI: 10.4103/ajm.AJM_3_19

Quick Response Code:

ABSTRACT

Infective endocarditis (IE) remains a prevalent disease with a high rate of morbidity and mortality. Recent changes have been noted in the profile of causative microorganisms. In this report, we describe a case of *Gemella*-related endocarditis and review the related literature. Our patient was an 81-year-old man who presented with dyspnea and fatigue. His initial examination revealed a new systolic murmur. Echocardiogram revealed moderate mitral regurgitation with 1-cm mass on the anterior mitral leaflet, and blood cultures grew *Gemella haemolysans.* Penicillin and gentamicin were initiated, and workup for possible source was positive for a colonic polyp with high-grade dysplasia. The patient subsequently developed cardiogenic shock and severe pulmonary edema. Comfort care measures were initiated, and he passed away thereafter. We reviewed PubMed for cases of *Gemella*-related endocarditis. We found 65 documented cases and added our patient's case to the analysis. Seventy-two percent of the cases occurred in men. The mean age was 51 years and 42% of the patients were older than 60 years. Fever was the most common presenting symptom and most of the cases presented subacutely. The mitral valve was the most affected site and 50% of the patients required surgical intervention. *G. morbillorum* was the most common subtype and a total of four cases were found to be associated with colorectal neoplasm. As a conclusion, *Gemella* species rarely cause IE. The absence of a clear source of bacteremia warrants further evaluation for a gastrointestinal source. The infection can be destructive and must be promptly treated to avoid complications.

Key words: Endocarditis, *Gemella haemolysans*, mitral, regurgitation, *morbillorum*

Key messages: Gemella endocarditis is a serious infection with significant morbidity and mortality. It must be promptly treated to avoid further complications.

INTRODUCTION

Infective endocarditis (IE) remains a concerning pathology given the increasing incidence and the growing rate of requiring valve replacement surgery.[1] Furthermore, the associated rates of morbidity and mortality are high, with reported short-term mortality, that is, within 30 days from the diagnosis, of 10%–30%, making IE a great burden on global health.[2,3]

IE is classified into acute and subacute depending on timing and severity. Acute IE usually has an aggressive course with a rapidly progressive illness, where subacute IE has usually a more indolent course and may extend over many months, which may lead to a delay in the diagnosis.[4] The classic clinical manifestation, which combines fever, heart failure,

Address for correspondence: Dr. Dima Youssef, Ascension Health, Saint John Hospital and Medical Center, 19251 Mack Avenue, Suite 340, Grosse Pointe Woods, Michigan 48236, USA.
E-mail: Dima.youssef@ascension.org

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Cite this article as: Youssef D, Youssef I, Marroush TS, Sharma M. Gemella endocarditis: A case report and a review of the literature. Avicenna J Med 2019;9:164-8.

© 2019 Avicenna Journal of Medicine | Published by Wolters Kluwer - Medknow

new cardiac murmurs, and embolic and immunologic phenomena, is rare.[5] Modified Duke criteria aid in making the diagnosis and include clinical, microbiological, pathological, and imaging features.[6,7] In a previous study, it was shown that modified Duke criteria helped with 10% increase in the frequency of cases being deemed clinically as definite IE, compared with Duke criteria, with no loss of specificity.[3,6]

Elderly patients can have atypical presentations and the diagnosis may become challenging.[8] Treatment of IE relies on microbial eradication by antibiotics. In some cases, surgery is indicated, mainly if the infection is not well controlled (evidence of an abscess or an enlarging vegetation), if there is indication for prevention of embolic events (as in left-sided IE with a very large vegetation >30 mm, or an evidence of an embolic event despite appropriate antibiotic therapy), and in the case of heart failure.[3,9]

The bacteriology of IE varies depending on the cohort examined; however, *Staphylococcus aureus* and *Streptococci* comprise most of the organisms involved.[9,10] Change in the causative organisms have been noted in recent years with emerging species that are often difficult to grow.[1,11,12]

Gemella species is present in the human oropharynx, the genitourinary system, and the gastrointestinal system. It has been implicated in several diseases primarily in adults, including meningitis and septic shock but rarely IE.[13,14] The genus currently includes six subspecies that cause similar clinical illness: *morbillorum, haemolysans*, *bergeriae*, *sanguinis*, *palaticanis*, and *cuniculi*, in addition to other subspecies that are restricted to animals.[15] *Gemella morbillorum* was initially thought to be part of the genus *Streptococcus* until 1988 when it was found to be related to *G. haemolysans* at the genus level.[16]

The literature on *Gemella* has been scarce and based mainly on case reports as the incidence is rare. In this paper, we report a case of IE caused by *G. haemolysans* and review the related literature, aiming to gather what is known about this infection in one source.

CASE REPORT

An 81-year-old man presented with dyspnea. He had a medical history of coronary artery disease, hypertension, chronic obstructive pulmonary disease (COPD), and atrial fibrillation. He underwent a coronary artery bypass grafting (CABG) 2 months preceding presentation but was in his usual state of health until 2 weeks before presentation when he developed weakness and exertional dyspnea. He denied any fever, rigors, or chest pain. On physical examination, he was afebrile and edentulous. On cardiac auscultation, he had an irregular heart rhythm with a 4/6 soft blowing systolic murmur in the left lower sternal border radiating to the axilla along with bilateral lung wheezing. His skin exam did not reveal any Osler nodes or Janeway lesions, and no Roth spots were noted in the eye examination.

Initial laboratory work showed a white cell count of 15,400/mm^3, a hemoglobin of 8.7 g/dL, a creatinine level of 1.74 mg/dL, a pro-brain natriuretic peptide of 11,341 pg/mL, and a procalcitonin level of 28.66 ng/mL (with normal value of below 0.15 ng/mL in healthy adults without kidney injury). A transthoracic echocardiogram was obtained to assess for a possible cardiac etiology for the patient's symptoms, and that revealed a normal ejection fraction; however, a new moderate mitral regurgitation with a 1 cm × 1 cm uniform, round and immobile mass on the atrial surface of the anterior mitral leaflet [Figure 1]. Figure 2 is included for comparison, and it shows a transthoracic echocardiogram that was obtained couple months before the current presentation, when he underwent CABG.

Because of concerns for endocarditis, the patient was started on vancomycin and ceftriaxone after blood cultures were obtained. Transesophageal echocardiogram showed an anterior leaflet mass measuring 1.3 cm × 0.8 cm, consistent

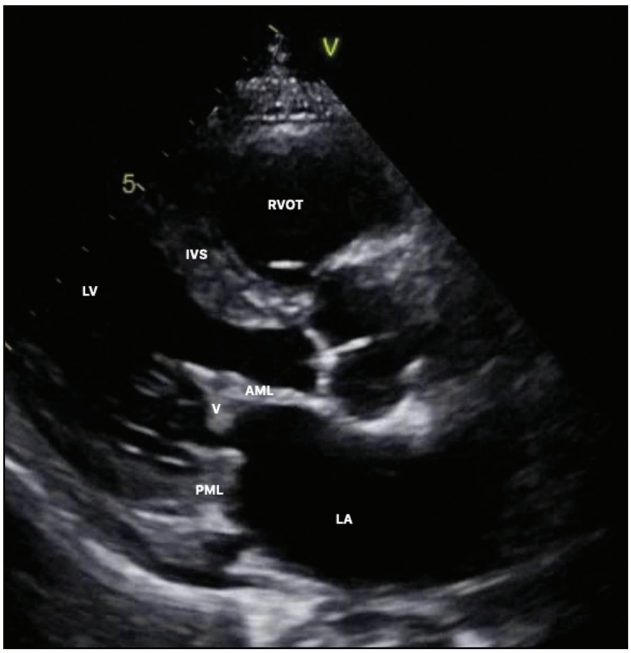

Figure 1: Transthoracic echocardiogram, parasternal long access view showing the vegetation on the anterior mitral leaflet. AML = anterior mitral leaflet, IVS = interventricular septum, LA = left atrium, LV = left ventricle, PML = posterior mitral leaflet, PW = posterior wall, RVOT = right ventricle outflow tract, V = vegetation

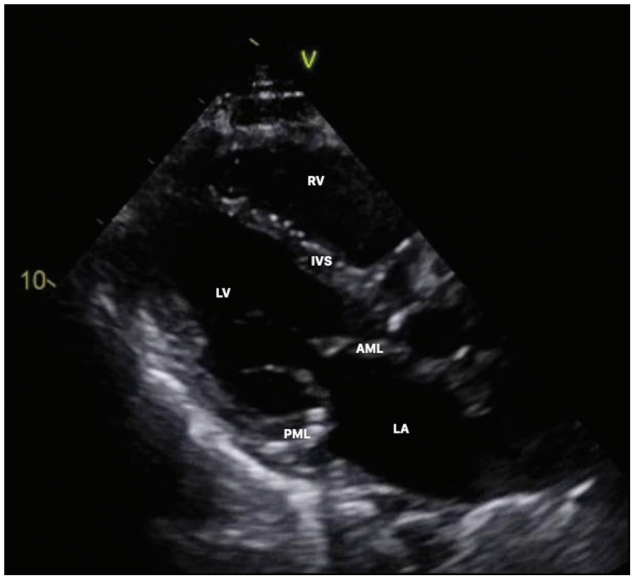

Figure 2: Transthoracic echocardiogram, parasternal long access view obtained couple months before current presentation. AML = anterior mitral leaflet, IVS = interventricular septum, LA = left atrium, LV = left ventricle, PML = posterior mitral leaflet, RV = right ventricle, V = vegetation

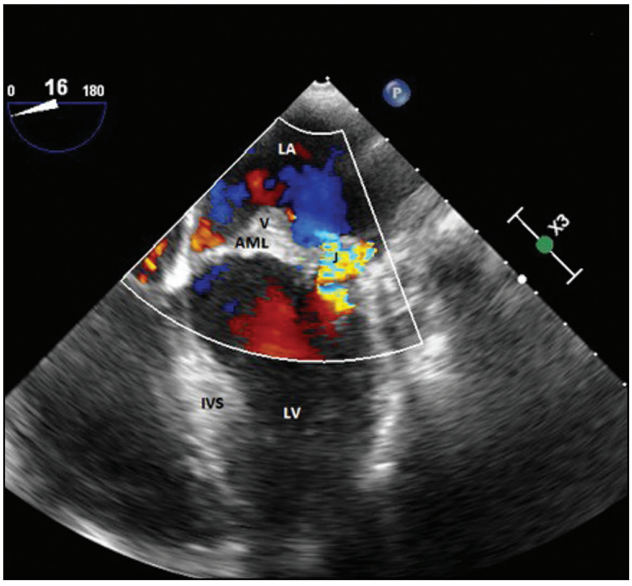

Figure 3: Four chamber view of transesophageal view showing mitral regurgitation jet and vegetation. AML = anterior mitral leaflet, IVS = interventricular septum, J = mitral regurgitation jet, LA = left atrium, LV = left ventricle, V = vegetation

with vegetation on the atrial aspect with moderate mitral regurgitation.

Preliminary report showed gram-positive cocci that turned out to be *G. haemolysans by* mass spectrometry (MS)-based molecular identification (Microflex, matrix-assisted laser desorption ionization time-of-flight [MALDI-TOF]), which was later confirmed by the Michigan State Laboratory. Follow-up antimicrobial susceptibility results showed the isolate to be highly sensitive to penicillin (≤0.03 mg/mL), ceftriaxone (≤0.06 mg/mL), meropenem (≤0.06 mg/mL), and vancomycin (≤0.5 mg/mL). The treatment was then changed to penicillin and gentamicin.

As a part of the workup to find a source for the bacteremia, and as the patient was edentulous, he underwent a colonoscopy, which showed a tubular villous adenoma that measured 9 cm with a focus of high-grade dysplasia.

The patient did not have any embolic phenomena. He was advised to undergo a surgical replacement of the mitral valve; however, he opted to pursue conservative management and was discharged to complete a 6-weeks course of ceftriaxone and 2 weeks of gentamicin. He returned to the hospital 3 days following discharge complaining of increasing dyspnea and was hypotensive. He was started on vasopressors. A repeat transesophageal echocardiogram showed a rupture in the mitral leaflet with increased mitral regurgitation and multiple regurgitation jets [Figure 3].

The patient subsequently developed cardiogenic shock and was enrolled in hospice and passed away couple of days later.

REVIEW OF THE LITERATURE

We reviewed PubMed for cases of *Gemella*-associated endocarditis using appropriate key words. The articles in languages other than English and those that do not include case reports were excluded. The articles were reviewed to gather information about patients' demographics, symptoms, microbiology, echocardiographic findings, and treatment options.

RESULTS

We found a total of 75 articles that included our key words in their titles, of these, 62 were included, depicting 65 cases, after adding our case, we analyzed a total of 66 cases. The characteristics of these cases are shown in Tables 1 and 2. The mean age was 50.5 years (range, 4–84 years) with the majority being men (46, 72%).

Onset of illness was subacute in majority of cases (37, 63%), and fever was the most common chief complaint in 40 (61%) patients. The mitral valve was the most affected valve (24 cases, 39%), followed by the aortic valve in 15 cases (24%).

The source of infection was described in 30 cases of which dental source (22, 73%) was the most common source.

Surgical intervention was pursued in 31 (50%) of the reported cases, of these 13 patients (42%) underwent aortic

Table 1: Characteristics of cases of Gemella infective endocarditis

Characteristics	Participants (*N* = 66)
Age group (years; *N* = 64)	50.5 ± 23
0–10	3 (5%)
11–20	5 (8%)
21–30	6 (9%)
31–40	7 (11%)
41–50	8 (13%)
≥51	35 (55%)
Gender (*N* = 64)	
Male	46 (72%)
Female	18 (28%)
Source (*N* = 30)	
Dental/oral	22 (73%)
Intravenous drug abuse	4 (13%)
Colonic	4 (13%)
Presentation	
Fever	40 (61%)
Fatigue	7 (11%)
Dyspnea	6 (9%)
Miscellaneous	13 (19%)
Gemella species (*N* = 63)	
G. morbillorum	34 (54%)
G. haemolysans	17 (26%)
G. sanguinis	6 (10%)
G. bergeriae	5 (8%)
G. taiwanensis	1 (2%)

Table 2: Valve affected, surgery, and outcomes of Gemella infective endocarditis

Characteristics	Participants (*N* = 66)
Valve affected (*N* = 62)	
Mitral valve	24 (39.1%)
Aortic valve	15 (24%)
Prosthetic mitral valve	9 (14%)
Others	14 (23%)
Surgery	
No	31 (50%)
Yes	31 (50%)
Aortic valve	13 (42%)
Mitral valve	13 (42%)
Mitral and aortic valve	5 (16%)
Others	7 (23%)
Outcomes (*N* = 57)	
Survived	47 (82%)
Died	10 (18%)
Outcomes based on treatment type (*N* = 53)	
Required surgery and died	24 (45%)
Conservative approach and died	23 (43%)
Required surgery and survived	5 (9%)
Conservative approach and survived	1 (2%)

valve replacement and 13 patients (42%) underwent mitral valve replacement, whereas 5 patients (32%) underwent both aortic and mitral valve replacement. Outcomes were available in 57 patients with a mortality rate of 18%. The mortality rate was similar with no significant difference between the group that proceeded with surgical intervention (45%) and the group that received conservative approach (43%).

G. morbillorum was the most common subtype in the 63 cases that reported the subtype (34, 54%), followed by *G. haemolysans* (17, 26%).

DISCUSSION

Gemella species is a gram-positive, facultative anaerobic bacterium that was first reported in 1917.[17] It was initially thought to be a part of the Neisseriaceae family[18,19] until 1961, when it was found to be sufficiently distinctive to form a different genus.[20] The virulence factors are not well studied; however, the production of exopolysaccharide may contribute to its capability of causing endocarditis.[21]

The demographic findings in our results may represent those of IE as a whole, recent data have shown a shift toward older patients and more males being affected with IE.[22] This can also be attributed to the higher frequency of predisposing conditions such as dental disease and colon cancer in older individuals.[23,24] The high number of cases caused by *G. morbillorum* may be due to the fact that it was the first subtype to be discovered, this finding may change over time with more cases reported.

Gemella isolates have shown to be susceptible to β-lactams and vancomycin, with less response to other antibiotics such as macrolides, levofloxacin, and clindamycin.[25-27] As it is impossible to clinically differentiate *Gemella* from other causes of IE, antibiotic therapy is empiric in acutely ill patients, with vancomycin being the best choice after obtaining sufficient blood cultures.[28] Once *Gemella* is isolated, choice of antibiotics and length of treatment depend on minimal inhibitory concentration of penicillin on susceptibility testing.[29] *Gemella* species is generally sensitive to penicillin G, and a combination of penicillin G and gentamicin is the current treatment of choice for these infections, whereas vancomycin can be used in patients with penicillin allergy. In our patient, the isolate was highly sensitive to penicillin, ceftriaxone, and vancomycin and the decision was made to discharge him on ceftriaxone and gentamicin given the ease of administration.

The source of bacteremia should be sought in all cases of Gemella IE, and potential risk factors include dental procedures, poor dentition, colorectal disease and procedures, bypass surgery, as well as immunocompromised status.[30] *Gemella* has been found to be more abundant in the stool of patients with colorectal cancer compared with healthy individuals,[31] and more abundant in the cancerous tissue specifically.[32] Some studies defend that the lesioned mucosa, that is undergoing chronic inflammation, is propitious to translocation of organisms including *Gemella*, leading to bacteremia and subsequently endocarditis.[33]

The organism can be difficult to be identified with standard techniques, and the 16S rRNA identification method seems to be the most accurate mean of diagnosis.[34] We detected the organism by MALDI-TOF MS, which shows strong potential as a new method for species identification of many bacteria in clinical microbiological laboratories.

CONCLUSION

Gemella spp. is a rare cause of IE, but it should be identified and treated properly as it can otherwise result in a significant morbidity and mortality. The main source of Gemella IE is dental; however, colonic etiologies should also be suspected in patients without apparent source. The infection can be destructive and must be promptly treated to avoid complications. In addition, optimal therapy should include valve repair or replacement in patients with clinical progression, despite appropriate antimicrobial therapy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Pant S, Patel NJ, Deshmukh A, Golwala H, Patel N, Badheka A, *et al*. Trends in infective endocarditis incidence, microbiology, and valve replacement in the United States from 2000 to 2011. J Am Coll Cardiol 2015;65:2070-6.
2. Ternhag A, Cederström A, Törner A, Westling K. A nationwide cohort study of mortality risk and long-term prognosis in infective endocarditis in Sweden. PLoS One 2013;8:e67519.
3. Bin Abdulhak AA, Baddour LM, Erwin PJ, Hoen B, Chu VH, Mensah GA, *et al*. Global and regional burden of infective endocarditis, 1990-2010: A systematic review of the literature. Glob Heart 2014;9:131-43.
4. Mylonakis E, Calderwood SB. Infective endocarditis in adults. N Engl J Med 2001;345:1318-30.
5. Furrer H, Malinverni R. [Clinical aspects and diagnosis of infectious endocarditis]. Praxis (Bern 1994) 1994;83:1309-15.
6. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, *et al*. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.
7. McDonald JR. Acute infective endocarditis. Infect Dis Clin North Am 2009;23:643-64.
8. Dhawan VK. Infective endocarditis in elderly patients. Clin Infect Dis 2002;34:806-12.
9. Vogkou CT, Vlachogiannis NI, Palaiodimos L, Kousoulis AA. The causative agents in infective endocarditis: A systematic review comprising 33,214 cases. Eur J Clin Microbiol Infect Dis 2016;35:1227-45.
10. Fowler VG Jr, Miro JM, Hoen B, Cabell CH, Abrutyn E, Rubinstein E, *et al*.; ICE Investigators. Staphylococcus aureus endocarditis: A consequence of medical progress. JAMA 2005;293:3012-21.
11. Brouqui P, Raoult D. Endocarditis due to rare and fastidious bacteria. Clin Microbiol Rev 2001;14:177-207.
12. Millar BC, Moore JE. Emerging issues in infective endocarditis. Rev Biomed 2004;15:191-201.
13. Purcell LK, Finley JP, Chen R, Lovgren M, Halperin SA. Gemella species endocarditis in a child. Can J Infect Dis 2001;12:317-20.
14. Ukimura A, Nishihara S, Suwa M, Hirota Y, Kitaura Y, Kawamura K, *et al*. Prosthetic ball valve endocarditis due to Gemella species. Jpn Circ J 1998;62:626-8.
15. Elsayed S, Zhang K. Gemella bergeriae endocarditis diagnosed by sequencing of rRNA genes in heart valve tissue. J Clin Microbiol 2004;42:4897-900.
16. Kilpper-Bälz R, Schleifer KH. Transfer of Streptococcus morbillorum to the genus Gemella as Gemella morbillorum comb. nov. Int J Syst Evol Microbiol 1988;38:442-3.
17. Facklam R, Elliott JA. Identification, classification, and clinical relevance of catalase-negative, gram-positive cocci, excluding the streptococci and enterococci. Clin Microbiol Rev 1995;8:479-95.
18. Thjötta T, Böe J. Neisseria hemolysans. A hemolytie species of Neisseria trevisan. Acta Pathol Microbiol Scand 1938;15:527-31.
19. Tunnicliff R. The cultivation of a micrococcus from blood in pre-eruptive and eruptive stages of measles. J Am Med Assoc 1917;68:1028-30.
20. Berger U. A proposed new genus of gram-negative cocci: Gemella. Int J Syst Evol Microbiol 1961;11:17-9.
21. Vasishtha S, Isenberg HD, Sood SK. Gemella morbillorum as a cause of septic shock. Clin Infect Dis 1996;22:1084-6.
22. Slipczuk L, Codolosa JN, Davila CD, Romero-Corral A, Yun J, Pressman GS, *et al*. Infective endocarditis epidemiology over five decades: A systematic review. PLoS One 2013;8:e82665.
23. Jiang Q, Liu J, Chen L, Gan N, Yang D. The oral microbiome in the elderly with dental caries and health. Front Cell Infect Microbiol 2018;8:442.
24. Millan M, Merino S, Caro A, Feliu F, Escuder J, Francesch T. Treatment of colorectal cancer in the elderly. World J Gastrointest Oncol 2015;7:204-20.
25. Baghdadi J, Kelesidis T, Humphries R. In vitro susceptibility of Gemella species from clinical isolates. Open Forum Infect Dis 2015;2:1737.
26. Buu-Hoï A, Sapoetra A, Branger C, Acar JF. Antimicrobial susceptibility of Gemella haemolysans isolated from patients with subacute endocarditis. Eur J Clin Microbiol 1982;1:102-6.
27. Kuriyama T, Karasawa T, Nakagawa K, Yamamoto E, Nakamura S. Bacteriology and antimicrobial susceptibility of gram-positive cocci isolated from pus specimens of orofacial odontogenic infections. Oral Microbiol Immunol 2002;17:132-5.
28. Sexton DJ. Antimicrobial therapy of native valve endocarditis. UpToDate. Waltham, MA: UpToDate; 2014.
29. Baddour LM, Wilson WR, Bayer AS, Fowler VG, Tleyjeh IM, Rybak MJ, *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;132:1435-86.
30. Lopez-Dupla M, Creus C, Navarro O, Raga X. Association of Gemella morbillorum endocarditis with adenomatous polyps and carcinoma of the colon: Case report and review. Clin Infect Dis 1996;22:379-80.
31. Wang T, Cai G, Qiu Y, Fei N, Zhang M, Pang X, *et al*. Structural segregation of gut microbiota between colorectal cancer patients and healthy volunteers. ISME J 2012;6:320-9.
32. Chen W, Liu F, Ling Z, Tong X, Xiang C. Human intestinal lumen and mucosa-associated microbiota in patients with colorectal cancer. PLoS One 2012;7:e39743.
33. Flynn KJ, Baxter NT, Schloss PD. Metabolic and community synergy of oral bacteria in colorectal cancer. mSphere 2016;1:e00102-16.
34. Stroup JS, Bransteitter BA, Reust R. Infective endocarditis caused by Gemella species. Infect Dis Clin Pract 2007;15:203-5.