Clinical Case Reports

CASE REPORT

Infective endocarditis and infected aneurysm caused by *Streptococcus dysgalactiae* subsp. *equisimilis*: a case report

Naoki Watanabe[1,2] iD, Shuji Bandoh[2], Tomoya Ishii[2], Kiyoshi Negayama[3], Norimitsu Kadowaki[2] & Kyoko Yokota[1]

[1]Department of Infectious Disease, Kagawa University, Kagawa, Japan
[2]Department of Internal Medicine, Hematology, Rheumatology and Respiratory Medicine, Kagawa University, Kagawa, Japan
[3]Department of Clinical Laboratory, Faculty of Medicine, Kagawa University, Kagawa, Japan

Correspondence
Naoki Watanabe, Department of Infectious Disease, Department of Internal Medicine, Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, 1750-1, Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0793, Japan.
Tel: +81 87 891 2145;
Fax: +81 87 891 2147;
E-mail: naoki-w@med.kagawa-u.ac.jp

Key Clinical Message

Endocarditis caused by *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) is rare. Infected aneurysm is one of the most serious complications of infective endocarditis. However, no reports have described SDSE-related infected aneurysm. We herein report a successfully treated case of SDSE-associated infective endocarditis with an infected aneurysm.

Keywords

Infected aneurysm, infective endocarditis, *Streptococcus dysgalactiae* subsp. *equisimilis*, transcatheter arterial embolization.

Introduction

Streptococcus dysgalactiae subsp. *equisimilis* (SDSE) belongs to the group C and group G streptococci. SDSE is a common colonizer of the pharynx, skin, gastrointestinal tract, and female genital tract and a part of the normal human flora [1]. It can cause wound infection, erysipelas, cellulitis, life-threatening necrotizing fasciitis, streptococcal toxic shock syndrome, pneumonia, arthritis, osteomyelitis, meningitis, endocarditis, and sepsis, thus sharing the clinical picture with group A streptococcus (GAS) [2]. Group C and group G streptococci have not been treated as pathogenic bacteria; recently, however, invasive infections caused by SDSE have gradually become recognized.

Case Report

A 31-year-old man visited our hospital for evaluation of dyspnea and malaise. He had been ill for 1 week prior to admission. His dyspnea gradually started to worsen 2 days prior to admission. One day before admission, he could not get out of the bathtub because of severe dyspnea. The following day, he was found in the bathtub by his family after about 10 h had passed and was transported to our hospital.

The patient had been diagnosed with mild dilated cardiomyopathy without coronary artery stenosis and valvular insufficiency 2 years previously, and diuretics were prescribed by the clinic. However, he stopped taking the diuretics and returning for regular checkups. On arrival to our hospital, his height was 163 cm, weight was 115.4 kg, and vital signs were as follows: blood pressure, 82/53 mmHg; regular heart rate, 125 beats/min; oxygen saturation, 100% (oxygen mask, 6.0 L/min); respiratory rate, 42 breaths/min, and body temperature, 38.7°C. Physical examination revealed peeling skin on his buttocks and pressure marks associated with the long bath time extending from the back over the buttocks. Wheezing and moist rales were heard in the lungs.

Laboratory examination showed the presence of inflammation (white blood cell count, 13,100 cells/μL; C-reactive protein, 16.7 mg/dL; procalcitonin, 41.95 ng/mL), renal impairment (blood urea nitrogen, 53.0 mg/dL; creatinine, 1.55 mg/dL), thrombocytopenia (platelet count, $3.9 \times 10^4/\mu$L), heart failure (N-terminal pro-brain natriuretic peptide, 49,804 pg/mL), and coagulation system abnormalities (D-dimers, 20.6 μg/mL; P-fibrin degradation products, 44.5 μg/mL).

Transthoracic echocardiography (TTE) at admission showed diffuse hypokinesis of wall motion and an ejection fraction of 56% without vegetation. An enlarged heart shadow and a patchy shadow were observed in the right middle lung field on a chest X-ray. Whole-body computed tomography (CT) showed nodules in the right middle lobe of the right lung, suspicious for septic emboli, along with splenomegaly.

Two sets of blood cultures were obtained. Under a preliminary diagnosis of disseminated intravascular coagulation and systemic inflammatory response associated with infection, intravenous administration of meropenem was initiated at 1 g every 8 h. The next day, both sets of blood cultures exhibited growth of Gram-positive streptococci (BD BACTEC blood culture system, Becton, Dickinson and Company, Sparks, Maryland, USA). The antimicrobial treatment was then switched from meropenem to combination therapy comprising ampicillin at 2 g every 8 h and clindamycin at 600 mg every 8 h for toxic shock. The Gram-positive culture was identified as SDSE (VITEK 2 system; BioMerieux Japan, Tokyo, Japan) on the third day. TTE on the third day revealed a reduction in the ejection fraction to 46%, emergence of severe mitral valve regurgitation, and a 5-mm vegetation on the anterior leaflet mitral valve (Fig. 1). Using the modified Duke criteria, we diagnosed IE (one major criterion and three minor criteria) caused by SDSE. The ampicillin and clindamycin were continued.

A whole-body CT scan on hospital day 12 revealed a hemorrhagic infarction of the right frontal lobe (Fig. 2A), abscesses on the right frontal and occipital lobes, and an aneurysm of the mesenteric artery (Fig. 2B). A rapidly progressive new aneurysm emerged (as shown by comparison of the CT examinations on days 1 and 12) during the clinical course of SDSE bacteremia, and radiological examination was compatible with an infected aneurysm. Therefore, we diagnosed infectious aneurysms caused by SDSE. On day 18, gentamicin was added at 60 mg every 24 h with dose adjustment according to the patient's renal function. Because of the possibility of brain hemorrhage and concern about worsening infection due to embolization, we decided not to perform surgical and radiological intervention. On hospital day 41, the patient complained of sudden abdominal pain, and an abdominal CT scan revealed that the infected aneurysm of the splenic artery had ruptured and caused massive bleeding (Fig. 3A); there was a significant increase in the size of the aneurysm in the upper mesenteric artery (Fig. 3B), and new aneurysms were present in the right colic artery. Transcatheter arterial embolization (TAE) for the aneurysms of the splenic and upper mesenteric arteries was performed (Fig. 4). A follow-up abdominal CT performed on day 68 demonstrated organized aneurysms of the right colic artery without intestinal ischemia or any additional bleeding.

The antimicrobial agents were adjusted according to the patient's renal function, and the ampicillin was increased to 12 g per day. The intravenous clindamycin
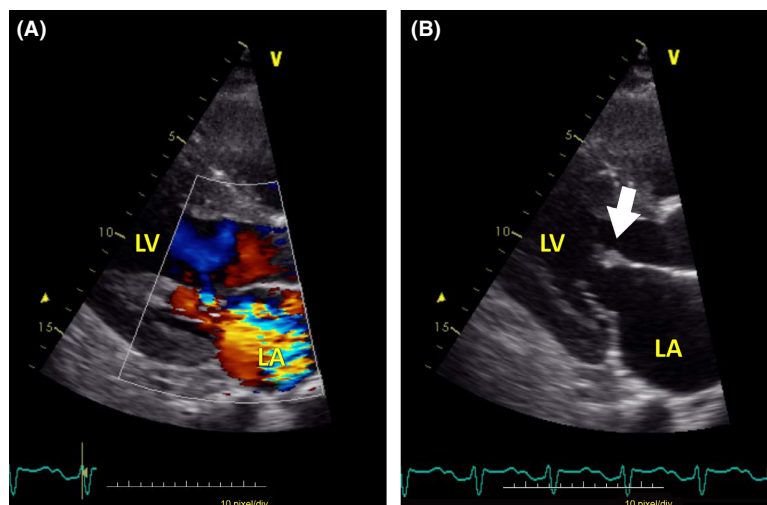

Figure 1. Transthoracic echocardiography with color Doppler examination (A) Color Doppler imaging shows turbulent retrograde flow in the left atrium. The regurgitation jet is evident. (B) The arrow shows a vegetation on the anterior leaflet mitral valve. LA: left atrium; LV: left ventricle.
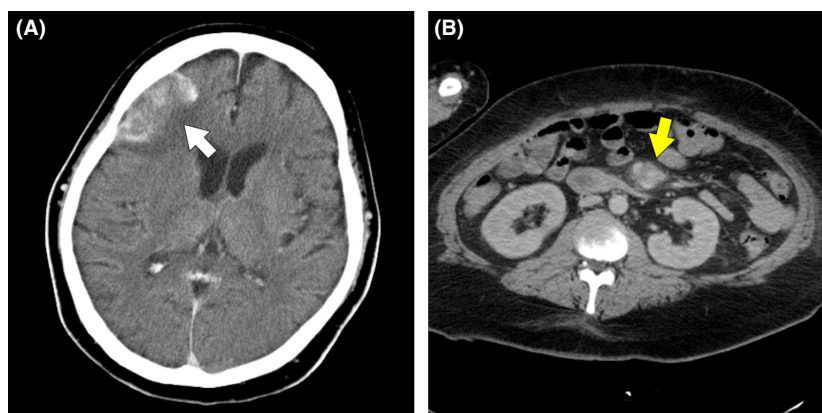
Figure 2. Computed tomography (CT) on hospital day 12 (A) Cranial CT shows infarction with bleeding in the right frontal lobe (white arrow). (B) Abdominal CT reveals the appearance of an aneurysm in the mesenteric artery (yellow arrow).
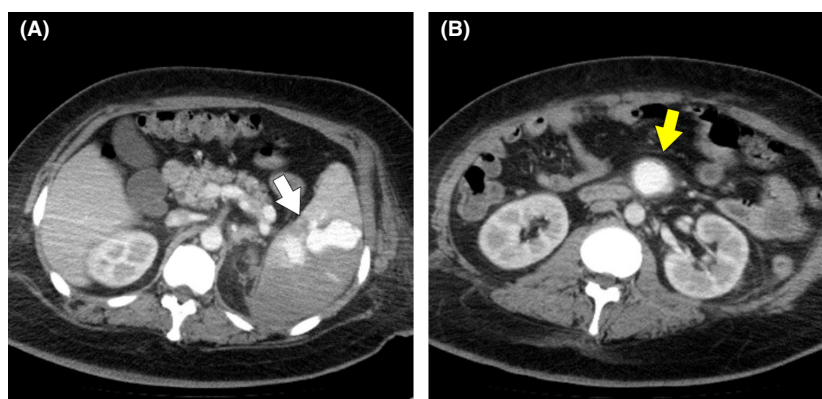

Figure 3. Contrast-enhanced computed tomography on hospital day 41 (A) Splenic bleeding is observed. The heterogeneity of splenic tissue represents differences in flow dynamics (white arrow). (B) The aneurysm of the mesenteric artery is expanded, and the density of the surrounding adipose tissue is increased (yellow arrow).

and gentamicin were continued for 10 weeks, and the ampicillin was continued for 11 weeks. Several blood cultures were performed throughout the treatment period, but none were positive. A follow-up TTE on hospital day 70 demonstrated organization of the vegetation. The patient was discharged in good clinical condition after 3 months of treatment.

Discussion

Streptococcus dysgalactiae subsp. *equisimilis* is a rare cause of IE and is reported in approximately 1.1–3.3% of all patients with IE [3–7]. Infected aneurysms are one of the most serious complications of IE.

An infected aneurysm is an aneurysm related to bacterial infection of the arterial wall. It is very rare compared with a noninfected aneurysm, but it is a very serious

medical condition with a high probability of rupture. The incidence of infected aneurysm is approximately 0.9–1.3% among all cases of aortic aneurysm [8, 9]. *Staphylococcus aureus* and *Salmonella* species are the most common pathogens involved [9].

Both surgical and conservative treatment approaches are available for the management of IE. The indications for and optimal timing of surgery for treatment of left-sided native-valve IE are controversial. The European Society of Cardiology guidelines on the prevention, diagnosis, and treatment of IE [10] and the American Heart Association guidelines of IE [11] have shown that surgical intervention should be considered in the following cases: presence of heart failure, uncontrolled infection, and an increased the risk of embolism. Although CT revealed multiple infarctions in the present case, we chose conservative treatment because of the risk of cerebral
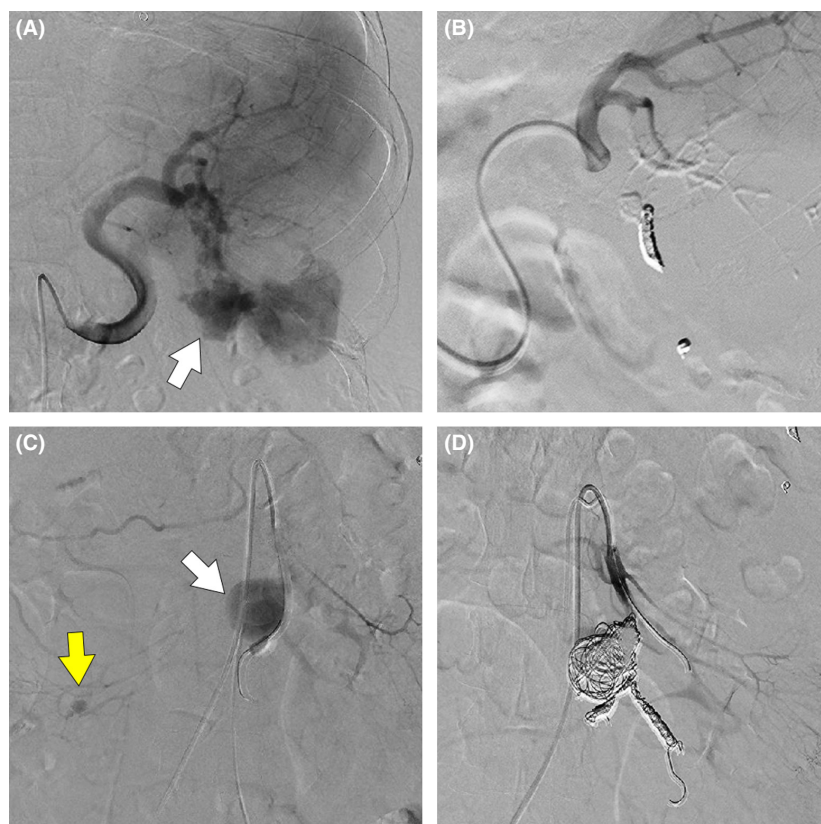
Figure 4. Angiogram and transcatheter arterial embolization (A) Splenic artery angiography shows a pseudoaneurysm (arrow). (B) Angiogram of splenic artery aneurysm after coil embolization. (C) Mesenteric artery angiography shows a giant aneurysm of the inlet portion (white arrow) and a small aneurysm in the right colic artery (yellow arrow). (D) Angiogram of the mesenteric artery aneurysm after coil embolization.

hemorrhage due to surgical intervention. Kang et al. [12] reported that surgery within 48 h in patients with IE significantly reduced in-hospital deaths or embolic events at 6 weeks by effectively decreasing the risk of systemic embolism. We did not exclude the possibility of preventing emerging embolism and aneurysm with early surgical intervention.

Laparotomy or TAE is an option for the treatment of infected aneurysms of ruptured abdominal visceral arteries. TAE can be performed quickly and is less invasive than laparotomy; therefore, it is an effective procedure for patients with significant comorbidities [13]. Sachdev et al. [14] reported that TAE tends to be preferred for patients with multiple comorbidities or in emergency cases of rupture. Generally, cerebral infected aneurysms can disappear or decrease in size after several weeks of antibiotic therapy [15]. However, aneurysms in abdominal visceral arteries have a high prevalence of rupture. Because of the difficulty of predicting a rupture, early intervention should be considered regardless of the aneurysm size or patient's symptoms [14, 16]. In the present case, we were able to control infected aneurysms of the splenic and upper mesenteric arteries with TAE.

Medical treatment for an infected aneurysm requires the administration of appropriate antibacterial agents. In general, this condition requires treatment with at least 6 weeks of parenteral and/or oral antimicrobial therapy [17, 18]. In addition, in patients with life-threatening infections (such as meningitis and endocarditis) due to group G streptococcus, aminoglycosides can be considered in addition to penicillin because an aminoglycoside–penicillin combination shows in vitro bactericidal synergy [19]. Furthermore, the usefulness of using a combination of clindamycin and a beta-lactam antibiotic has been reported in severe GAS infections. A similar report about group G streptococcus can also be found in the literature [20]. In the present case, we used a combination therapy of ampicillin, gentamicin, and clindamycin.

Invasive SDSE infections, most of which are characterized by bacteremia, are now increasingly observed worldwide, as are those caused by GAS and group B streptococcus. There are currently few reports of invasive SDSE infection such as sepsis with unknown focus, cellulitis, septic arthritis, pneumonia, necrotizing fasciitis, meningitis, infectious endocarditis, streptococcal toxic shock syndrome, abscesses at sites other than the skin,

and osteomyelitis. These symptoms are extremely compatible with fulminant streptococcal infection.

Additionally, GAS and SDSE share virulence properties [21]. Furthermore, there are several reports of infected aneurysms caused by GAS or group B streptococcus [22, 23]. Together, these findings suggest that SDSE may cause infected aneurysms. With respect to virulency, this isolate was further investigated by sequencing the emm amplicon, and the emm genotype stG245 was identified. Following stG6792 and stG485, respectively, stG245 is the third most common emm genotype among Japanese isolates of group G streptococcus. The mortality rates reportedly do not differ among the emm genotypes [24].

Most (90–96%) patients with SDSE bacteremia have an underlying disease such as diabetes mellitus, cardiovascular disease, malignancy, immunosuppression, and/or breakdown of the skin [2]. Our patient had mild dilated cardiomyopathy and severe obesity. Because of the severity of the patient's disease, we suspect that severe obesity increases the risk of infection and induces severe reactions. Calle et al. [25] reported an increased risk of death associated with severe obesity as well as a gradient of increasing risk associated with moderate obesity. Although one report stated that obesity is associated with a poor prognosis in patients with skin infections, the association between obesity and bacteremia has not been well evaluated [26, 27]. Our patient showed peeling of the skin on his buttocks because of a prolonged rest period in the bathtub. We speculate that the portal of entry for SDSE was the skin lesions on the buttocks.

The number of infections caused by SDSE has recently been increasing. We treated a rare case of SDSE infection with IE related to an infected aneurysm. This case was successfully treated with radiological intervention and prolonged antibiotics. To our knowledge, there are no other reports of infected aneurysms caused by SDSE. Obesity has not been reported as a risk factor for SDSE. Based on the present case, obesity might be a possible risk factor for severe infection. Evaluation of more cases is necessary to clarify the pathological mechanism of and risk factors for this disease.

Consent

Written informed consent was obtained from the patient regarding publication of this case report and the accompanying images.

Acknowledgments

Authorship

NW: made the clinical diagnosis, managed the patient, and wrote and edited the manuscript. SB, TI, and NK: helped to draft the manuscript and reviewed the literature. KN: coordinated and worked with the reference laboratory to establish the microbiological diagnosis. KY: also made the clinical diagnosis, managed the patient, and supervised manuscript drafting. All authors have read and approved the final manuscript.

Conflict of Interest

None declared.

References

1. Sinner, S. W., and A. R. Tunkel. 2009. Viridans streptococci, Groups C and G streptococci, and Gemella species. Pp. 2667–2680 in G. Mandell, J. Bennett and R. Dolin, eds. Principles and practice of infectious diseases, 7th ed. Churchill Livingstone, Philadelphia, PA.

2. Rantala, S. 2014. *Streptococcus dysgalactiae* subsp. equisimilis bacteremia: an emerging infection. Eur. J. Clin. Microbiol. Infect. Dis. 33:1303–1310.

3. Cohen-Poradosu, R., J. Jaffe, D. Lavi, S. Grisariu-Greenzaid, R. Nir-Paz, L. Valinsky, et al. 2004. Group G streptococcal bacteremia in Jerusalem. Emerg. Infect. Dis. 10:1455–1460.

4. Liao, C. H., L. C. Liu, Y. T. Huang, L. J. Teng, and P. R. Hsueh. 2008. Bacteremia caused by group G Streptococci, Taiwan. Emerg. Infect. Dis. 14:837–840.

5. Broyles, L. N., C. Van Beneden, B. Beall, R. Facklam, P. L. Shewmaker, P. Malpiedi, et al. 2009. Population-based study of invasive disease due to beta-hemolytic streptococci of groups other than A and B. Clin. Infect. Dis. 48:706–712.

6. Rantala, S., J. Vuopio-Varkila, R. Vuento, H. Huhtala, and J. Syrjanen. 2009. Clinical presentations and epidemiology of beta-haemolytic streptococcal bacteraemia: a population-based study. Clin. Microbiol. Infect. 15:286–288.

7. Takahashi, T., K. Sunaoshi, K. Sunakawa, S. Fujishima, H. Watanabe, K. Ubukata, et al. 2010. Clinical aspects of invasive infections with *Streptococcus dysgalactiae* ssp. equisimilis in Japan: differences with respect to *Streptococcus pyogenes* and *Streptococcus agalactiae* infections. Clin. Microbiol. Infect. 16:1097–1103.

8. Chan, F. Y., E. S. Crawford, J. S. Coselli, H. J. Safi, and T. W. Jr Williams. 1989. In situ prosthetic graft replacement for mycotic aneurysm of the aorta. Ann. Thorac. Surg. 47:193–203.

9. Muller, B. T., O. R. Wegener, K. Grabitz, M. Pillny, L. Thomas, and W. Sandmann. 2001. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries:

experience with anatomic and extra-anatomic repair in 33 cases. J. Vasc. Surg. 33:106–113.

10. Habib, G., B. Hoen, P. Tornos, F. Thuny, B. Prendergast, I. Vilacosta, et al. 2009. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur. Heart J. 30:2369–2413.

11. Baddour, L. M., W. R. Wilson, A. S. Bayer, V. G. Jr Fowler, A. F. Bolger, M. E. Levison, et al. 2005. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. Circulation 111:e394–e434.

12. Kang, D. H., Y. J. Kim, S. H. Kim, B. J. Sun, D. H. Kim, S. C. Yun, et al. 2012. Early surgery versus conventional treatment for infective endocarditis. N. Engl. J. Med. 366:2466–2473.

13. Tulsyan, N., V. S. Kashyap, R. K. Greenberg, T. P. Sarac, D. G. Clair, G. Pierce, et al. 2007. The endovascular management of visceral artery aneurysms and pseudoaneurysms. J. Vasc. Surg. 45:276–283; discussion 83.

14. Sachdev, U., D. T. Baril, S. H. Ellozy, R. A. Lookstein, D. Silverberg, T. S. Jacobs, et al. 2006. Management of aneurysms involving branches of the celiac and superior mesenteric arteries: a comparison of surgical and endovascular therapy. J. Vasc. Surg. 44:718–724.

15. Corr, P., M. Wright, and L. C. Handler. 1995. Endocarditis-related cerebral aneurysms: radiologic changes with treatment. AJNR Am. J. Neuroradiol. 16:745–748.

16. Stone, W. M., M. Abbas, K. J. Cherry, R. J. Fowl, and P. Gloviczki. 2002. Superior mesenteric artery aneurysms: is presence an indication for intervention? J. Vasc. Surg. 36:234–237.

17. Ranbarger, K. R., J. M. Fichelle, G. M. Tabet, P. M. Cormier, J. C. Farkas, C. Laurian, et al. 1993. Infected infrarenal aortic aneurysms: when is in situ reconstruction safe? J. Vasc. Surg. 17:635–645.

18. Heyd, J., R. Meallem, Y. Schlesinger, B. Rudensky, I. Hadas-Halpern, A. M. Yinnon, et al. 2003. Clinical characteristics of patients with psoas abscess due to non-typhi Salmonella. Eur. J. Clin. Microbiol. Infect. Dis. 22:770–773.

19. Lam, K., and A. S. Bayer. 1984. In vitro bactericidal synergy of gentamicin combined with penicillin G, vancomycin, or cefotaxime against group G streptococci. Antimicrob. Agents Chemother. 26:260–262.

20. Pillai, A., S. Thomas, and C. Williams. 2005. Clindamycin in the treatment of group G beta-haemolytic streptococcal infections. J. Infect. 51:e207–e211.

21. Brandt, C. M., and B. Spellerberg. 2009. Human infections due to *Streptococcus dysgalactiae* subspecies equisimilis. Clin. Infect. Dis. 49:766–772.

22. Thawait, S. K., A. Akay, R. H. Jhirad, and N. El-Daher. 2012. Group B streptococcus mycotic aneurysm of the abdominal aorta: report of a case and review of the literature. Yale J. Biol. Med. 85:97–104.

23. Gardiner, B. J., J. Wong, M. Yii, T. Buckenham, and T. M. Korman. 2013. Streptococcus pyogenes aortic aneurysm infection: forgotten but not gone. Infect. Dis. Rep. 5:e11.

24. Wajima, T., M. Morozumi, S. Hanada, K. Sunaoshi, N. Chiba, S. Iwata, et al. 2016. Molecular characterization of invasive *Streptococcus dysgalactiae* subsp. equisimilis, Japan. Emerg. Infect. Dis. 22:247–254.

25. Calle, E. E., M. J. Thun, J. M. Petrelli, C. Rodriguez, and C. W. Heath Jr. 1999. Body-mass index and mortality in a prospective cohort of U.S. adults. N. Engl. J. Med. 341:1097–1105.

26. Carratala, J., B. Roson, N. Fernandez-Sabe, E. Shaw, O. del Rio, A. Rivera, et al. 2003. Factors associated with complications and mortality in adult patients hospitalized for infectious cellulitis. Eur. J. Clin. Microbiol. Infect. Dis. 22:151–157.

27. Huttunen, R., and J. Syrjanen. 2013. Obesity and the risk and outcome of infection. Int. J. Obes. (Lond). 37:333–340.