

Case Report of *Staphylococcus lugdunensis* Native Valve Endocarditis and Review of the Literature

H H Teong,^{*MD (Canada), MRCP (UK)}, Y S Leo,^{**FAMS, M Med (Int Med) MRCP (UK)}, S Y Wong,^{***FAMS, MBBS, M Med (Int Med)},
L H Sng,^{+MBBS, FRCPA}, Z P Ding,^{++FAMS, MBBS, M Med (Int Med)}

Abstract

Introduction: Coagulase-negative staphylococci, commonly *Staphylococcus epidermidis*, cause 5% of native valve endocarditis. We describe a case due to *Staphylococcus lugdunensis*, a coagulase-negative staphylococcus identified in 1988, as a first report in Southeast Asia. It was previously misidentified as *S. aureus* because it is sometimes slide coagulase positive, but always tube coagulase negative, resulting in its delayed recognition as a pathogen. We also reviewed 36 other cases reported in the English literature from 1988 to 1999. **Clinical Picture:** Our patient was admitted 3 times over 4 months for unresolved weight loss and fever before the coagulase-negative staphylococcus bacteraemia was eventually considered significant. **Treatment and Outcome:** He was treated with 4 weeks of high-dose intravenous penicillin and 2 weeks of gentamicin and did not require urgent valve replacement. **Conclusion:** A positive blood culture of coagulase-negative staphylococcus is not always a contaminant. *S. lugdunensis* can cause aggressive native valve endocarditis resulting in high mortality, especially without surgical intervention.

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Key words: Bacteraemia, Coagulase-negative staphylococcus, Endocarditis, *Staphylococcus lugdunensis*

Introduction

Coagulase-negative staphylococci cause 5% of native valve endocarditis.^{1,2} Of the 30 species identified currently, *Staphylococcus epidermidis* is a well-recognised cause of native valve endocarditis; however, it more commonly causes prosthetic valve endocarditis. *Staphylococcus lugdunensis* was first described by Freney et al in 1988.³ Most infections due to *S. lugdunensis* involve the skin and soft tissues⁴ although it has also been reported to cause other infections including brain abscess,⁵ bacteraemia,⁵ vascular prosthetic infections,⁵ chronic osteomyelitis,⁵ peritonitis^{5,6} and toxic shock syndrome.⁷ Cases of native valve endocarditis due to *S. lugdunensis* were reported in the late 1980s. The largest series of 11 cases was published in 1993.⁸ We describe the first report of a case of native valve endocarditis due to *S. lugdunensis* in Southeast Asia

and review the 36 other cases reported so far in the English literature from 1988 to 1999.

Case Report

Our patient was a 22-year-old American male Caucasian technician who was working on a 3-month project in Singapore from September to December 1997. He was previously in good health except that he had had an incidental heart murmur of uncertain cause and significance since childhood.

He first became unwell with diarrhoea in August 1997 when he was still in the United States, from which he recovered uneventfully. In September 1997, shortly after his arrival in Singapore, he was admitted to a hospital with a low-grade fever, dyspnoea, right pleuritic chest pain and a cough productive of purulent, blood-stained sputum. The

* Registrar

Department of Internal Medicine

+ Associate Consultant

Department of Pathology

Singapore General Hospital

** Clinical Director

Communicable Disease Centre

Tan Tock Seng Hospital

*** Consultant Infectious Disease Physician

Gleneagles Medical Centre

++ Senior Consultant Cardiologist

National Heart Centre

Address for Reprints: Dr Hui-Hwang Teong, Department of Internal Medicine, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

E-mail: zhfteong@mbox3.singnet.com.sg

physical examination was unremarkable except for a low-grade fever and a soft systolic ejection murmur at the upper right sternal edge. Investigations showed a normochromic normocytic anaemia of 11 g/dL and a mild leukocytosis of $12.9 \times 10^9/L$. The chest radiograph was unremarkable. A diagnosis of acute bronchitis was made and he was treated with amoxicillin with good response. The one set of blood cultures taken grew coagulase-negative staphylococcus which was interpreted as a contaminant and he was discharged after 3 days of hospitalisation.

On his outpatient follow-up visit, he reported a persistent cough productive of greenish sputum for which he was given a course of clarithromycin. He denied a history of smoking. However, his symptoms worsened and he developed haemoptysis and a significant weight loss of 3 kg over a month. He was re-hospitalised in November 1997. During this second admission, an end-diastolic murmur was detected at the aortic area, but there were no peripheral stigmata of endocarditis such as splinter haemorrhages, Janeway lesions or Osler's nodes. Laboratory investigations showed a persistent normochromic and normocytic anaemia of 10.8 g/dL. The anaemia workup suggested anaemia of chronic illness as both serum iron and total iron binding capacity levels were both high. Haemoglobin electrophoresis was negative and occult blood was not detected in his stool samples. The erythrocyte sedimentation rate was 74 mm/h; the rheumatoid factor and one set of blood cultures were negative. Transthoracic and trans-oesophageal echocardiography showed severe aortic regurgitation with aortic valve prolapse and a small rounded defect in the interatrial septum suggestive of either a patent foramen ovale or a perforation; no vegetations were detected. Chest radiograph and computed tomography of the thorax showed consolidative changes in the left lateral basal segment, as well as patchy opacities in the right upper and lateral basal segments. Sputum cultures and serology tests for mycoplasma and legionella were negative. Bronchoscopy revealed a polypoidal stricture at the left lower lobe. The bronchoalveolar lavage culture was negative and the histology report of a bronchial biopsy revealed acute-on-chronic bronchitis. He was treated for pneumonia with intravenous cefuroxime and erythromycin, followed by oral cefuroxime. He was discharged after documented resolution of the left lower zone consolidation on the chest radiograph and he was given an appointment with the cardiologist to monitor his valvular condition.

He was re-admitted in December 1997 for unresolved weight loss and recurrence of fever. During this admission, he had both a grade 4/6 systolic ejection and end-diastolic murmurs at the aortic area. The jugular venous pulse was not elevated. Examination of the lungs and the abdomen was unremarkable. His total white count was $5.1 \times 10^9/L$,

haemoglobin was 11.4 g/dL and platelet count was $84 \times 10^9/L$. All 6 sets of blood cultures grew a coagulase-negative staphylococcus, which was later identified as *S. lugdunensis*. The chest radiograph showed cardiomegaly with pulmonary congestion and a small left pleural effusion. A repeat transthoracic echocardiogram showed an old vegetation on the right coronary cusp of the aortic valve, with severe aortic regurgitation (Fig. 1). He was treated intravenously with 24 million units/day of crystalline benzyl penicillin and 80 mg of gentamicin (for synergism) every 8 hours for the first 2 weeks, followed by crystalline benzyl penicillin for the remaining 2 weeks. His fever subsided 3 days after the commencement of the antibiotics. The trough gentamicin level of $1.4 \mu\text{g/mL}$ was within the nontoxic levels of 0 to $2 \mu\text{g/mL}$ while the peak gentamicin level of $4.1 \mu\text{g/mL}$ was within the synergistic peak levels of 3 to $5 \mu\text{g/mL}$.⁹ As the patient was haemodynamically stable, he did not require urgent aortic valve repair. During the entire course of the illness, there was only one isolated embolic phenomenon observed: a small vasculitic lesion along the lateral aspect of the right foot, which resolved spontaneously. One set of blood cultures performed about 48 hours after cessation of the antibiotic treatment was negative. The thrombocytopenia due to splenomegaly (seen on the computed tomography of the abdomen) resolved partially. On discharge, the patient was well and his cardiovascular state was stable. Further follow-up of the patient was not possible as he had decided to return to the United States for further treatment.

The organism isolated from this patient formed yellow opaque colonies that were weakly β -haemolytic on sheep blood agar. The Gram smear showed Gram positive cocci in clusters. The catalase, slide coagulation tests and latex agglutination using FA Staph (Carr-Scarborough

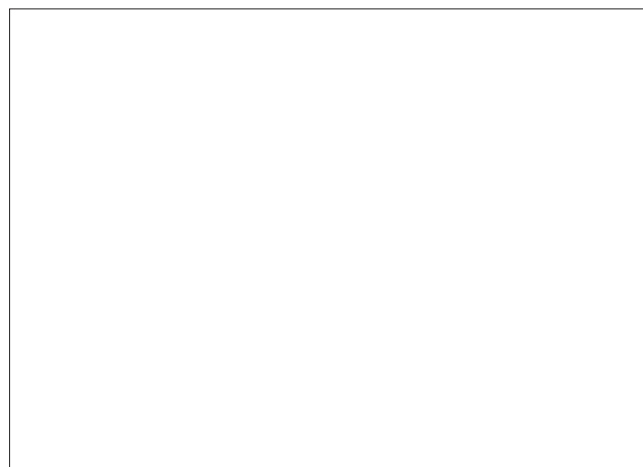


Fig. 1. Parasternal long axis view of the heart showing an old vegetation on the ventricular aspect of the aortic valve (right coronary cusp). (LA: left atrium; LV: left ventricle; RV: right ventricle; white arrow: old vegetation)

Microbiologicals, GA) were positive; the tube coagulase test was negative. Further screening tests of pyrrolidonyl aminopeptidase (PYR) (Carr-Scarborough Microbiologicals, GA) and ornithine decarboxylase were positive. A final identification of *Staphylococcus lugdunensis* was confirmed using API 20 Staph (BBL, Cockeysville, MD) (profile number: 6716150). Susceptibility testing was performed using the disk diffusion method according to the National Committee of Clinical Laboratory Standards (NCCLS) performance standards.¹⁰ The isolate was sensitive to penicillin, gentamicin, chloramphenicol, clindamycin, fusidic acid and vancomycin. The β -lactamase test using a nitrocefin disk (BBL, Cockeysville, MD) was negative.

Discussion and Literature Review

Staphylococcus lugdunensis was described by Freney in 1988,³ being named after the French city Lyon (Latin adjective of Lugdunum) where the organism was first recognised. Besides residing on the skin, it has also been reported to be present in respiratory secretions and urogenital specimens.⁴ Vandenesch et al⁸ suggested based on a limited study that in contrast to *S. epidermidis*, *S. lugdunensis* preferentially colonises the perineum rather than the entire skin surface. Herchline et al⁴ reported in a retrospective survey that excluding *S. aureus* and *S. epidermidis*, *S. lugdunensis* constituted only 10.1% of all clinical staphylococcal isolates. In 60% of these cases, the organism was isolated as part of a mixed flora. However, it was considered as a culture contaminant or coloniser in only 15.4% of clinically reviewed specimens. Therefore, when isolated, its potential as the possible causative agent of infection should be seriously considered.

Historically, misidentification of *S. lugdunensis* as *S. aureus* probably resulted in its delayed recognition as a pathogen. It has been shown that 2 out of 3 *S. lugdunensis* isolates were previously first identified as *S. aureus* (Groupie Francis d' Etude sur l'Endocardite Infectieuse, 1991, unpublished data). Apart from their similar morphology, *S. lugdunensis* may produce clumping factor (bound coagulase) like *S. aureus*; this results in positive slide coagulase and latex agglutination tests. Commercial identification systems are convenient and give rapid results; however, these are expensive and some may misidentify *S. lugdunensis* as other *Staphylococcal* species.⁸ A negative tube coagulase test (which detects free coagulase) and positive PYR, ornithine decarboxylase and mannitol fermentation tests³ will reliably distinguish *S. lugdunensis* from other clumping factor producing staphylococcus species. Commercially available identification systems such as the API ID 32 Staph system can also be used. Otherwise, a simple and convenient scheme described by Hebert can be adopted, characterising *S. lugdunensis* as pyrrolidonyl-arylamidase-positive, novobiocin-susceptible,

polymyxin-resistant and bacitracin-resistant.¹¹

In the largest series of 11 cases, Vandenesch et al⁸ reported that the majority of *S. lugdunensis* strains studied were susceptible to most antimicrobials as was the isolate in this case. However, β -lactamase production and tetracycline resistance were noted in 2 strains. Other authors have also reported β -lactamase production and reduced susceptibility to other antimicrobials.^{5,12} Of the reviewed cases that survived, the patients were reported to receive about 4 to 6 weeks of antibiotics such as penicillin, cloxacillin, vancomycin and cefazolin and 1 to 2 weeks of gentamicin. The British Society for Antimicrobial Chemotherapy, however, recommended in 1998¹³ that native valve endocarditis due to coagulase-negative *Staphylococcus* including *S. lugdunensis* should be treated with a 4-week course of penicillin, flucloxacillin or vancomycin depending on the sensitivity testing and 1 week of gentamicin on full therapeutic levels. This is similar to the recommended treatment for endocarditis due to *S. aureus* as the former infection could sometimes be just as severe as the latter.

Thirty-six cases of *S. lugdunensis* endocarditis have been reported^{8,14-32} in the English literature (Table I). The mean age of the patients was 54 years with an age range of 22 to 81 years. The proportion of males was slightly higher at 59%. None of these cases admitted intravenous drug abuse. Both native valve, normal and diseased, and prosthetic valve endocarditis were described. Native valves were more commonly involved (84%); this is in contrast to

TABLE I: SUMMARY OF *S. LUGDUNENSIS* ENDOCARDITIS FROM 1988 TO 1999 REPORTED IN THE ENGLISH LITERATURE

Valve type	Surgery ⁺	Outcome	
		Recovery (n = 20)	Death (n = 17)
Mitral (n = 14) ^{8,14,17,18,20,21,24,25,29,31}	Yes	6	1
	No	1	6
Aortic (n = 9) ^{8,15,22,23,30,current case}	Yes	5	1
	No	1	2
Tricuspid (n = 3) ^{27,28}	Yes	3	0
	No	0	0
Pulmonary (n = 1) ³²	Yes	0	0
	No	1	0
Mixed (n = 4) ^{8,14,23}	Yes	2	1
	No	0	1
Prosthetic (n = 6) ^{8,14,16,19}	Yes	1	1
	No	0	4
All (n = 37)	Yes	17	4
	No	3	13

+ includes valve replacement, valvuloplasty and removal of infected pacemakers

S. epidermidis which infects prosthetic valves more often than native valves.³³ The 37 cases including our patient involved mitral (38%), aortic (24%), tricuspid (8%), pulmonary (3%), mixed (11%) and prosthetic (16%) valves. The sources of infection suspected included a dental abscess,²² cutaneous infections,^{8,14,23} infected vascular access,^{20,21,32} infected pacemakers,^{8,27,28} and recent vasectomies.^{23,31} However, the portals of entry for many cases were unknown (46%).

In 4 cases of *S. lugdunensis* endocarditis, vasectomies had been performed 1 to 3 months prior to the diagnosis of endocarditis.^{23,31} This association correlated with it being a common perineal organism. In our patient, it is speculative to suggest that the earlier episode of gastroenteritis could have promoted the portal of entry for the *S. lugdunensis* through breaks in the perianal area. Other alternative portals of entry may have been the many cuts that the patient had sustained on his hands from his technical work, or even during the bronchitis episode since the organism has also been reported in respiratory secretions.

Most of the available clinical data suggest that *S. lugdunensis* is an aggressive pathogen. Most patients had a short duration of symptoms, usually for less than 3 weeks. There was often gross valvular destruction, with abscess formation, requiring valve replacement. In our review of the 37 cases, 57% required surgical intervention including valve replacement, valvuloplasty or removal of infected pacemakers. There was a high mortality rate compared to the reported mortality of 6%³⁴ in endocarditis due to viridans streptococcus. Vandenesch et al⁸ reported a mortality rate of 70% in their review of 20 cases. We analysed the 37 cases and found an overall mortality rate of 46%. These figures are closer to that reported for *S. aureus* native valve endocarditis (39% to 53%).² Of the fatal cases, 81% were seen in patients who did not receive any surgical treatment compared to 19% who received surgical treatment. Deaths were more common in the older age group, who tended not to undergo surgery. It is interesting to note that most deaths occurred in the earlier reports. Perhaps increased recognition of this organism and its virulence has led to earlier and more aggressive management including surgery and hence better outcome.

In comparison to other cases described, the clinical course of our patient appeared to be less aggressive in nature as he responded fairly quickly to medical treatment. He had symptoms for at least 4 months before a definitive diagnosis could be reached. The multiple courses of antibiotics he had received prior to the diagnosis of endocarditis might have attenuated the severity of his illness, but at the same time delayed the diagnosis and proper management.

This case illustrates the importance of serial blood cultures

and careful interpretation of blood culture results. It is a well-recognised phenomenon that a busy House Officer either sends one set of blood cultures before starting antibiotics or may inoculate multiple bottles from a single venipuncture due to time constraint. Either blood taking procedures described above can only be counted as 1 specimen and hence produce enormous difficulties in the proper interpretation of a growth of a coagulase-negative staphylococcus. Similarly, as in several other case reports in the literature, the initial positive blood culture with a coagulase-negative staphylococcus was regarded as a contaminant and its clinical significance was overlooked, causing a delay in our patient's diagnosis. Thus, whenever a coagulase-negative staphylococcus is cultured from the blood, one should exclude serious infections, e.g., endocarditis, line infection, vertebral osteomyelitis and so forth, before disregarding the result.

In conclusion, we present the first case report of *Staphylococcus lugdunensis* native valve endocarditis in Southeast Asia. This case underscores the importance of serial blood cultures in the presence of a patient with an underlying predisposing cardiac lesion and careful interpretation of coagulase-negative staphylococci in the blood. This is facilitated by the provision of relevant details with the request for blood cultures, e.g. "endocarditis", or "known valvular disease of heart" as in this present patient.

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