

## Progressive *Staphylococcus lugdunensis* endocarditis despite antibiotic treatment

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### Progrediente infektiöse Endokarditis durch *Staphylococcus lugdunensis* trotz antibiotischer Therapie

**Zusammenfassung.** Bei einem 68-jährigen Mann mit Fieber, Schüttelfrost und einem diastolischen Herzgeräusch wurde eine durch *Staphylococcus lugdunensis* verursachte Aortenklappenendokarditis diagnostiziert. Unter antibiotischer Therapie verbesserte sich das klinische Bild zunächst. Am siebten stationären Behandlungstag wurden große Abszesse mit transösophagealer Echokardiographie nachgewiesen, die sich von der Aortenwurzel bis zur freien Wand des linken Ventrikels ausdehnten. Der notfallmäßige operative Eingriff verlief erfolgreich und eine gerüstfreie Bioprothese wurde implantiert. *Staphylococcus lugdunensis* verursacht infektiöse Endokarditiden mit aggressivem klinischen Verlauf, die trotz adäquater antibiotischer Therapie zur Destruktion von Herzklappen, Abszedierung und embolischen Komplikationen neigen. Die hohe Letalität bei Patienten unter alleiniger antibiotischer Therapie kann durch frühzeitigen prothetischen Klappenersatz gesenkt werden

**Schlüsselwörter:** Infektiöse Endokarditis, Coagulase-negative Staphylokokken, *Staphylococcus lugdunensis*, intrakardialer Abszess, transösophageale Echokardiographie.

**Summary.** A 68-year old man with fever chills and a diastolic murmur was diagnosed with aortic-valve endocarditis caused by coagulase-negative *Staphylococcus lugdunensis*. The clinical condition initially improved with antibiotic therapy. On day seven, transoesophageal echocardiography revealed large abscesses extending from the aortic root to the left ventricular wall. Emergency cardiac surgery was performed successfully and a stentless bioprosthetic valve was inserted. *S. lugdunensis* endocarditis is known for its aggressive clinical course with valve destruction, abscess formation and embolic complications despite appropriate antibiotics. Antibiotic treatment alone is associated with a high mortality rate which can be reduced by early valve replacement.

**Key words:** Infective endocarditis, coagulase-negative staphylococci, *Staphylococcus lugdunensis*, intracardiac abscess, transoesophageal echocardiography.

### Introduction

Thirty-two species with 28 subspecies of coagulase-negative staphylococci (CNS) can be currently differentiated. Most are harmless commensals of the human skin flora, but some are facultatively pathogenic causing a variety of clinical pictures. CNS play a major role in nosocomial infections, foreign-body infection, prosthetic-valve endocarditis [1–3] and are the most common contaminants of blood cultures [4].

The coagulase-negative *Staphylococcus (S.) lugdunensis* has pathogenetic properties similar to *S. aureus*. Infections caused by *S. lugdunensis* are mainly community acquired and usually take a fulminant clinical course. Toxic-shock syndrome, septic shock, peritonitis, brain abscess, infective endocarditis (IE), osteomyelitis, and infections of vascular prostheses have been reported [5–8].

### Case report

A 68-year-old male was admitted to the hospital with a 4-week history of sporadic fever attacks and chills. The temperature was 39.5 °C, pulse 88 per minute, and blood pressure 130/70 mm Hg at admission. The physical examination revealed a diastolic murmur (grade 2) of high frequency in the fourth intercostal space along the left sternal border. There was slight pretibial oedema. Pulmonary examination and chest radiograph were normal. From the case history we learned that arterial hypertension and moderate aortic-valve regurgitation had been known for many years. Five weeks before admission he had an out-patient hand surgery without antibiotic prophylaxis.

Abnormal laboratory tests included a white-cell count of  $15.3 \times 10^9$ /liter (normal  $< 9 \times 10^9$ /liter) with 73% polymorphonuclear neutrophils and haemoglobin 8.4 mmol/liter (normal 8.7–10 mmol/liter). The erythrocyte sedimentation rate was 42 mm/h, C-reactive protein 152 mg/L (normal  $< 5$  mg/L), aspartate aminotransferase 80 U/liter (normal 14–59 U/liter), ferritin 929 µg/liter (normal 20–306 µg/liter), blood glucose 8.4 mmol/liter (normal 3.3–5.5 mmol/liter) and troponin T was qualitatively positive.

The initial ECG revealed sinus rhythm at 96 beats per minute with evidence of left ventricular hypertrophy with repolarisation abnormalities. Transthoracic echocardiography showed slight calcification of the aortic-valve leaflets and Doppler-evidence of moderate aortic regurgitation. The subsequent transoesophageal echocardiography (TEE) revealed a tiny separation between the layers of the posterior aortic wall, measuring about 1.7 cm in length and resembling an early aortic-root abscess.

After multiple blood specimens were taken for culture, intravenous vancomycin 1 g i.v. b.i.d. was initiated. On the next day rifampin 300 mg orally t.i.d. and cefuroxime 1.5 g t.i.d. were added. On the third day three blood cultures yielded growth of CNS. On day five all isolates were identified as *S. lugdunensis* by routine microbiological procedures and were susceptible to all standard antibiotics tested in vitro including vancomycin, rifampin, penicillin and oxacillin/methicillin.

Fever and chills resolved and the clinical condition seemed to improve with antibiotics. However, on day four the patient complained of recurring chest discomfort, refractory to nitroglycerine. Troponin T was still positive but the other serum markers typical for myocardial damage (e.g. creatine kinase and its isoenzyme MB) remained within the normal limits.

Daily ECG tracings did not show any changes until first-degree atrioventricular block developed on day seven. C-reactive protein remained high at 153 mg/L and the nitroglycerine-refractory chest pain persisted. On repeated TEE a slight pericardial effusion had developed, the lamella-like structure of the aortic wall was replaced by a big septated intracardiac abscess (3.9 × 2.8 cm) which spread from the non-coronary sinus of Valsalva to the left auricle (Fig. 1). Another ovalar abscess (1.1 × 0.7 cm) was located beside the left coronary sinus of Valsalva.

Emergency cardiac surgery was performed. About 200 ml of serosanguineous pericardial effusion and a perforation of the left ventricular lateral wall, covered by a small thrombus, were found. The aortic valve showed focal fibrous thickening with

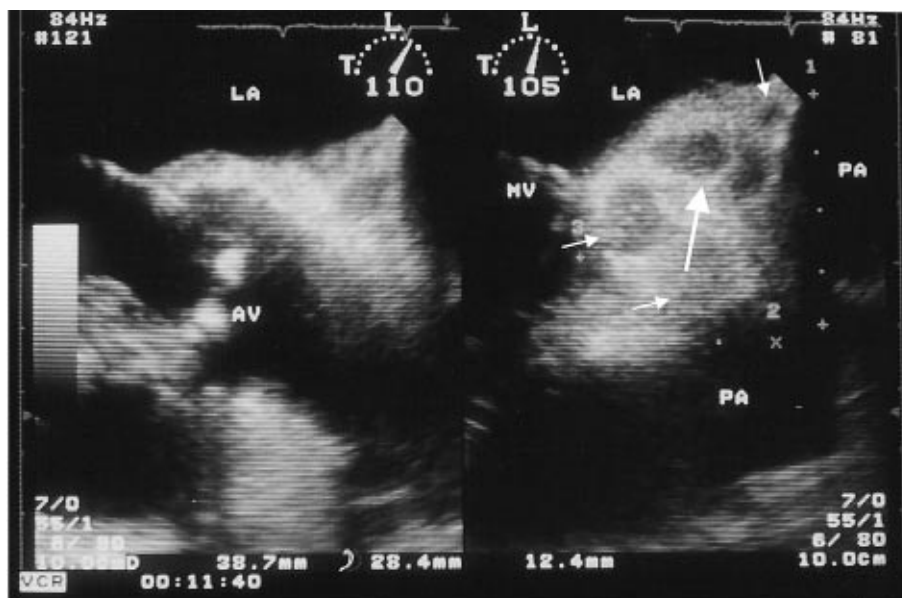
some calcifications but no vegetation. The subvalvular abscess cavities adjacent to the left and the non-coronary sinus of Valsalva were debrided and a stentless bioprosthesis (Prima) was inserted. Cultures from excised tissue did not grow *S. lugdunensis*.

After surgery the patient remained afebrile and all laboratory markers of inflammation returned to normal within four weeks. Anticoagulation was started with dicoumarol. Vancomycin was given intravenously and rifampin orally for 4 weeks followed by a 6-month course of oral cefuroxime, flucloxacillin, fusidic acid and clindamycin given alternately (changing every four weeks). Three weeks after surgery a small fistula with a high-velocity diastolic jet from the aortic root to the right atrium was detected by TEE. Six months after cardiac surgery the patient underwent coronary angiography and right-heart catheterization. Coronary artery disease and a significant left-to-right shunt were excluded. During a four-year follow-up period, the patient remained stable without recurrence of infective endocarditis and without diastolic overloading of the right ventricle.

## Discussion

*S. lugdunensis* was first described in 1988 [5] and is often confused with *S. aureus*, since they are morphologically similar on blood agar [9], and *S. lugdunensis* may produce fibrinogen-affinity factor (clumping factor) but is coagulase negative [5]. *S. lugdunensis* can be differentiated from other CNS by ornithine decarboxylation [9, 10]. Up to 29 percent of American isolates produce  $\beta$ -lactamases [10, 11], whereas 95 percent of the European strains are highly susceptible to  $\beta$ -lactam antibiotics [5].

*S. lugdunensis* was found in ten percent of the staphylococcal isolates from human specimens that were not *S. aureus* or *S. epidermidis* [8]. *S. lugdunensis* preferentially colonizes the perineum and was not isolated from nasal swabs [12]. 15% of *S. lugdunensis* isolated from



**Fig. 1.** TEE: The formerly lamella-like structure of the aortic wall is replaced by a big septated abscess (3.9 cm × 2.8 cm, arrows). LA left atrium; AV aortic valve; MV mitral valve, PA pulmonary artery

clinical specimens are thought to be contaminants or colonising organisms [8], whereas up to 85% of other CNS are regarded as contaminants of blood cultures [4]. 55% of clinically relevant isolates of *S. lugdunensis* are obtained from skin surface-related sites and 17% from blood and blood-related devices [8]. In a retrospective analysis *S. lugdunensis* accounted for 18% of tube coagulase-negative staphylococci causing infective endocarditis and 44% of tube coagulase-negative staphylococci causing native-valve endocarditis [13].

The clinical course of IE caused by CNS other than *S. lugdunensis* is in most cases subacute, often resembling that of viridans streptococci [1]. In the first year after valve surgery CNS cause about 40–50% of cases of prosthetic-valve endocarditis, but they cause only 5% of native-valve endocarditis [11]. The mortality is about 20% in both surgically and medically treated patients [14]. Although IE caused by *S. lugdunensis* is rare, it preferentially involves native valves leading to a fulminant course. Even with appropriate antibiotics [3, 15, 16] the infection may not be adequately controlled, reflected in one study by a mortality rate of 90% in patients with medical treatment alone and 50% in patients who underwent early valve replacement [12].

In addition to blood-culture results TEE is essential for the diagnosis of IE. *S. lugdunensis* endocarditis is characterized by complications such as abscess formation, gross valve destruction and embolisation. Most abscesses in IE occur at the aortic valve [17]. Involvement of the non-coronary sinus of Valsalva induces conduction abnormalities because the atrioventricular node and the His bundle travel through the interventricular septum close to the non-coronary cusp of the aortic valve. Thus, the newly developed first-degree heart block in our patient was indicative of an abscess localized at the non-coronary cusp of the aortic valve, bearing in mind the tiny separation of the posterior aortic wall in the first TEE examination. First- or second-degree heart block is reported in up to 10% of patients with abscess-forming IE. When only the aortic valve was involved, complete heart block occurred in 11 percent of patients [18], therefore daily ECG tracing is mandatory in IE with aortic-valve involvement.

The perivalvular involvement increases the septic burden, leading to unresponsiveness to antibiotics and persistence of infection. Abscesses pave the way for fistulas which may occur between any adjacent cardiac chambers or vessels, causing intracardiac shunts that might worsen the haemodynamic situation by volume overload. In our patient the large confluent abscesses spread to the lateral wall of the left ventricle and caused contained myocardial rupture and pericarditis, which explained the nitroglycerin-resistant chest pain. A small fistula occurred between the aortic root and the right atrium three weeks after surgery, causing no significant left-to-right shunt.

Increased troponin T is sensitive and specific of myocardial damage associated with coronary artery disease, but it is not synonymous with ischemia [19]. The elevation of troponin T in our patient reflects the destruction of myocytes; however, further studies should assess the role of troponin T in IE with abscess formation.

Systemic embolisation occurs in 20 to 50% of all cases of IE, with 25% and 42% reported with CNS [1] and *S. lugdunensis*, respectively [20]. The absence of visible vegetations in TEE indicated a low risk for this complication in our patient.

This case report and the review of the literature suggest that CNS isolated from patients with suspected or proven endocarditis should be promptly identified to the subspecies level. In patients with infective endocarditis caused by *S. lugdunensis*, early valve replacement is indicated even if the clinical condition seems to improve with adequate antibiotic treatment.

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