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(REVIEW ARTICLE)

Staphylococcus lugdunensis: A wolf in sheep's clothing? Review of the case reports from the last decade

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Abstract

Staphylococcus lugdunensis is a coagulase-negative *Staphylococcus* which can be isolated as part of the normal skin flora in humans. However, it has also been identified as a significant pathogen encoding a diverse array of virulence factors for adhesion, cytotoxicity and innate immune evasion. Infections from this pathogen include endocarditis with significant valve damage and abscess formation, skin and soft tissue infections, endophthalmitis and prosthetic joint infections. In this review article, all the case reports implicating this opportunistic pathogen during the last 10 years (2013-2023) are summarized. In the past decade, *S. lugdunensis* has been associated with skin and soft tissue infections, cases of endocarditis, orthopedic and ocular infections in adults and children. Given the pathogenic potential and wide spectrum of clinical disease associated with *S. lugdunensis*, this opportunistic pathogen should not be disregarded as a contaminant.

Keywords: *Staphylococcus lugdunensis*; Endocarditis; Endopthalmitis; Infections; Pathogen

1. Introduction

Staphylococcus lugdunensis, a coagulase-negative *Staphylococcus* (CNS), is part of the human normal skin flora, but has also emerged as an opportunistic pathogen causing various types of infections; from benign soft tissue infections to native valve endocarditis, osteomyelitis and arthritis [1]. First reported in 1988, this pathogen is a virulent *Staphylococcus* species often associated with endocarditis. Despite its susceptibility to antimicrobials, clonal expansion and carriage of virulence factors combined with biofilm-producing ability, render this species an important pathogen that should not be ignored in clinical practice [2].

The aim of the this review was to document all the case reports implicating this opportunistic pathogen during the last 10 years (2013-2023). A search in Pubmed was performed using the terms *Staphylococcus* and *lugdunensis.* Among the displayed results, case reports were selected and the 10-year filter was applied, resulting in 113 articles. One report of veterinary nature was excluded.

2. Skin and soft tissue infections

As a member of the staphylococcal family, *S. lugdunensis* can be found as part of the normal skin flora. However, it has been identified as the cause of skin and soft tissue infections in several cases. *S. lugdunensis* has been isolated from ulcers [3] [4] [5], pyoderma [6], abscesses [7], cutaneous nodules [8] and deeper sites, including cervical epidural abscess [9], necrotizing fasciitis [10] [11] and soft-tissue abscess with deep muscle invasion [12]. Some cases are very severe; according to Mallat et al, a 36-year-old male with no significant past medical history presented to the emergency

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room with abdominal pain, diarrhea, nausea and vomiting in the past 24 hours. Fulminant soft tissue infection resulted in a deterioration of symptoms and urgent laparotomy showed diffuse bowel and liver ischemia and infarction of the terminal ileum and ascending colon. The hospital course was complicated by multiorgan system dysfunction requiring hemodialysis, but the patient finally recovered [13].

Infections often occur on patients with serious underlying conditions, such as HIV [14] or end stage renal disease on hemodialysis [15]. Delpon et al described a case of a psoas abscess in a patient with a medical history of diabetes mellitus and rheumatoid arthritis, which was treated successfully with intravenous cloxacillin [16]. In another study, the cases of 16 patients with skin infections were analyzed. The most frequent site of infection was the inguinal-perineal region and pustules were the most common presentation. In spite of the good response to treatment, infection recurred in 3 patients, two of which were on anti-TNF therapy [17]. Infections can have a slow development, as in the case of a 54-year-old woman with rheumatoid arthritis treated with methotrexate with fever and swelling on her right cheek and upper eyelid in whom a dermal filler was injected into her cheeks 17 years prior [18].

Polymicrobial infections have also been reported, as in the case of a 14-year-old boy suffering from a wound infection caused by *Vibrio alginolyticus* and *S. lugdunensis* after stepping on a sea urchin. Initial treatment with cephalosporin was unsuccessful, thus antibiotic therapy was switched to ciprofloxacin, followed by trimethoprim/sulfamethoxazole, resulting in a painful scar [19]. Even though soft tissue infections are usually treated successfully, fatalities have occurred. A 57-year-old male with a polymicrobial surgical site infection of *S. lugdunensis* and *Clostridium* perfringens after resection of a soft tissue sarcoma of the lateral thigh, developed fulminant necrotizing fasciitis with an additional gas gangrene. The patient suffered a severe sepsis with consecutive hemolysis and multiorgan failure [20].

Diagnosis is often more complicated, as in the case of 46-year-old female with an infection in the fourth finger of the right hand after an accidental wound. In this case, a catalase-negative strain was isolated and identification was confirmed with MALDI-TOF mass spectrometry and sequencing of the mutated catalase gene [21].

2.1. Endocarditis

Although cases of prosthetic valve endocarditis have been reported [22] [23] [24] [25], most recorded infections involve native heart valves [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36]. In many patients valve replacement was necessary to successfully fight the infection [37] [38]. In others, patient's condition did not allow surgery and antibiotic therapy alone did not have the desirable outcome [39]. In 2020, a case of *S. lugdunensis* native valve endocarditis in a 83-year-old patient with confirmed COVID-19 was described. The patient received antibiotic and supportive therapy, but her condition continued to deteriorate, and she eventually passed away after 20 days [40].

Another rare complication of infective endocarditis by *S. lugdunensis* is transient global amnesia, as described in a 35-year-old woman with hippocampal infarction by Sakihara et al [41]. Other heart-related infections include pseudoaneurisms after cardiac surgery [42] [43], infection of vascular graft after bypass operation [44] and mycotic aneurysm of the superior mesenteric artery in association with *S. lugdunensis* endocarditis [45] [46]. A unique case of pericarditis in a 69-year-old woman with sepsis and disseminated intravascular coagulopathy due to *S. lugdunensis* was reported in 2021 [47].

In some cases the infection is very aggressive with severe complications, including embolic strokes [48] [49] [50], meningitis [26] and myocardial infarction caused by coronary embolism [51] and septic shock [52]. A case of acquired left ventricle to right atrial shunt (named Gerbode defect) has been described in a patient with staphylococcal aortic valve endocarditis [53]. Antibiotic treatment often leads to recovery, even in severe cases, as in a 43-year-old male diabetic patient who presented with an aggressive form of infective endocarditis involving the tricuspid, mitral and aortic valves following a gluteal abscess due to infection with *S. lugdunensis*. In this case, antibiotic treatment in combination with open heart surgery led to patient discharge in a stable condition [54]. On the contrary, there have been reports of patients who died, as one patient who suffered from endocarditis after perforation of the sinus of Valsava [55].

Polymicrobial infections have also been reported, including cavernous sinus thrombosis due to *Streptococcus mitis* and *S. lugdunensis* [56] and recurrent infective endocarditis due to *Aggregatibacter aphrophilus* and *S. lugdunensis* [57]. Diagnosis is therefore very complicated, as in the case of a 66-year-old man with infective endocarditis on the basis of a personal history of ischaemic dilated cardiomyopathy treated with an implantable cardioverter defibrillator. Transoesophageal echocardiography showed multiple vegetations on the pacemaker auricular wire, as well as a hydatid-like image that could be confused with an *Echinococcus* cyst [58].

During the last 10 years, five case reports of heart-related *S. lugdunensis* infections in children have been published. The youngest involved a male preterm infant (born at 27 weeks gestation) who developed fulminant late-onset sepsis due to *S. lugdunensis* with persistent bacteremia secondary to an infected aortic thrombus. After a complicated clinical course including severe respiratory distress syndrome that evolved into chronic lung disease along with multiple episodes of tracheitis, an episode of medical necrotizing enterocolitis followed by *S. lugdunensis* septicemia and the diagnosis of an infected aortic thrombus, the infant finally responded to therapy and recovered without complications [59]. Other reports involve a newborn with sepsis and endocarditis following lotus birth [60] and a 2-year-old boy who developed endocarditis while receiving chemotherapy for severe Langerhans cell histiocytosis through a totally implantable venous access port [61]. Infective endocarditis was also diagnosed in another 2-year-old boy who underwent repeat right ventricular outflow tract reconstruction with a bovine jugular vein graft [62] and in a previously healthy 15-year-old male [63]. Infections in children generally had a favorable clinical outcome after the appropriate treatment.

Infective endocarditis in pregnancy is generally associated with high maternal and fetal morbidity and mortality and is estimated to complicate approximately 1 in 100,000 pregnancies. Conolly et al described a case of a 33-year-old woman who presented at 30 weeks and 3 days gestation in her third pregnancy, with a history of feeling generally unwell, an episode of temporary speech disturbance, right shoulder tip pain, left subscapular pain on inspiration and chest discomfort. A pathologic echocardiogram combined with blood cultures positive for *S. lugdunensis* led to the diagnosis of infective endocarditis. The patient deteriorated, with worsening cardiac function, and a caesarean section was performed. Her baby had multiple limb abnormalities, subsequently diagnosed as arthrogryposis multiplex congenita. After an aortic valve replacement with a mechanical valve, the patient was eventually discharged with her baby [64].

2.2. Orthopedic infections

Although uncommon, *S. lugdunensis* orthopedic infections have been reported. Simpler cases include native joint septic arthritis of the knee [65] [66] [67] or the hip [68], chronic pain and lesion in the distal radius [69], asymptomatic chronic periprosthetic joint infection of the hip [70], septic iliopsoas bursitis after intra-articular methylprednisolone injection to the hip [71] and phalangeal osteomyelitis [72]. More complicated cases have also been reported in the last decade. In a patient suffering from osteomyelitis of the foot, bone cultures obtained during surgery were positive for two different *S. lugdunensis* strains, with different antimicrobial susceptibilities [73]. Polymicrobial infections are in fact rare, as in the case of co-infection from *S. lugdunensis* and *Aspergillus clavatus* [74]. Other diagnostic problems include the presence of virulent small-colony variants, which are genetically indistinguishable, but differ in size and antibiotic susceptibility from the parent strain and can be responsible for chronic persistent infection and failure of antibiotic treatment [75] [76]. Patients often have a complicated medical history, as in a case of a patient with disseminated musculoskeletal infection (including epidural abscess) in the context of anti-TNF use due to rheumatoid arthritis [77], or in the case of another on chronic hemodialysis with recurrent osteomyelitis of the lumbar spine [78]. In some cases osteomyelitis is complicated with bacteremia [79]. Reactive arthritis has also been described in the presence of bacteremia [80] or perianal abscess [81]. Infections may also develop after orthopedic surgeries, as in two cases of *S. lugdunensis* septic arthritis following arthroscopic anterior cruciate ligament reconstruction, where both patients successfully recovered with early arthroscopic irrigation and debridement in addition to long-term parenteral and oral therapy [82].

2.3. Ocular infections

Ocular infections caused by *S. lugdunensis* are uncommon, but a few cases have been reported in the last decade. Endophthalmitis is the most frequently recorded eye infection, either after intravitreal injections [83] [84] [85] [86] or in patients with several eye conditions [87] and with various visual outcomes. The incidence of S. lugdunensis keratitis is even lower, with only one severe case of suppurative keratitis in a 77-year-old woman [88] and a case of keratitis due to *Candida albicans* and *S. lugdunensis* after a motor vehicle accident reported in the last 10 years [89]. Kingston et al reported a case of a patient who developed necrotizing scleritis after glaucoma and cataract surgery [90].

2.4. Other types of infections

S. lugdunensis has been associated with a variety of different infections in the last decade. Less severe cases with good clinical outcome include primal lung abscess [91], urinary tract infection in adults [92] [93] or neonates [94] and cochlear implant infection in a 6-year-old girl [95]. Moreover, bilateral nasopharyngeal mucopyoceles were discovered on MRI in a patient with chronic headache [96] and in a rare case, a young male presented with scrotal pain and swelling, was found to have epididymo-orchitis with scrotal pyocele on imaging. Wound cultures grew *S. lugdunensis* and the patient clinically improved after being treated with appropriate antibiotics [97].

More complicated case reports include brain abscess without endocarditis or bacteremia [98], meninigitis after surgery for Rathke's cleft cyst by transsphenoidal approach [99], a pituitary abscess following endoscopic endonasal drainage of a suprasellar arachnoid cyst [100] and *S. lugdunensis* bacteremia in a patient receiving treatment for acute myeloid leukemia, which led to temporary interruption of therapy [101]. A patient with recurrent pneumonia was eventually diagnosed with common variable immunodeficiency [102]. Recurrent bacteremias in another patient revealed the presence of a prominent tortuous vessel coursing from the ascending aorta and main pulmonary artery to the left atrium [103]. In another case, computed tomography of an 80-year-old man presented to the emergency department with complaints of abdominal pain and fevers revealed the presence of a large lymphocele and cultures of lymphocele fluid grew *S. lugdunensis* [104]. A case of infected endometrioma during pregnancy following assisted reproductive technology was reported in 2019 [105], as well as an infection of a venticuloperitoneal shunt [106]. Similarly, a case of *S. lugdunensis* intracranial abscess in a pediatric hydranencephalic patient caused by a ventriculoperitoneal shunt related infection was described in 2013 [107]. A case of septic embolism secondary to *S. lugdunensis* bacteremia without infective endocarditis in an early geriatric-aged patient with a medical history of human immunodeficiency virus (HIV) was described in 2022 [108]. A newborn in Ethiopia developed hospital acquired pneumonia from a methicillin resistant strain, along with septicemia [109].

Polymicrobial infections include a case of a unilateral subdural empyema in a previously healthy 16-year-old patient due to *Streptococcus constellatus* and *S. lugdunensis* [110], as well as *S. lugdunensis* and *Trichophyton tonsurans* infection in synthetic hair implants [111]. Also, *Candida albicans* and *S. lugduensis* superinfection of liver cysts in a patient with autosomal dominant polycystic kidney disease under prednisolone treatment has been reported [112]. A 56-year-old woman with a medical history of obesity and diabetes mellitus was diagnosed with bacteremia and blood cultures were found positive for *Staphylococcus warneri* and *S. lugdunensis* in 2016 [113]. Odontogenic periorbital and orbital necrotizing fasciitis where cultures grew multiple organisms, most notably *Streptococcus milleri* group and *S. lugdunensis* was diagnosed in a 39-year-old man [114].

3. Conclusion

S. lugdunensis is an important opportunistic pathogen with the ability to cause endocarditis and a variety of other infections. Even though the microorganism remains susceptible to antimicrobials and treatment is successful in most cases, its aggressive nature suggests that it should not be disregarded as a contaminant.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

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