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Case Report

A Case of Vascular Graft Infection Caused by *Staphylococcus lugdunensis* after Femoropopliteal Bypass Operation

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A 79–year-old man who had undergone a right femoropopliteal (FP) bypass operation 6 weeks previously was diagnosed with vascular graft infection caused by *Staphylococcus lugdunensis*. Another FP bypass operation was performed, with long-term administration of antibiotics, and the patient eventually recovered well without any recurrences for over 2 years. Although *S. lugdunens* is classified as coagulase-negative *Staphylococcus*, its pathogenicity has been reported to be equal to that of *S. aureus*. Based on the literature review, the organism characteristically colonizes the inguinal area of human skin; thus, operations such as FP bypass grafting may place patients at a relatively high risk for infection by *S. lugdunensis*, a potentially high-pathogenicity organism.

Key words: coagulase-negative *Staphylococcus* (CNS), femoropopliteal (FP) bypass, *Staphylococcus lugdunensis*, vacuum-assisted closure (VAC) therapy, vascular graft infection (VGI)

Generally, coagulase-negative *Staphylococcus* (CNS) is considered relatively less pathogenic than *Staphylococcus aureus*. In fact, CNS rarely causes severe diseases in clinical situations. However, *Staphylococcus lugdunensis*, though microbiologically classified into CNS, has high pathogenicity, comparable to that of *S. aureus*, with a poor prognosis [1]. To date, various kinds of *S. lugdunensis* infection cases such as infective endocarditis (IE), skin and soft tissue infection, and bone and joint infection have been reported. As with other CNS organisms, it often manifests in conjunction with prosthetic devices; infections related to artificial joints, ventriculo-peritoneal shunts, heart valves, and pacemakers have been also described [2]. Recently, Choi *et al.* reported that approximately 60% of nosocomial *S. lugdunensis* bacteremia cases were caused by central line infection [3]. However, there has been no well-documented report concerning vascular graft infection (VGI) so far. Here, we report a case of *S. lugdunensis* VGI after a femoropopliteal (FP) bypass grafting operation.

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Case Report

A 79–year-old man (Height: 167 cm, Body weight: 60 kg) with a history of hypertension (for 9 years), arteriosclerosis obliterans (ASO), and vascular graft bypass of the left lower extremity (9 years previously), presented at our hospital with 2 days' history of right leg lassitude and coldness. The ankle brachial index (ABI) was 0.29 on right side and 0.99 on left side. He was diagnosed with ASO of the right femoral artery (Fontaine class 2) and received a right FP bypass operation using a Gore-Tex graft. In the nor-

mal clinical course after surgery, clinical symptoms and ABI showed improvement, and he was discharged without any complications.

Approximately 6 weeks later, the patient returned to the hospital complaining of mild fever and right femoral pain. Upon examination, a surgeon observed exudate leaking from the surgical wound, although the concurrent laboratory examination had not detected elevation of inflammatory markers. Irrigation and oral antibiotic (cefcapene pivoxil) was initiated; however, high fever emerged and the patient was readmitted 60 days after the initial operation.

His vital signs on readmission were as follows: blood pressure, 130/68 mmHg; heart rate, 96 beats per minute; body temperature, 39.0℃. Physical examination revealed redness and tenderness of the inner aspect of his right thigh. The patient did not exhibit any symptoms relating to IE such as cardiac murmur or embolization of peripheral vessels. His transthoracic echocardiogram was negative for vegetation on valves. Laboratory testing revealed an elevated inflammatory status (white blood cell count, 9,900/mm^3; and C-reactive protein level, 10.2 mg/dL), but no other specific results. The infected graft was completely removed, and another right FP bypass operation was performed, again with synthetic Gore-Tex graft. This time the bypass was routed via the lateral side of the infected femoral region to avoid re-infection. The surgical wound was left open and vacuum-assisted closure (VAC) therapy was initiated. Gram staining of the abscess pooled around the infected graft revealed inflammatory cells and Gram-positive cluster-forming cocci, and linezolid (600 mg every 12 h) was initiated intravenously.

Later, *S. lugdunensis* was detected from two sets of blood cultures, the abscess obtained from the surgical site, and a thrombus inside the graft (Microscan Walkaway, SIEMENS, CA, USA). According to the result of antibiotics susceptibility testing (Table 1), the antibiotic was changed to vancomycin 2 weeks after the operation, and a total of 8 weeks of intravenous antibiotic therapy was successfully given. VAC therapy was regularly performed every 3 to 4 days and continued for approximately 8 weeks. Complete healing of the local wound was finally achieved and the patient was discharged without any subsequent infectious complications over 2 years.

Table 1 Antibiotic susceptibility testing of *S. lugdunensis*

Antibiotics	MIC (μg/mL)
Penicillin G	>8
Ampicillin	>8
Cefazolin	≦8
Cefotiam	≦8
Flomoxef	≦4
Imipenem	≦1
Gentamicin	>8
Arbekacin	2
Minocycline	≦2
Clindamycin	≦0.5
Levofloxacin	≦0.5
Fosfomycin	>16
Sulfamethoxazole/Trimethoprim	≦1
Vancomycin	2
Teicoplanin	≦2
Linezolid	≦2

MIC, minimum inhibitory concentration.

Discussion

S. lugdunensis was first detected in 1988 and differentiated from the closely related but more virulent *S. aureus* by its inability to produce free coagulase [4]. Among over 40 recognized species of CNS, this organism is unique in 2 major points.

First is its similarity to *S. aureus* with respect to pathogenicity and biochemical properties: *S. lugdunensis* has the potential to cause infections as severe as those attributable to *S. aureus*. In fact, a recent guideline suggests that *S. lugdunensis* bacteremia should be managed the same way as *S. aureus* bacteremia [5]. In contrast to other CNS organisms, *S. lugdunensis* is known to possess the same virulence factors as *S. aureus*, such as delta toxin-like hemolytic peptide, vitronectin (DNase and lipase), esterases, lysosome resistance, biofilm formation, and others [1]. The biochemical properties of *S. lugdunensis* also resemble those of *S. aureus*. The organism can be easily mistaken for *S. aureus* if identification is based only on the latex agglutination test. *S. lugdunensis* can be differentiated from *S. aureus* by ornithine decarboxylase detection, generation of acid from D-mannitol, and the pyrrolidonyl aminopeptidase test (Table 2).

The second distinctive characteristic of *S. lugdunensis* is its antibiotic susceptibility. According to the Clinical and Laboratory Standards Institute, its resistance to oxacillin is the same as that of *S. aureus*.

While other CNS organisms are generally resistant to oxacillin, *S. lugdunensis* is generally susceptible to most anti-staphylococcal antibiotics, including penicillin. Beta-lactamase production is found in only approximately 25% of strains, and methicillin resistance is uncommon [6]. The pathogen in the present case was a methicillin-sensitive strain.

To date, a variety of *S. lugdunensis* infections have been reported. Frank *et al.* summarized clinical cases caused by *S. lugdunensis* in their review article in 2008 [7], and concluded that IE, mainly involving native valves, is a major clinical manifestation. According to Liu *et al.*, who conducted a retrospective literature review and summarizend 67 cases of *S. lugdunensis* IE between 1988 and 2008 [8], more than 80% occurred as left-sided valvular IE, 66.7% required valve replacement operations, and the mortality was 38.8%. We further investigated recent *S. lugdunensis* infection cases by performing an English-language search of PubMed from 2008 to September 2013, using the keyword phrase "*Staphylococcus lugdunensis*". On the basis of 243 cases from 49 articles, it was revealed that skin and soft tissue infection, followed by IE, is the most common manifestation of *S. lugdunensis*, as shown in Fig. 1 [1, 9–14].

Table 2 Biochemical characteristics of *S. aureus* and *S. lugdunensis*

	S. aureus	*S. lugdunensis*
Oxidase	(−)	(−)
Ornithine decarboxylase	(−)	(+)
Sucrose	(+)	(+)
Maltose	(+)	(+)
D-mannitol	(+)	(−)
D-mannose	(+)	(+)
D-trehalose	(+)	(+)
D-ribose	(+)	(−)
Agglutination test	(+)	(−)
Clumping test	(+)	(+)
Thermostable nucleases	(+)	(−)
pyrrolidonyl aminopeptidase test	(−)	(+)

As with other CNS organisms, *S. lugdunensis* is a normal flora of the human skin and has high potential to become involved with indwelling medical devices [2]. Importantly, *S. lugdunensis* characteristically resides at the perineum and inguinal area [15–19]. Vascular grafts originating in the groin area as in the present case generally have the highest rates of infection among the various types of vascular grafts. Therefore, we assume that FP bypass places patients

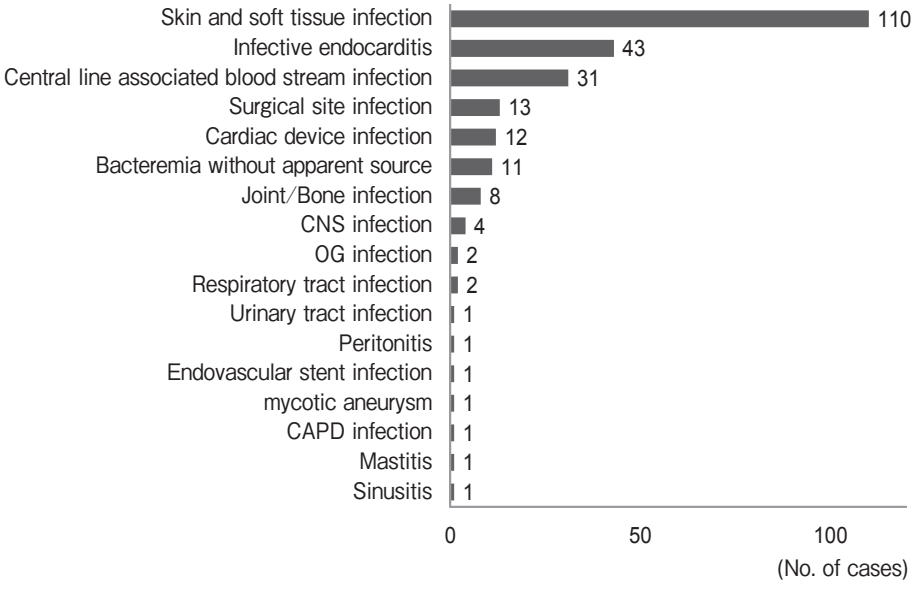

Fig. 1 A summary of previously reported cases of *Staphylococcus lugdunensis* infection. The summary is composed of 243 cases derived from 49 publications including case reports, case series, and reviews concerning *Staphylococcus lugdunensis* infection that were reported from 2008 through September 2013. The designation "skin and soft tissue infection" includes cellulitis, necrotizing fasciitis, subcutaneous abscess, and iliopsoas abscess. CNS, central nervous system; OG, obstetrics and gynecology; and CAPD, continuous ambulatory peritoneal dialysis.

at a relatively high risk for *S. lugdunensis* infection. Although *S. lugdunensis* infections of indwelling medical devices have been reported [2], a literature review found no previous case involving VGI. The infections caused by this organism are known to have the potential to cause severe infection as discussed above. Thus, we consider that VGI caused by *S. lugdunensis* should be separated from other etiologies.

In general, antimicrobial therapy alone without surgery is associated with a high mortality [20]. Graft excision and revascularization through a non-infected site are essential for treatment of VGI. Revascularization can be accomplished by extra-anatomic bypass or partial graft excision and *in situ* reconstruction with arterial allografts, autologous veins, or antibiotic- or silver-bonded prosthetic grafts [21]. Among these, the incidence of infection in arterial allografts or autologous veins is lower than in prosthetic vascular grafts [22]. The efficacy of rifampicin-bonded grafts in preventing graft infection has been reported by 3 randomized controlled trials [23–25]. In our case, revascularization was performed using a non-antibiotic-bonded prosthetic vascular graft. However, considering the risk of reinfection, the previously proven method could be an option.

Since the patient's skin, particularly at the inguinal area, is a major source of *S. lugdunensis*, improving preoperative skin management is important for prevention. Preoperative bathing with a detergent alone can be of use [26]. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant *Staphylococcus aureus* has been reported in ICU patients [27, 28], and such a method can be applied for the prevention of *S. lugdunensis* infection. In addition, 2% chlorhexidine-based preparations are reported to be superior to 10% povidone-iodine in preventing surgical site infection [29], although 0.5 to 1% chlorhexidine solution is commonly used in Japan. Skin preparation using such an appropriate antiseptic agent is evaluated as critical to prevention in guidelines [30–32]. In the inguinal area, hair removal can be of concern. Removing hair using a razor is no longer recommended [32]; if needed, a hair clipper should be used so as not to damage the skin tissue. It is considered that scars made by the procedure of removing hair are vulnerable to surgical site infection. Compliance with all these fundamental principles can lead to more effective infection prophylaxis. On the other hand, the selection of prophylactic antibiotic might be less important since *S. lugdunensis* is generally sensitive to various kinds of antibiotics.

In summary, this is the first well-documented case report of VGI caused by *S. lugdunensis*. FP bypass operation can place patients at a relatively high risk for *S. lugdunensis* infection since the organism characteristically resides at the inguinal area and the operation embeds prosthetic devices. We need to pay more attention to the clinical characteristics of cardiovascular infections caused by this potentially fatal organism, *S. lugdunensis*.

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