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Surgical management of *Staphylococcus capitis* prosthetic valve infective endocarditis: Retrospective review of a 10-year single center experience and review of the literature

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ABSTRACT

Background: Staphylococcus capitis (*S. capitis*) is a subtype of coagulase-negative staphylococci and a commensal of the skin of the human scalp and forehead. *S. capitis* has been occasionally reported in infective endocarditis and rarely in prosthetic valve endocarditis (PVE). The purpose of this report is to present the clinical course and the surgical management of a series of four patients with *S. capitis* PVE.
Methods: The medical records of 190 adult patients with a definite diagnosis of infective endocarditis by the Duke modified criteria and who underwent surgery at our center between January 2008 and December 2018 were retrospectively reviewed.
Results: There were four cases of *S. capitis* infective endocarditis among 190 patients. All were male with an average age of 70.25 years (range, 58–80 years). The four cases were PVE: 3 aortic (1 mechanical and 2 biological bioprostheses) and 1 mitral (bioprosthesis). Their mean Euroscore II was 32.43 (range, 9.19–50.8). Three patients had underlying diseases (diabetes mellitus = 2, chronic obstructive pulmonary disease = 3, chronic kidney disease = 1, peripheral arterial disease = 2, ischemic heart disease = 1, dilated cardiomyopathy = 1). Preoperative clinical presentation was characterized by the occurrence of sepsis in three patients and heart failure and sepsis in one patient. Two patients presented with vegetation (mitral bioprosthesis, aortic bioprosthesis). A prosthetic dehiscence was present in all patients, and two presented with a localized annular abscess. All but one patient received triple antibiotic treatment with vancomycin plus rifampicin plus gentamycin. Surgery was performed on an urgent basis in all patients, and the in-hospital mortality rate was 50%.
Conclusions: While limited by the small number of patients, our series highlights the aggressive clinical course of *S. capitis* PVE with a mortality rate close to that of *Staphylococcus aureus* PVE. Therefore, early surgical management is recommended to improve the clinical outcome of this serious disease.

Introduction

Staphylococcus capitis (S. capitis) is a coagulase-negative Staphylococcus (CoNS). CoNS are well-known for their ability to produce biofilm, which is an important determinant of virulence in the development of staphylococcal device-related infections [1]. Indeed, CoNS infections are frequently associated with the use of indwelling lines and devices. Moreover, CoNS are the most common cause of early prosthetic valve endocarditis (PVE) [2–6]. However, in contrast to other CoNS, *S. capitis* has a low ability to adhere to foreign body surfaces [7,8]. PVE due to S. capitis is therefore highly uncommon and it has only been described in a few case reports.

This study describes the clinical characteristics of a series of four patients with *S. capitis* PVE, with a particular emphasis on the man-

Abbreviations: CoNS, coagulase-negative *Staphylococcus*; IE, infective endocarditis; ICU, intensive care unit; LOS, length of stay; POD, postoperative day; PVE, prosthetic valve endocarditis; *S. capitis*, *Staphylococcus capitis*.

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agement of this rare entity. It also provides a review of the literature of published cases of *S. capitis* PVE.

Methods

This single-center retrospective observational study was approved by our local ethics committee (Chairperson Pr V. Seutin, Ref:2020/157). Only adult patients (age >18 years) were considered for the study. Among 190 adult patients diagnosed with IE according to the modified Duke Criteria [9] and operated on in our center between January 2008 and December 2018, four cases (2.1%) of *S. capitis* infective endocarditis (IE) were identified.

The patients' records were retrospectively reviewed by evaluating the following characteristics: age at the time of diagnosis, sex, previous heart disease, comorbidities, status of the diseased prosthesis, days from signs/symptoms onset to start of treatment, antibiotic therapy, surgical treatment for endocarditis, days from diagnosis to surgical treatment, type of surgery, complications, and in-hospital mortality. Early-onset PVE was defined as a case that occurred within 1 year after valve replacement [2]. The surgical risk was calculated using the logistic European system for cardiac operative risk evaluation II (Euroscore II). For mortality, only early mortality was considered for analysis in this study and was defined as a death that occurred during hospitalization regardless of cause or within 1 month of discharge. Early surgery was defined based on the American Heart Association guidelines as a surgery performed during initial hospitalization and before completion of a full course of antibiotics.

Microbiological identification of *S. capitis* was performed by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics). Antimicrobial susceptibility testing and minimal inhibitory concentrations (MIC) were determined by using a VITEK® 2 microbial ID/AST testing system (Biomérieux) following the European committee on antimicrobial susceptibility testing (EUCAST) breakpoint guidelines [10].

Quantitative variables are reported as mean (range).

A literature review of published cases of *S. capitis* PVE was performed using the Medline database with the following keywords: *endocarditis, S. capitis, PVE*. Only reports written in English were selected. Additional cases were identified from the reference lists of the selected articles.

Results

Clinical characteristics (Table 1)

All four patients were male with a mean age of 70.25 years (range, 58–80 years). They all suffered from PVE (3 aortic and 1 mitral); they were all considered as early PVE and healthcare-acquired. Three patients had underlying comorbidities, including diabetes mellitus (n = 2), chronic kidney disease (n = 1), chronic obstructive pulmonary disease (n = 3), ischemic cardiomyopathy (n = 1), dilated cardiomyopathy (n = 1), and peripheral arterial disease (n = 2). There were no intravenous drug users in our cohort.

Microbiological data

S. capitis grew in at least 3 blood samples from all of the patients in our cohort. It was resistant to methicillin but sensitive to vancomycin in all four patients, and their valve cultures were all negative.

Echocardiographic data

All four patients underwent both transthoracic and transesophageal echocardiography, whose specific findings are presented in Table 2. Moderate to severe paravalvular leak with partial prosthetic dehiscence was present in all patients. Vegetations were only found on echocardiography for the patient with mitral PVE (4 × 6 mm). However, vegetation not described at echocardiography was discovered in the operating room in another patient. A localized annular abscess was present in two patients. There was no leaflet perforation.

Clinical evolution

The mean time between the initial surgery and the re-admission to our center was 3.5 months (range, 1.8–7.5 months). The clinical course was acute in all four patients (< 4 weeks), with fever and sepsis as a common feature at admission. Heart failure developed in one patient. There was no embolic event in our series.

Antibiotic therapy

The mean time between signs/symptoms onset and the beginning of treatment was only 3.75 days (range, 2–7 days). All patients, except one, received a triple combination of vancomycin plus gentamycin plus rifampicin for 6 weeks, following the recommendations of the infectious disease team. One patient with chronic kidney disease received a combination of vancomycin and rifampicin (patient 1—Tables 1 and 2).

Surgical management

Indications for surgery were heart failure with moderate to severe paravalvular leak for one patient, and persistent sepsis with prosthesis dehiscence and paravalvular leak for the other three patients. The mean time between PVE diagnosis and surgery was 14 days (range, 2–33 days). Two patients required debridement of a localized annular abscess. Valve replacement was carried out with implantation of 1 mitral mechanical valve (1 patient), 1 aortic mechanical valve, and 2 aortic bioprostheses.

The mean cardiopulmonary bypass time was 95.67 min (range, 77–121 min), while the mean cross-clamp time was 51.67 min (range, 44–63 min). The mean intensive care unit (ICU) length of stay (LOS) was 11.5 days (range, 2–19 days), while the mean hospital LOS was 12.5 days (range, 6–19 days). There were 2 in-hospital deaths (overall mortality of 50%). The first was a patient with preoperative heart failure who presented a cardiogenic and septic shock in the ICU and died at postoperative day (POD) 17. The second was a patient with aortic PVE who underwent implantation of a bioprosthesis. After sedation was discontinued in the ICU, he presented an episode of seizure and delayed awakening. The neurological investigations were negative. Yet, his clinical condition worsened with the occurrence of a severe septic shock and he died at POD 19.

Discussion

PVE is a life-threatening condition and has been reported to occur in 3–4% of patients within 5 years of their surgery, with a similar incidence for bioprosthetic and mechanical valves [11]. In a recent report, the most common causative organism of PVE was *Staphylococcus aureus*, followed by the CoNS, *Enterococcus* and *Streptococcus viridans* [12]. However, CoNS are the prevalent isolate in early PVE [2–6].

S. capitis is a usually multi-susceptible and low-virulence commensal species. It has been implicated in a broad range of human infections, including pneumonia, urinary tract infection, cellulitis,

Table 1
Clinical characteristics of the four patients with *Staphylococcus capitis* prosthetic valve endocarditis.

Case	Age	Sex	Valve	Euroscore II	Underlying disease	Antibiotics	Surgery	Complications	Outcomes
1	74	M	Mitral bioprosthesis	50.8	Dilated cardiopathy COPD CKD PAD	Rifampicin Vancomycin	MVR (mechanical)	Heart failure Septic shock	Died (POD17)
2	69	M	Aortic bioprosthesis	40.82	Diabetes COPD PAD Ischemic cardiopathy	Rifampicin Vancomycin Gentamycin	AVR (bio-prosthesis)		Recovered
3	80	M	Aortic bioprosthesis	28.89	COPD Diabetes	Rifampicin Vancomycin Gentamycin	AVR (bio-prosthesis)	Septic shock	Died (POD19)
4	58	M	Aortic mechanical valve	9.19		Rifampicin Vancomycin Gentamycin	AVR (mechanical)		Recovered

AVR, aortic valve replacement; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; MVR, mitral valve replacement; PAD, peripheral arterial disease.

Table 2
Echocardiographic data of the four patients with *Staphylococcus capitis* prosthetic valve endocarditis.

Case	Vegetation	Size(mm)	Paravalvular insufficiency	Abscess	Perforation	Preop LVEF	Preop transvalvular gradient
1	Yes	4 × 6 mm	++++	No	No	25 %	3.8 mmHg
2	No	n/a	+++	Yes (localized)	No	70 %	n/c
3	Not on echo but in the OR	n/a	++++	Yes (localized)	No	60 %	66/45 mmHg
4	No	n/a	+++	No	No	45 %	34/15 mmHg

Echo, echocardiography; LVEF, left ventricular ejection fraction; n/a, not applicable; n/c, not calculated; preop, preoperative; OR, operating room.

meningitis in patients with ventriculoperitoneal shunts [13], and in catheter-related bloodstream infections in neonates [14]. However, *S. capitis* is an uncommon cause of endocarditis. The first case of *S. capitis* native valve endocarditis was described in 1992 by Bandres and Darouiche [15]. There were at least 12 additional cases reported since then [16–25]. All of the patients were male. The most frequently infected valves were the mitral (7 out of 13) and aortic (5 out of 13) valves. All patients were treated with appropriate antibiotics and only one required surgery during the acute phase [25]. The mortality rate was 23% (3 out of 13).

To date, at least three cases of *S. capitis* cardiac device-related endocarditis have been reported [26–28]. The time intervals between implantation and diagnosis in these three patients were three years [26], seven years [28], and 15 years, respectively [27]. For all three, the pacemaker was successfully removed. In one octogenarian patient, the tricuspid valve had to be replaced due to extensive destruction [27]. An unusual location of *S. capitis* IE has also been reported by Demarie et al. [29]. In fact, they described the case of a 46-year-old patient with multiple comorbidities and a history of repaired congenital heart disease who developed *S. capitis* IE on an intracardiac Dacron patch. The patient was managed successfully by appropriate antibiotics followed several weeks later by surgery.

To the best of our knowledge, there are at least 8 cases of *S. capitis* PVE reported in the English literature [30–33]. The first case was reported in 1996 and involved a 65-year-old woman after her third mitral valve replacement. The patient was successfully managed by prompt valve re-replacement and antibiotics [30]. Dominguez Rodriguez et al. described the case of a 55-year-old man with aortic and mitral bioprostheses IE due to *S. capitis*. This patient was also managed by antibiotics and a double valve surgical replacement [31]. Nalmas et al. reported two cases of aortic PVE caused by *S. capitis* complicated by an aortic root abscess and peripheral septic emboli with fatal outcomes in both patients, despite early surgical intervention [32]. To date, the largest case series of *S. capitis* PVE has been reported by Takano et al. It involved four patients (three aortic and one mitral). All four patients survived after antibiotic therapy and surgery [33]. All but one reported cases of *S. capitis* PVE were early PVE and occurred within 7 months of valve replacement surgery. Our paper describes 4 additional cases of *S. capitis* early PVE operated in our center over a 10-year period. In our series, the cases occurred with a median delay of 3.5 months after surgery (range, 1.8–7.5 months), which suggests that a contamination process during the initial surgery is probably the source of the infection. The key features of these cases of *S. capitis* PVE (including our case series) are summarized in Table 3.

In general, the clinical presentation of PVE may be nonspecific, leading to a delayed and difficult diagnosis. Furthermore, the modified Duke criteria have a lower sensitivity in cases of suspected PVE [34]. Another characteristic of PVE is the occurrence of local complications, such as an annular abscess and prosthesis dehiscence in up to 60% of patients [35]. Despite its reported weak ability to adhere to foreign bodies, the review of cases of *S. capitis* PVE demonstrated a high occurrence of local complications, such as the presence of vegetations, prosthetic valve annulus destruction with abscess, and dehiscence in all of the patients (8/8) [30–33]. This trend is confirmed in our cohort where all patients had at least one of these local complications.

The results of valve culture are rarely mentioned in the series of *S. capitis* PVE reported in the literature. Although valve culture has been shown to have a limited diagnostic power in IE compared to blood cultures and sequencing techniques [36,37], it has recently

Table 3
Staphylococcus capitis prosthetic valve endocarditis: reported cases in the literature.

References	Age	Gender	Previous surgery	Onset of symptoms after surgery	Local complications	Timing surgery after diagnosis	Surgery performed	Antibiotics	In-hospital outcomes
Ref 30	65	F	MVR (3x)	3 weeks	Paravalvular leak Dehiscence	8 weeks	MVR	Imipenem+VCM	Survived
Ref 32	72	M	AVR (CABG)	3 months	Root abscess Dehiscence	4 d	ARR	VCM+GM+RMP	Died
	48	F	AVR + MV repair	4 months	Root abscess Vegetation	4 d	AVR	VCM+GM+RMP	Died
	79	F	AVR	24 d	Annular abscess, Vegetation Dehiscence	12 d	AVR	AMK >LZD>TeiC Min	Survived
Ref 33	79	F	AVR	40 d	Vegetation	14 d	AVR	VCM +Min	Survived
	76	M	AVR	53 d	Vegetation Abscess Dehiscence	8 d	AVR	Teic > VCM> LZD LVFX	Survived
	68	F	MVR/AVR	106 d	Dehiscence Abscess	8 d	MVR	VCM+GM+LVFX.	Survived
Ref 31	55	M	MVR/AVR	7 years	Vegetations	30 d	MVR/AVR	VM+GM+RMP	Survived
	74	M	MVR	2.4 months (73 d)	Vegetation Dehiscence	33 d	MVR	VM+RMP	Died
PR	69	M	AVR	2.5 months (75 d)	Dehiscence Abscess	2d	AVR	VM+GM+RMP	Survived
	80	M	AVR	1.8 months (57 d)	Vegetation Dehiscence Abscess	7d	AVR	VM+GM+RMP	Died
	58	M	AVR	7.5 months (228 d)	Dehiscence	14 d	AVR	VM+GM+RMP	Survived

AMK, amukin; AVR, aortic valve replacement; ARR, aortic root replacement; CABG, coronary artery bypass; GM, gentamycin; LVFX, levofloxacin; LZD, linezolid; Min, minocycline; MVR, mitral valve replacement; PR, present report; RMP, rifampicin; VCM, vancomycin, TEIC, teicoplanin.

been described as an independent predictor of in-hospital mortality in active left-sided IE [38].

Indeed, Garcia-Granja et al. showed in a recent report that patients with positive blood cultures who undergo surgery during the active phase of the disease, and in whom the same microorganism is isolated from the blood and valve culture, have a particularly poor prognosis, with nearly 2-fold in-hospital mortality compared to those with a negative valve culture [38]. In the two cases of aortic PVE with aortic root abscess reported by Nalmas et al., urgent surgical procedures were performed in both patients after a few days of antibiotics, and culture of both valves grew *S. capitis* [32]. However, in the case report of Terada et al., the surgery was performed after an initial course of 4 weeks of antibiotics and the valve culture was negative [30]. In our case series, the valve cultures were all negative. This is probably due to the fact that antibiotic therapy was started in all patients before surgery, with a mean duration of 16.75 days (ranging from 7 days to 37 days).

As other CoNS, *S. capitis* is a ubiquitous skin commensal. Thus, repeated blood cultures are required to distinguish a true bacteremia by *S. capitis* from a contaminant. *S. capitis* was the only organism that grew in at least 3 blood samples in all four patients of our cohort, confirming the diagnosis of *S. capitis* PVE.

S capitis is commonly resistant to β-lactam antibiotics such as methicillin. In all reported cases of *S. capitis* PVE in the literature, as well as in our case series, all isolates were methicillin resistant. In addition, certain specific strains of S. capitis encountered in neonatal intensive care units have been associated with heteroresistance to vancomycin, which may increase the failure rate of medical therapy [39]. The antibiotic therapy regimen in our series consisted of gentamycin plus vancomycin plus rifampicin for all patients, except one who received a combination of vancomycin and rifampicin because of chronic kidney disease.

While *S. capitis* native valve IE is usually managed conservatively with antibiotics during the acute phase [23], prompt surgery is recommended to improve the clinical outcome of patients with complicated PVE [33]. In the case series of four patients with *S. capitis* PVE of Takano et al., the time interval between the diagnosis of PVE and surgery ranged from 0 to 5 days. The author attributed their good clinical outcomes (100% survival) to the early initiation of surgery combined with an appropriate antibiotics therapy [33]. Unfortunately, despite a relatively early surgical removal of the infected prostheses combined with antibiotics, the overall mortality of our series was relatively high compared to the series of *S. capitis* PVE cases published in the literature (50% (n = 2/4) vs 25% (n = 2/8)) [30–33]. This may be explained, at least in part, by the elevated number of comorbidities of the patients, as reflected by their high predicted mortality according to the EuroSCORE II (mean Euroscore = 32.43, range 9.19–50.8).

Conclusion

Although uncommon, S. capitis PVE can exhibit a severe morbidity and mortality similar to *Staphylococcus aureus* PVE. We believe that early surgical removal of the infected prosthesis combined with an appropriate antibiotic therapy remains the best approach to improve the clinical outcomes of patients with complicated *S. capitis* PVE.

Our study is limited by its retrospective and observational design. Furthermore, the number of patients is small due to the rarity of *S. capitis* PVE. In addition, our cohort is exclusively composed of surgical patients with no comparison to a group managed medically.

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Competing interests

None declared.

Ethical approval

Approval from an ethics committee and consent to participate were not required since this study was retrospective. Nevertheless, the study was approved by the Ethical review committee of the University Hospital Center of Liege, Belgium (Chairperson Prof V. Seutin, ref: 2020/157).

Consent for publication

Not applicable.

Availability of data and materials

The dataset used and analyzed during this study is available from the corresponding author on reasonable request and after removal of all personal information.

Author contributions

Dr. Vincent Tchana-Sato designed the study, collected and analyzed the data, and wrote the manuscript. Dr. Gregory Hans wrote and reviewed the manuscript. Dr. Frederic Frippiat reviewed and revised the manuscript. Dr. Ines Zekhnini collected and analyzed the data. Dr. Racaru Dulgheru reviewed the manuscript. Pr. Jean Paul Lavigne revised the manuscript. Pr. Jean Olivier Defraigne reviewed and revised the manuscript.

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