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Review

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Native and Prosthetic Valve *Staphylococcus capitis* Endocarditis: A Review of the Literature

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Abstract

Infective endocarditis (IE) is a rare but serious disease. Coagulase-negative staphylococci (CoNS) are among the least prevalent causes of IE. *Staphylococcus capitis*, a species of CoNS, although described in the literature before has only been seen in a few cases. Even with such few cases, complications and mortality have still been demonstrated. In our review, we look at the epidemiology, diagnosis, management, and literature prevalence of CoNS in native and prosthetic valve IE.

Keywords: *Staphylococcus capitis*; Endocarditis; Native endocarditis; Prosthetic valve endocarditis

Introduction

Infective endocarditis (IE) is among the rarest forms of infections. Of the bacteria that are known to be causative, coagulase-negative staphylococci (CoNS) are among the least prevalent. Notwithstanding the low prevalence, CoNS can cause serious infections such as endocarditis, catheter-related bacteremia, and prosthetic joint infections [1, 2]. In this review of the literature, we look at the epidemiology, diagnosis, management, and outcomes of *Staphylococcus capitis* (*S. capitis*), a species of CoNS, in both native valve and prosthetic valve endocarditis.

Methods

PubMed was searched with all article types included. No date limitation was placed. All case reports and review articles pertaining to *S. capitis* were analyzed for review inclusion with exclusion being non-accessibility of the article. Pertinent search terms included "*Staphylococcus capitis*", "*Staphylococcus capitis* endocarditis", and "infective endocarditis".

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Epidemiology

Due to the wide presentation and affected populations, there is variability in the prevalence and incidence of IE. In recent studies, the incidence of IE has been described as anywhere from 3 to 7 per 100,000 person-years. The most common implicated pathogen has been *Staphylococcus aureus* [1]. CoNS are a heterogenous group of commensal organisms considered abundant in the skin flora. *S. capitis*, a species of CoNS that occupies a specific niche on the skin of the head, accounts for approximately 5% of CoNS clinical isolates. Its typical infection profile includes urinary tract infections, catheter-related bacteremia, and cellulitis [3].

In terms of prevalence, Murdoch et al looked at pathogen isolates of 2,781 patient with endocarditis in both drug and non-drug abusers. Native valve IE was seen in 1,881 patients, with 237 being due to persons who inject intravenous drugs and 1,644 being unrelated to intravenous drug injection. In patients with native valve IE, only 155 or 12% were due to CoNS, with 3% being secondary to intravenous drug abuse. Intracardiac-device IE was seen in 735 patients. Of these 735 patients, the prevalence of prosthetic valve IE due to CoNS was 95 patients or 17% [4]. The risk factors for IE vary greatly. In terms of non-clinically acquired IE, intravenous drug usage is a significant etiology. Clinically acquired etiologies include need for vascular access especially for long-term therapies, valvular prosthesis, implantable intracardiac devices, and non-cardiac prosthesis [5]. IE has been described mostly in the elderly population with males being affected more than females [6, 7]. In a study by Jensen et al, looking at 8,905 patients over a 20-year interval, median age was 70.2. In terms of gender prevalence, males accounted for 65.2% of the study population [8].

Diagnosis

Diagnosis of IE consists of a clinical, laboratory, and imaging approach. In terms of clinical approach, the first step is

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obtaining a history. In our review, the patients had symptoms such as fever, dyspnea on exertion, cold intolerance [9], malaise [10], palpitations [11], and back pain [12]. The modified Duke criteria have been shown as one of the major diagnostic criteria for IE. According to the criteria, for definitive clinical IE diagnosis patients must meet two major criteria, one major criterion and three minor criteria, or five minor criteria. Major criteria include positive blood culture with typical microorganisms known for IE from two separate blood cultures, a single positive blood culture with *Coxiella burnetii* or anti-phase 1 immunoglobulin G (IgG) antibody titer 1:800 or greater, evidence of endocardial involvement, and echocardiogram with IE findings. Minor criteria include predisposition to IE such as intravenous drug use or prior heart condition, fever, any exam findings of septic emboli, immunologic phenomena, and positive blood culture inconsistent with major criteria or serology demonstrating active infection with IE organism. In terms laboratory approach, obtaining blood cultures are key in confirming the causative pathogen. Other laboratory markers that can help guide diagnosis include the complete blood count with differential and inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate [1]. Aside from clinical and laboratory diagnosis, echocardiography has been shown to be a major imaging modality in confirming diagnosis. The two main echocardiographic modalities are transthoracic and transesophageal. The preliminary diagnostic choice due to feasibility is transthoracic echocardiography (TTE). The sensitivity of TTE is approximately 80%. Transesophageal echocardiography (TEE) has been shown to have approximately 95% sensitivity [13].

S. capitis Native Valve Endocarditis

Native valve endocarditis secondary to *S. capitis* infection has been described in 12 patients. In terms of patient demographics, all patients were male. The median age was 55.8 years, with the youngest patient age of 29 and oldest patient age of 79. Comorbidities among the patient population included coronary artery disease, hypertension, diabetes mellitus, prior cerebrovascular accident, renal insufficiency, cardiomyopathy, ventricular septal defect, prior endocarditis, mitral regurgitation with prior mitral annuloplasty, esophagitis, aortic sclerosis, and epilepsy. In regard to valvular location, the most prevalent was mitral with six cases. Aortic involvement was seen in five patients. Tricuspid valve was seen in one patient. Two patients underwent surgical management, while the other 11 underwent medical treatment alone with antibiotics. Vancomycin was the most commonly used antibiotic appearing in the regiment of seven patients. Gentamicin was used in five patients. Rifampin was used in four patients. Nafcillin, penicillin, ampicillin, and cloxacillin were used each in two patients. Amoxicillin, netilmicin, ceftriaxone, and pefloxacin were used each in one patient. Complications included heart failure in two patients, embolic phenomenon to the leg in two patients, arrhythmia in one patient, multiorgan failure in one patient, and facial nerve palsy with hemiplegia in one patient. In terms of mortality, two patients died with one patient having mitral involvement and the other aortic involvement (Table 1) [3, 14-22].

S. capitis Prosthetic Valve Endocarditis

Prosthetic valve endocarditis secondary to *S. capitis* infection has been described in 12 patients. In terms of demographics, seven patients were male and five were female. The median age was 68.6 years, with the youngest patient age of 48 and oldest patient age of 80. Comorbidities among the patients included coronary artery disease, atrial fibrillation, hypertension, cardiomyopathy, chronic obstructive pulmonary disease, chronic kidney disease, and peripheral artery disease. In regard to prosthetic valvular infection, the most prevalent was aortic with 10 cases. Mitral valve involvement was seen in four cases. One out of the 12 cases demonstrated both aortic and mitral valve prosthesis involvement. All patients underwent surgical management which consisted mostly of valve replacement. All patients were treated with antibiotics. Vancomycin was used in 10 patients; rifampin was used in seven patients; gentamicin was used in six patients; linezolid, teicoplanin, minocycline, and levofloxacin were used each in two patients; imipenem and amikacin were used each in one patient. Complications included heart failure in three patients, aortic root abscess in two patients, shock in two patients, aortic annular abscess in one patient, mitral annular abscess in one patient, embolic phenomenon to the leg in one patient, embolic phenomenon to the spleen in one patient, and adverse cerebrovascular event in one patient. Mortality was seen in four patients with one having mitral valve involvement and three having aortic valve involvement (Table 2) [9-12, 23].

Management

The primary preventive measures against IE are avoidance of intravenous drug use, prudent use of bioprosthetic devices, judicious catheter placement, and removal of unnecessary catheters in patients particularly those who are immunosuppressed [24]. Medical management includes identifying the pathogenic isolate in order to tailor antibiotic regimen. The most commonly used antibiotics found in our review in both native and prosthetic valve endocarditis were vancomycin, gentamicin, and rifampin [3, 9-12, 14-23]. For patients with complicated right-sided IE and left-sided IE with methicillin- or oxacillin-susceptible isolates, nafcillin or oxacillin can be used for 6 weeks with dosing of 12 g per 24 h intravenously in four to six equally divided doses. Cefazolin can be used in patients with non-anaphylactoid penicillin allergy for 6 weeks duration. The dosage is 6 g per 24 h intravenously in three equally divided doses. If anaphylaxis is a concern for both penicillin and cephalosporins, then vancomycin can be implemented. For oxacillin-resistant species, vancomycin at 30 mg per kilogram per 24 h intravenously in two equally divided doses or daptomycin at greater or equal to 8 mg per kilogram per dose can be used for 6 weeks. In regard to dosing and duration for prosthetic valve IE the dose for nafcillin or oxacillin is 12 g

Table 1. Native Valve Endocarditis

Reference	Patient	Gender	Age	Comorbidities	Location	Vegetation	Abscess	Antibiotic management	In-hospital surgical management	Complications	In-hospital mortality
[3]	1	Male	35	Epilepsy, hypertension, dilated cardiomyopathy	Aortic valve	Yes	No	Vancomycin, rifampin	No	Heart failure	No
[14]	1	Male	72	Cerebrovascular accident, peripheral vascular disease	Mitral valve	Yes	No	Vancomycin, gentamicin	No	No	No
[15]	1	Male	53	Not available	Mitral valve	Yes	No	Amoxicillin, netilmicin, ceftriaxone	No	Popliteal artery embolism	No
[16]	1	Male	63	Ventricular septal defect, prior endocarditis	Tricuspid valve	Yes	No	Cloxacillin	No	Heart failure	No
[17]	1	Male	46	End-stage renal disease	Aortic valve	Yes	No	Vancomycin, rifampin	No	Lower extremity gangrene	No
	2	Male	35	Not available	Aortic valve	Yes	No	Vancomycin, rifampin	No	No	No
[18]	1	Male	73	Hypertension, esophagitis	Mitral valve	Yes	No	Ampicillin, cloxacillin, gentamicin	No	Hemiplegia, facial palsy	Yes
[19]	1	Male	29	Not available	Mitral valve	No	No	Penicillin, gentamicin	No	No	No
	2	Male	62	Not available	Mitral valve	No	No	Vancomycin, penicillin, gentamicin, pefloxacin, rifampin	Yes	No	No
[20]	1	Male	79	Diabetes mellitus, renal insufficiency, coronary artery disease, hypertension, aortic sclerosis, mitral regurgitation	Aortic valve	Yes	No	Vancomycin, nafcillin	No	Multiorgan failure	Yes
[21]	1	Male	70	Hypertension, diabetes mellitus	Aortic valve	Yes	No	Nafcillin, gentamicin	No	Arrhythmia	No
[22]	1	Male	53	Mitral regurgitation (prior mitral annuloplasty)	Mitral valve	Yes	No	Ampicillin, vancomycin	Yes	No	No

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Table 2. Prosthetic Valve Endocarditis

Reference	Patient	Gender	Age	Comorbidities	Location	Vegetation	Abscess	Antibiotic management	In-hospital surgical management	Complications	In-hospital mortality
[9]	1	Male	72	Coronary artery disease, hypertension, atrial fibrillation	Aortic valve	No	Yes	Vancomycin, gentamicin, rifampin	Yes	Heart failure, aortic root abscess	Yes
	2	Female	48	Hypertension	Aortic valve	Yes	Yes	Vancomycin, gentamicin, rifampin	Yes	Leg embolism, heart failure, shock, aortic root abscess	Yes
[10]	1	Female	79	Not available	Aortic valve	Yes	Yes	Vancomycin	Yes	None	No
	2	Female	79	Not available	Aortic valve	Yes	No	Vancomycin, rifampin, minocycline	Yes	None	No
	3	Male	76	Not available	Aortic valve	Yes	Yes	Teicoplanin, vancomycin, linezolid, levofloxacin	Yes	Aortic annular abscess	No
	4	Female	68	Not available	Mitral valve	No	No	Vancomycin, gentamicin, levofloxacin	Yes	Mitral annular abscess, heart failure	No
[11]	1	Female	65	Not available	Mitral valve	No	No	Imipenem, vancomycin	Yes	None	No
[12]	1	Male	55	Not available	Aortic and mitral valve	No	No	Vancomycin, gentamicin, rifampin	Yes	Spleen embolism, cerebral infarct	No
[23]	1	Male	74	Dilated cardiomyopathy, chronic obstructive pulmonary disease, chronic kidney disease, peripheral artery disease	Mitral valve	Yes	No	Rifampin, vancomycin	Yes	Heart failure, shock	Yes
	2	Male	69	Diabetes mellitus, chronic obstructive pulmonary disease, peripheral artery disease, ischemic cardiomyopathy	Aortic valve	No	Yes	Rifampin, vancomycin and gentamicin	Yes	None	No
	3	Male	80	Chronic obstructive pulmonary disease, diabetes mellitus	Aortic valve	Yes	Yes	Rifampin, vancomycin, and gentamicin	Yes	Shock	Yes
	4	Male	58	None	Aortic valve	No	No	Amikacin, linezolid, teicoplanin, minocycline	Yes	None	No

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per 24 h intravenously for 6 or greater weeks, rifampin 900 mg per 24 h intravenously or orally in three equally divided doses for 6 or greater weeks, and gentamicin 3 mg per kilogram per 24 h intravenously or intramuscularly divided into two or three doses for 2 weeks. For oxacillin-resistant strains, the dosing for vancomycin is 30 mg per kilogram per 24 h in two equally divided doses for 6 or greater weeks and rifampin and gentamicin with same dosing and duration as native valve IE [1]. For uncomplicated right-sided IE cases, a 2-week duration can be used. Surgical management is indicated in instances where a patient is presenting with acute heart failure, periannular abscess, large vegetation greater than 15 mm, or signs of cerebrovascular compromise [25].

Discussion

Aside from having a large clinical burden, the economic burden imposed by *S. capitis* IE has been shown to be upwards of $2.34 billion [26]. The aim of our study was to guide health care professionals by outlining the epidemiology, diagnosis, and management as it pertains not only to IE but specifically *S. capitis* IE. Furthermore, given its rarity we sought to consolidate the literature of prior described cases in order to appreciate the impact of *S. capitis* as a cause of IE. Our review of the literature looking at cases of *S. capitis*-related native and prosthetic valve endocarditis found that: 1) Although cases have been described in the literature of *S. capitis* causing endocarditis the quantity is small; 2) For cases involving the native valve medical management alone overall had good outcomes, with a few cases noted to have poor outcomes; 3) Surgical management was important in treating prosthetic valve IE; 4) The most common comorbidities in patients developing *S. capitis* IE was hypertension, diabetes mellitus, and renal insufficiency; and 5) The most common complication was heart failure. The antibiotics used for medical management were largely consistent with the recommendations in the American Heart Association (AHA) endocarditis treatment guidelines which recommend 6 weeks of therapy with vancomycin plus rifampin, with addition of gentamicin for the first 2 weeks for methicillin- or oxacillin-resistant CoNS involved in prosthetic valve endocarditis [1]. When complications did exist, they were devastating with shock and eventual death. Aside from characterizing cases of *S. capitis* IE, we looked at the epidemiology, diagnosis, and management of IE. Although, sample size was a major limitation of our study, from our knowledge we included most cases of *S. capitis* endocarditis reported in the literature.

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Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Author Contributions

Dr. Thakker drafted and was the main editor of the manuscript, as well as, creation of tables. Drs. Chatila, Reynoso, and Karnath played a key role in reviewing the quality of information, assisted in editing of the manuscript, and organization of information in the tables.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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