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Original Article

Pathologic findings in native infective endocarditis

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ABSTRACT

Background: There are few studies on the histologic findings in native infective endocarditis, especially regarding mimics of autoimmune valvulitis.
Methods: We prospectively studied 106 surgical specimens from 95 patients with a clinical diagnosis of infective endocarditis on native valves, and compared gross and histologic findings with culture results, underlying valve disease, risk factors and time interval from symptom onset to surgical intervention.
Results: There were 41 (39%) aortic, 33 (31%) mitral, 9 (9%) tricuspid, 1(.9%) pulmonic and 11 (10%) multiple valve replacements. Underlying valve disease was present in 26 (27%) patients (non-calcified bicuspid aortic valve, 10 (38%) cases; mitral valve prolapse, 5 (19%) cases; calcified trileaflet aortic valve, 5 (19%) cases; calcified bicuspid aortic valve, 2 (8%) cases; post-rheumatic mitral valve disease, 2 (8%) cases; hypertrophic cardiomyopathy-related mitral valve disease, 1 (4%) case, trileaflet aortic insufficiency 1 (4%) case) and associated with streptococcal infection ($p = .001$). Absence of underlying valve disease was associated with intravenous drug abuse ($p = .01$) and dialysis dependent renal disease ($p = .006$). Intravenous drug abuse was associated with staphylococcal infection ($p = .03$). Vegetations were present in 80 (75%) of cases, and on the nonflow surface of the valve in 65 (81%) of these. Gram-stain positivity and neutrophilic microabscesses were associated with staphylococcal infection ($p = .03$). Epithelioid macrophages with palisading features mimicking necrobiotic granulomas were seen in 42 (40%) valves and more frequently associated with streptococcal infection ($p = .03$). As expected, the presence of valve necrosis and acute inflammation decreased with an increase in time with respect to symptomatic onset.
Conclusion: Histologic findings that mimic autoimmune inflammation are frequent in infective endocarditis and associated with streptococcal infection. Risk factors for infective endocarditis include calcific valve disease.

Introduction

The incidence of infective endocarditis has been estimated at about 161 per million population annually [1]. Infective endocarditis continues to be an underdiagnosed and undertreated disease, despite a mortality rate far superior to that of acute coronary syndromes [2]. Surgery is necessary in up to 50% of cases and is generally indicated if there is systemic embolization, paravalvular extension of infection or irreversible valve damage resulting in insufficiency and heart failure. In most cases that require surgery, valve replacement is performed, with valve-sparing repairs and vegectomies when possible. Currently, the recommended treatment approach to infective endocarditis includes early surgical intervention, including patients that would have been considered too high risk [3]. Therefore, it is not surprising that the rate of surgical intervention of infective endocarditis has been increasing over time [1].

Although the incidence of infective endocarditis has remained constant, there has been a decrease in its association with underlying valve disease, i.e. rheumatic heart disease. A recent pathology series from a tertiary center identified trends in underlying organisms and valve disease among infective endocarditis cases; highlighting the current changes occurring in the epidemiology of these two areas [4]. Although there have been reviews on the pathogenesis and pathologic features of infective endocarditis, there are few reports specifically characterizing the histologic findings and correlating to clinical and microbiological data [5].

Methods

Patients with a diagnosis of active or healed infective endocarditis involving a native cardiac valve removed at surgery between

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Table 1
Clinical and microbiologic features, 95 patients with endocarditis.

Underlying causes	*n*	Mean age	M:F	Valve[g]	% embolic	% strepto-cocci	% staphylo-cocci	% cult neg	% other
Underlying valve disease alone[a]	20	51	16:4	Ao 8 M 9 Mult 3	11	70[f]	25	5	0
Conditions leading to chronic active bacteremia, underlying normal valve	55	50	34:21	Ao 21 M 18 T 9 Mult 6 P 1	25	24	54	13	9
Intravenous drug use	24	44	13:11	Ao 10 T 8 M 4 Mult 1 P 1	38	25	67	8	0
End stage renal disease – dialysis	24	55	17:7	M 11 Ao 7 Mult 5 T 1	21	25	54	8	12.5
Renal transplant	3	56	2:1	M 2 Ao 1	0	0	0	33	67
Intravenous drug abuse and end stage renal disease	2	51	2:0	Ao 2	0	0	50	50	0
Active chronic bacterial infections[b]	2	59	0:2	Ao 1 M 1	0	50	0	50	0
Valve disease[c] with predisposing condition[d]	15	53	4:2	Ao 9 M 5 Mult 1	33	33	17	17	33
No active bacteremia or valve disease[e]	14	57	10:4	Ao 8 M 5 Mult 1	27	71[f]	7	14	7
Total	95	51	64:31	Ao 41 M 33 Mult 11 T 9 P 1	23	40	39	12	9

[a] Bicuspid aortic valve, non calcified (8); calcified bicuspid aortic valve (1), mitral valve prolapse (5); rheumatic mitral disease (2); trileaflet aortic insufficiency secondary to aortic aneurysm (1), nodular calcific aortic stenosis (2); hypertrophic cardiomyopathy (1). Two patient had recent dental work, one diskitis, and one meningitis with diskitis.
[b] Suppurative pharyngitis complicated by mastoiditis; urosepsis complicating metastatic colon carcinoma.
[c] Trileaflet nodular calcific aortic stenosis (3), bicuspid aortic valve, non-calcified (2), calcified bicuspid aortic valve (1).
[d] IVDA (3), ESRD (2), chronic total parenteral nutrition (1). One patient with trileaflet nodular calcific aortic stenosis had end-stage renal disease.
[e] 7 patients had diabetes; 1 bad dental care; 1 chronic obstructive lung disease; 1 Grave's disease; 1 myasthenia gravis; 1 rheumatoid arthritis; 1 intrauterine fetal demise.
[f] $p = .001$ vs. patients with chronic bacteremia.
[g] Ao, aortic; M, mitral; P, pulmonic; T, tricuspid; Mult, multiple.

Table 2
Underlying valve disease, 26 patients.

Underlying disease	M:F	Age, years, mean	Organism
Bicuspid aortic valve, non-calcified valve (9)[a]	8:1	38	Streptococci (6) Staphylococci (3)
Bicuspid aortic valve, with nodular calcifications (2)[b]	2:0	68	Streptococcus (1) Corynebacterium (1)
Nodular calcific aortic disease, trileaflet valve (5)	4:1	67	Culture negative (2) Multiple (1) Streptococci (1) Staphylococci (1)
Mitral valve prolapse (5)	4:1	50	Streptococci (5)
Rheumatic mitral valve disease (2)	1:1	63	Streptococci (1) Staphylococci (1)
Hypertrophic cardiomyopathy (2)	0:2	43	Streptococci (1) Staphylococci (1)
Ascending aortic aneurysm with aortic insufficiency, trileafet valve (1)	1:0	56	Streptococci (1)

[a] The existence of pre-existing insufficiency was difficult to ascertain because of the superimposed infectious process. One patient had a dilated ascending aorta by intraoperative transesophageal ultrasound, but no patient had ascending aneurysm repair.
[b] Nodular calcification seen grossly and histologically.