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Unexpected Death as a Result of Infective Endocarditis

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ABSTRACT: Thirteen cases of infective endocarditis (IE) diagnosed for the first time at autopsy or, in those patients with a previous diagnosis of IE, not thought to be active at the time of death, are presented. Of the six patients who died within 24 h of the onset of symptoms, two died of obstruction of a valve orifice, two died of sepsis, one died of sepsis and alcoholic cardiomyopathy, and one died of a coronary artery embolus. Of the five patients with symptoms lasting more than 24 h, three died of sepsis and congestive heart failure. One died from sepsis alone and one died from congestive heart failure (CHF). In two patients whose duration of symptoms is unknown, one died of sepsis and CHF, and in the other the mechanism of death is unknown. Predisposing factors present in 11 of 13 patients included alcoholism (three), intravenous (IV) drug abuse (three), prosthetic valves (three), aortic stenosis (two), past rheumatic fever (one), and nonstenotic congenitally bicuspid valves (two). The reasons for no antemortem diagnosis were a missed or incorrect clinical diagnosis in three patients seen by a physician shortly before death, no signs or symptoms or found dead (four), nonspecific signs and symptoms (three), refusal of medical treatment (one), and a solitary lifestyle (one); there was insufficient information about one patient. Individuals with needle tracks, generalized petechiae, Osler's nodes, splinter hemorrhages, intravenous catheters, pacemaker wires, and infected aortic-valve (A-V) shunts are at risk of IE. Blood and the vegetations should be cultured. The attending physician should be notified of the diagnosis in such cases.

KEYWORDS: pathology and biology, infective endocarditis, death

Classically acute infective endocarditis (IE) manifests itself by the dramatic onset of a changing heart murmur, high fever, and severe malaise. In practice, however, the onset of IE is often variable and nonspecific. Presenting signs and symptoms can vary from the insidious onset of weakness, anorexia, headache, fatigue, and vertigo to the sudden occurrence of fever, chills, and abdominal or central nervous system symptoms [*1*]. We present 13 patients dying of IE whose diagnoses were first made at autopsy. All died outside a hospital or shortly after admission. The histories and autopsy findings are compared with those presented in previously published papers.

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Case Reports

Case 1 (BMMC)

A 47-year-old man who lived alone and had few friends was found dead by police, who had been called by the patient's doctor because he had failed to keep an appointment. He was being evaluated for malabsorption. There was evidence of fecal incontinence with hematochezia and hematemesis. The scene investigation and autopsy findings indicated that he had been dead approximately 6 days. Past history was positive for gastrointestinal bleeding and malabsorption. At autopsy, the aortic valve contained a vegetation measuring 1 by 0.5 cm. Gram-positive cocci were present within the vegetation. Microabscesses were noted within the myocardium, and there were numerous septic emboli within the central nervous system and one septic embolus within a kidney. The combined lung weight was 2000 g as a result of marked pulmonary edema.

Case 2 (BMMC)

A 32-year-old man found dead at home at 3:00 a.m. had a 20-year history of alcohol abuse. He had marked mental status deterioration, including hallucinations, for several days before his death. His sister felt that these were symptoms of alcohol withdrawal. He had been anorexic and was confined to bed for the last five days of life. He was taken several times during that week by his family to a hospital emergency room but was not admitted because he was thought to be intoxicated. On the day of death an ambulance had been summoned, but he was not transported because the ambulance attendants thought that the family would be able to take care of him and that he would get better on his own in several days.

The autopsy showed the presence of vegetations on the right and noncoronary cusps of the aortic valve with a perivalvular abscess that extended into the right ventricular cavity. *Streptococcus pneumoniae* was cultured from the blood, and gram-positive diplococci were seen in gram-stained sections of the vegetation. There was marked pulmonary edema (combined lung weight 1500 g), focal bronchopneumonia, meningitis, and ventriculitis. The liver showed alcoholic hepatitis. The alcohol and drug screen were negative.

Case 3 (BMMC)

A 26-year-old white woman was seen in an outpatient medical clinic because of mild sinus congestion manifested by postnasal drip at 8:10 a.m. on the morning of death. An examination by a physician's assistant showed her lungs were clear to percussion and auscultation. Her temperature was 98°F (36.6°C), her pulse was 100/min, and her blood pressure was 142/80 mm of mercury. She did not complain of shortness of breath. Her heart was normal in size, rate, and rhythm. She was treated with Septra DS™ and Entex LA™. On the way home she complained of fatigue and had difficulty walking up the steps to get to her room. Her girlfriend heard her fall in the bathroom at approximately 10:45 a.m. Upon arrival of the paramedics she was in cardiopulmonary arrest with fixed and dilated pupils. Resuscitation was unsuccessful.

Her medical history included an episode of rheumatic fever at age 14 requiring 3 months of hospitalization. She had been well since except for occasional headaches.

The autopsy, conducted 20 h after death, revealed a 2.1-cm vegetation attached by a broad base to the posterior leaflet of the mitral valve, causing nearly total occlusion of the mitral valve orifice. The chordae tendineae of the mitral valve were fused, thickened, and shortened. There was commissural fusion extending nearly to the lunulae of the left and right aortic-valve (A-V) cusps, which contained a 0.3- by 0.2-cm vegetation. The commissure between the left and noncoronary cusps was minimally fused. There were

multiple old and subacute microinfarcts of the left ventricle, with occasional intramyocardial arterial emboli and multiple old infarcts of the kidneys. Gram and Gomori's methenamine silver (GMS) stains of the vegetations revealed no organisms, and blood cultures and bacterial and fungal cultures of the mitral valve vegetations yielded no growth.

Case 4 (New Mexico)

This 42-year-old Caucasian woman was pronounced dead on arrival at a hospital emergency room. She had a history of hypertension. The circumstances of her collapse, including the duration of any symptoms, are unknown.

The autopsy revealed the presence of numerous vegetations on the mitral valve, with the greatest dimensions ranging from 0.1 to 2.0 cm. The lungs were moderately edematous (combined lung weight 1025 g). The spleen weighed 175 g. No cultures were taken and gram stains were not done.

Case 5 (New Mexico)

A 60-year-old Latin American man who had the sudden onset of cold, chills, dizziness, chest pain, numbness in the arms and shoulders, and shortness of breath died shortly after arrival at a clinic. There was no other pertinent medical history.

Autopsy findings included calcific aortic stenosis with a 1.5-by 1.0-by 1.0-cm red-brown vegetation firmly attached to the right aortic valve cusp and extending into the valve orifice. Alpha streptococcus was cultured from the blood.

Case 6 (New Mexico)

An eleven-year-old Caucasian girl with a two-day history of nausea and one-day history of vomiting died at home approximately 15 min after vomiting some soup. She had undergone replacement of her native aortic valve with a porcine bioprosthesis five years before death.

Autopsy findings revealed the presence of a 0.6-cm vegetation on one of the cusps of the bioprosthetic aortic valve. The left main and left circumflex coronary arteries contained occlusive septic emboli. The 530-g heart showed left ventricular hypertrophy. There were bilateral pleural effusions and pulmonary edema. Microscopically there were septic emboli within the coronary arteries. *Streptococcus viridans* was isolated from the vegetation.

Case 7 (St. Louis)

This 29-year-old Caucasian woman had an onset of left chest pain that radiated down the left arm. Three weeks before she had undergone placement of a bioprosthetic valve in the tricuspid position resulting from IE caused by intravenous (IV) drug abuse. She was evaluated in a hospital emergency room where an electrocardiogram (EKG) was interpreted as negative and she was diagnosed as having musculoskeletal pain. Twelve hours later she again went to an emergency room for shortness of breath and shortly after arrival had a cardiac arrest from which she could not be resuscitated.

Pertinent autopsy findings revealed a Hancock bioprosthesis in the tricuspid position with a 2-cm vegetation on the ventricular surface of the valve occluding the valve orifice. There was moderate pulmonary edema with a combined lung weight of 1460 g, liver congestion, and splenomegaly (340 g). No organisms were seen on gram stain of the vegetation. No cultures were taken.

Case 8 (St. Louis)

This two-year-old Caucasian girl was sleeping with her mother. The mother awoke to discover the child vomiting. Shortly afterward the child collapsed and was pronounced dead approximately 1 h later at a hospital emergency room.

The child's physician had been following her since birth for a small ventricular septal defect that was felt to be hemodynamically insignificant. She had chronic anemia treated with iron and had had an episode of pneumonia four and one-half months before death.

At autopsy the 200-g heart had a 0.4- by 0.3-cm defect through the membranous portion of the interventricular septum. There was vegetations up to 2 cm thick along the periphery of the congenitally bicuspid aortic valve. The vegetations extended through the valve ring to form a 6- by 4-mm vegetation on the surface of the mitral valve. The 350-g spleen was congested. There was an acute takeoff of the left main coronary artery.

Microscopically there were microabscesses within the myocardium. *Streptococcus intermedius* was cultured from the aortic valve. Gram-positive cocci were present.

Case 9 (St. Louis)

This 45-year-old black man was found unresponsive and hypotensive at 5:45 a.m. He was taken to a local hospital, where he had a cardiac arrest and was pronounced dead at 8:20 a.m. on the day of admission. He had a past history of IV drug abuse and chronic alcoholism. Four days before death he was seen in the emergency room of the same hospital and was diagnosed as having possible endocarditis, pleural effusion, and cirrhosis of the liver. He left the hospital against medical advice. Five months before death he was admitted for a four-month hospital stay for treatment of heroin and cocaine addiction, ethanol abuse, seizures, hypertension, biliary obstruction, and status post gunshot wound of the abdomen. He was discharged two and one-half weeks before death.

At autopsy, the 470-g heart had multiple vegetations on the tricuspid valve, with the largest measuring 2 cm in greatest dimension. There was a perforated thin fibrous membrane within the right atrium which contained 1 to 2-mm vegetations. There were multiple small vegetations on the atrial surface of the mitral valve. There was no evidence of preexisting valve disease. The three major coronary arteries showed 95% atherosclerotic narrowing. The lungs showed marked congestion and edema (combined weight 1595 g). There was micronodular cirrhosis of the liver and marked splenomegaly (710 g).

Microscopically there were microabscesses in the myocardium, kidney, brain, and spinal cord. The lungs contained pneumonia and diffuse alveolar damage. Cultures were not taken, and gram stains of the vegetations demonstrated gram-positive cocci. Blood ethanol was 35 mg/dL, and blood morphine was 0.22 μg/mL.

Case 10 (St. Louis)

This 69-year-old black man was found dead lying on the sidewalk by a passerby at 1:19 a.m. A pint of whisky was present in a trouser pocket. Two other liquor bottles were found adjacent to the body. The deceased appeared well when seen approximately 20 min before being found.

At autopsy, the 670-g heart showed biventricular hypertrophy and dilatation. There was mild to moderate myxomatous degeneration of the tricuspid valve, and two vegetations measuring up to 1.5 cm were found on its atrial surface. A 0.6-cm friable vegetation was on the anterior mitral valve leaflet. There was marked pulmonary congestion (combined lung weight 1100 g) and splenomegaly (460 g). Microscopically, the base of the vegetations showed organization. Gram-positive cocci were seen but cultures were not taken. Blood ethanol was 179 mg/dL.

Case 11 (St. Louis)

This 30-year-old Caucasian woman who had had a "cold" for two weeks collapsed in her backyard. Two weeks before death, after complaining of transient left-sided numbness, she had an electroencephalogram (EEG), which was unremarkable. There was a history of a small ventricular septal defect that was felt to be clinically insignificant.

At autopsy, the 320-g heart contained a 0.5-cm septal defect through the membranous portion of the interventricular septum. The congenitally bicuspid aortic valve contained vegetations measuring up to 1 cm; these were most prominent on the anterior cusp. There was a vegetation on the tricuspid valve. A small renal infarct was noted. The 200-g spleen was congested. The combined lung weight was 740 g.

Microscopically, the vegetation of the aortic valve extended into the subvalvular tissue with abscess formation. There was a septic embolus within the left kidney. Gram-positive cocci were present in the vegetation. Cultures were not obtained.

Case 12 (St. Louis)

This 21-year-old black woman collapsed after arguing with her boyfriend for approximately 20 min. She grabbed her chest and fell to the floor. She was pronounced dead in a local emergency room.

Two years before death she had an episode of IE caused by aortic stenosis. One year before death she was treated for IE but received an incomplete course of antibiotics. Eight months before death she was treated for IE. Echocardiography showed a vegetation on the aortic valve.

At autopsy, the 410-g heart contained a vegetation occluding the left coronary artery at the ostium. Vegetations were noted on all aortic valve cusps. The vegetation from the left cusp had extended into the sinus of Valsalva occluding the ostium. Bacterial and fungal cultures and tissue stains failed to demonstrate any organisms. There was a jet lesion on the interventricular septum. Aortic stenosis was present. Recent and old infarcts were present within the left kidney. The spleen weighed 240 g.

Case 13 (St. Louis)

This 29-year-old black man with a history of IV drug abuse collapsed in the bathroom of his home. Earlier in the day he was seen in a clinic complaining of dyspnea and left chest pain after climbing one flight of stairs. He was given prednisone and sent home. The chest pain continued up to the time of his collapse. He was pronounced dead on arrival at a local hospital.

His past history included positive *Staphylococcus aureus* brain abscess. Three years before death a murmur of aortic insufficiency was noted. From three to one and one-half years before death he had three episodes of IE. Fifteen months before death his aortic valve was replaced. He subsequently was treated for pericarditis, pericardial effusion, and anemia. He underwent a six-week course of antibiotic treatment for a staphylococcal endocarditis which was discontinued three weeks before death.

At autopsy, a Bjork-Shiley prosthetic valve was present in the aortic position. There was an aortic ring abscess involving approximately one half of the valve circumference. There was a vegetation on the anterior mitral valve leaflet. The heart weighed 650 g, and there were subendocardial fibrosis, bilateral remote renal infarcts, and multiple remote splenic infarcts. Neither the blood nor vegetations were cultured.

Discussion

We have identified 13 cases of death as a result of IE in three forensic pathology practices (see Table 1 for a summary of each case). Six cases were from St. Louis. Out of about 2625 autopsies, there were 3/7000 autopsied cases from New Mexico and 3/2372 from Grand Rapids. The patients ranged in age from 2 to 69 years, with a median age of 30 and a mean age of 34. There were six males and seven females. Specific organisms were identified in four cases: *Streptococcus pneumoniae* in one instance and alpha streptococci in the other three. In eight cases no cultures were obtained. Gram stains were performed on the tissue in 10 cases, demonstrating the presence of gram-positive cocci in seven cases and failing to demonstrate organisms in the other three. In two cases, tissue gram stains were not performed, but gram-positive cocci (*Streptococcus viridans* and alpha-streptococcus) were cultured from the blood or vegetations. In one case, neither tissue organism stains or cultures were obtained.

IE presented clinically in different ways in our patients. Four patients were found dead, four were seen to suddenly collapse, two had the acute onset of heart failure, and two presented with systemic symptoms, and nausea and vomiting, respectively. The available history on the final patient stated that she was brought in dead to a hospital.

One third [*2,3*] to two thirds [*4*] of hearts are reported to have no preexisting disease before the onset of infection. In four of our cases there was no underlying valve disease, and in one case the description given was insufficient to make this determination.

Cardiac abnormalities predisposing to IE include rheumatic heart disease, congenital heart disease (especially tetralogy of Fallot, ventricular septal defect, patent ductus arteriosus, congenital aortic stenosis, and coarctation of the aorta), floppy mitral valve, degenerative heart disease (such as senile calcific aortic stenosis and mitral annulus calcification), hypertrophic obstructive cardiomyopathy, indwelling cardiac catheters and pacemakers, recent cardiac surgery, prior IE, and prosthetic valves [*1–6*]. Rheumatic heart disease, congenital heart disease, and floppy mitral valve most commonly predispose the patient to IE [*3,6*].

Predisposing cardiac factors in our cases included prior IE in three, prior rheumatic fever in one, aortic stenosis in two, prosthetic valves in three, and nonstenotic congenitally bicuspid valves in two. In each of these latter two patients there was also a ventricular septal defect that was considered hemodynamically insignificant; in Case 8, this defect did not play a role in the genesis of the IE, and in Case 11, the tricuspid valve appears to have been infected by continuous spread from the aortic valve through the defect.

In three patients there were infected prosthetic valves: one at the tricuspid position and two at the aortic level. Prosthetic valve infection accounts for up to 16% of all cases of IE [*2*]. About half the cases occur within two months of surgery, usually as a result of contamination of the valve at the time of placement, while the late-occurring half result from blood-borne organisms [*5,7*]. In early occurring IE *Staphylococcus* species, gram-negative bacteria, and fungi, chiefly *Candida*, predominate, while the *Streptococcal viridans* group, Group D enterococci, and staphylococci cause late-occurring IE [*5*]. In two of our cases, continued IV drug abuse probably led to valve infection. Annular abscesses, present in one of our cases, can lead to valvular dehiscence and extension into surrounding heart structures [*2*]. Valve stenosis, as found in our Case 7, tends to occur in mitral valve prostheses, while infected aortic valve prostheses are prone to incompetence. Atkinson and Virmani describe a 22-year-old man with occlusion of a Starr-Edwards aortic valve by *S. aureus* endocarditis [*2*]. Overall mortality of IE in all prosthetic valves is 60% and is even higher when infection occurs soon after valve placement [*5*]. The rates of infection and complications in mechanical and heterograft prostheses are equal [*2*].

TABLE 1—*Summary of 13 deaths by IE.*

Case	Location[a]	Age/Sex	Valve[b]	Organism	Signs/SX[c]	Predisposing Factors[d]	Autopsy Findings[e]	Reason for No Diagnosis
1	BMMC	47/M	AV	G(+) cocci in valve	found dead, evidence of hematemesis at scene	none	pulmonary edema; combined lung weight 2000 g; septic emboli in CNS and kidney; spleen 220 g	reclusive lifestyle
2	BMMC	32/M	AV	*S. pneumoniae* in blood; G(+) diplococci in valve	anorexia, disorientation, malaise × 5 days	alcoholism	perivalvular abscess, meningitis and ventriculitis, focal pneumonia, pulmonary edema; spleen 190 g	failure of patient and family to recognize illness; CNS SX mistaken for delerium tremens
3	BMMC	26/F	MV and AV	none cultured in blood or valve; gram negative, GMS negative	sinusitis; SOB, fatigue immediately before collapse	rheumatic changes MV and AV; microinfarcts	pulmonary edema; spleen 250 g	no signs or SX
4	New Mexico	42/F	MV	no cultures or gram stains done				
5	New Mexico	60/M	AV	alpha streptococcus from blood	sudden onset of dizziness, SOB, angina, numbness in arms and shoulders, cold chills	calcific aortic stenosis	LVH (0.7 cm LV)	sudden onset of SX

6	New Mexico	11/F	AV	*S. viridans* from valve	two-day history N&V; died 15 min after last vomiting episode	Prosthetic porcine AV; 5 years PTD	bilateral pleural effusions; emboli in LCA and LCx; LVH (530 g); no infarct on microscopic; septic emboli in several coronary arteries LM and LCx	nonspecificity of SX
7	St. Louis (bioprosthesis)	29/F	TV	none seen on gram stain	12-h history of chest pain, seen in ER; returned with SOB, collapsed in ER 12 h later.	IV drug abuse; valve replacement for IE	splenomegaly	misdiagnosed as musculoskeletal pain
8	St. Louis	2/F	MV and AV	*S. intermedius*	vomited, then became unresponsive	congenital bicuspid AV and small VSD	splenomegaly; myocardial microabscesses	sudden unexpected death
9	St. Louis	45/M	TV, R. atrium MV	gram-positive cocci	found unresponsive at home	IV drug abuse; alcoholism	microabscesses in myocardium, kidney, brain, and spinal cord; pneumonia and diffuse alveolar damage; splenomegaly; cirrhosis.	refused medical treatment
10	St. Louis	69/M	MV and TV	gram-positive cocci	found dead on sidewalk	alcoholism	alcoholic cardiomyopathy; splenomegaly	sudden death, "street person"
11	St. Louis	30/F	AV TV	gram-positive cocci	found collapsed in yard; "cold" for last two weeks of life; transient left-sided numbness two weeks before death	bicuspid AV, VSD through membranous septum	extension of abscess into subvalvular zone with abscess formation; septic embolus in kidney	sudden death

TABLE I—*Continued.*

Case	Location[a]	Age/Sex	Valve[b]	Organism	Signs/SX[c]	Predisposing Factors[d]	Autopsy Findings[e]	Reason for No Diagnosis
12	St Louis	21/F	AV	organism not demonstrated by culture or microscopy	collapsed while arguing; two past episodes of IE, poorly treated	aortic stenosis	recent and old left kidney infarct; occlusion of LCA ostium by embolus	sudden death (coronary artery embolus)
13	St. Louis	29/M	Bjork-Shiley prosthesis. AV position + anterior MV leaflet	Gram-positive cocci (presumed *Staphylococcus aureus*)	collapsed in bathroom at home; three prior episodes of IE; seen in ER night before death with DOE and left chest pain; chest pain last month of life	IV drug abuse	aortic ring abscess, cardiomegaly, and aortic ring abscess; multiple remote infarcts of spleen and kidneys	no clinical suspicion

[a]BMMC = Blodgett Memorial Medical Center.
[b]AV = aortic valve; MV = myocardial valve; TV = tricuspid valve; R = right.
[c]SX = symptoms; SOB = shortness of breath; NV = nausea and vomiting; ER = emergency room; DOE = dyspnea on exertion.
[d]PTD = prior to death; VSD = ventricular septal defect.
[e]LVH = left ventricular hypertrophy; LCA = left coronary artery; LCx = left circumflex coronary artery; LM = left main coronary artery.

Bacteremia or fungemia leading to IE can result for IV drug abuse, hemodialysis, dental procedures, urinary or gastrointestinal tract instrumentation, infected indwelling catheters, and infections [*1,3*]. Immunosuppression from any cause, especially alcoholism, diabetes, neoplasm, or chemotherapy, renders one susceptible to IE [*1,3–6*]. In our cases, IV drug abuse served as a source of bacteria in three patients. Two of these had prosthetic valves. One IV drug abuser was also an alcoholic.

Of our patients 3 were alcoholics, contrasting with 4 alcoholics out of 541 patients with IE reported by Bayliss [*3*]. Alcoholics are particulary prone to pneumococcal endocarditis, as in our Case 2. Alcoholics are well known to be immunodeficient with granulocytopenia and deficient granulocyte delivery to infected sites. There is poor clearance of bacteria from the lungs and reticuloendothelial system, depression of cell mediated immunity, and deficient antibody response to new antigens [*8*]. Alcoholics are probably overrepresented in our series because they are less likely to come to medical attention in the course of their IE.

There were a variety of reasons the antemortem diagnosis of active IE was not made except in one case (Case 9). One patient, obviously ill before death, lived alone and apparently was too sick to obtain medical help. Three patients who sought medical attention for symptoms suggestive of IE were misdiagnosed: in one there was no clinical suspicion and he was sent home with a prescription for prednisone; in one the symptoms were mistaken for delirium tremens; and in one case the patient was felt to have musculoskeletal pain. Three patients had nonspecific symptoms: one had nausea and vomiting; one had a "cold" the last few weeks of life; and one had sinusitis. Four patients either had no evidence of IE until just before death or were found dead. One patient, Case 9, refused medical therapy in spite of a diagnosis of "possible endocarditis." In one case we had insufficient information to determine why an antemortem diagnosis was not made.

In 70 to 90% of cases of IE, death results from congestive failure because of left-sided valve destruction [*1,2,4,6,7,9*]. Other less common causes include embolism, rupture of mycotic aneurysm, dysrhythmias, sepsis and acute pneumonia, and coronary ostial occlusion [*10,11*].

This contrasts with our series in which four patients died of sepsis (manifested by multiple abscesses, positive blood cultures, or both) and congestive heart failure (CHF), three died of sepsis alone, two of coronary emboli, two of valve orifice obstruction, one of sepsis and alcoholic cardiomyopathy, and in one patient there were insufficient data to determine the mechanism of death.

Atkinson and Virmani [*2*] state that 90% of cases of IE involve the left-sided valves; in our series of the ten patients with native valves, left-sided valves were involved exclusively in seven cases and in combination with right-sided valves in the other three. In our series the aortic valve only was infected in four patients, the mitral and aortic valves in two, the mitral valve only in one, the aortic and tricuspid valves in one, the mitral and tricuspid valves in one, and the tricuspid valve, a right atrial membrane, and mitral valve in one.

There have been few cases of sudden death caused by IE reported in the literature. Most large series of IE contain few or no sudden deaths. Greenberg et al. [*10*] and Dowling and Buja [*11*] reported cases of sudden death as a result of coronary ostial occlusion by aortic valve cusp vegetations. In each case there was propagation of the vegetation from the left coronary cusp directly into the left coronary ostium. One of the patients reported by Straus and Hamburger [*12*], a 35-year-old man, died suddenly 6 years after an episode of *Streptococcus pneumoniae* endocarditis. Autopsy revealed healed aortic and mitral rheumatic valvulitis, with a ruptured anterior aortic valve cusp and pulmonary edema. Walker and Hudson [*13*] reported a sudden death resulting from a ruptured mycotic aneurysm of the splenic artery in a patient with mitral IE caused by *Staphylococcus aureus*. Of the 22 deaths in the series reported by Pesanti and Smith [*14*],

3 were sudden, but the results of autopsies (if performed) were not mentioned. Perivalvular abscesses are likely to cause sudden death because of their propensity to initiate conduction defects. Myocardial ischemia or infarct, myocarditis, or myocardial abscesses can lead to ventricular ectopy [*5*].

Six of our patients died suddenly (within 24 h of the onset of symptoms). Two died of sepsis, one died of obstruction of the mitral valve orifice, one had occlusion of a porcine valve in the tricuspid position, one died of a coronary artery embolus, and the mechanism of death in the sixth patient was most likely sepsis with a contribution from alcoholic cardiomyopathy. In five patients there was evidence of IE for at least one day before death, although the patients were not under a physician's care at the time of their death. Of these five non-sudden deaths, three patients (Cases 1, 2, and 13) died of sepsis and CHF. Sepsis was manifested by abscesses in the myocardium and elsewhere, and CHF was diagnosed by pulmonary edema at autopsy and clinical evidence of CHF. One patient, Case 11, died of sepsis alone. Patient 6 died from coronary artery emboli. In two patients, the interval between onset of symptoms and death is unknown—one patient died of sepsis and CHF, and the mechanism of death in the other is unknown.

Complications of IE can be cardiac or extracardiac [*1,2,4,6,7,15*]. Cardiac complications include valve destruction, ruptured chordae tendineae or papillary muscles, myocardial and perivalvular abscesses, sinus of Valsalva aneurysm, myocardial injury (inflammatory and ischemic), pericarditis, and intracardiac fistula from rupture of a Valsalva sinus aneurysm. Myocardial infarcts may result from coronary emboli or from thrombosis caused by perivascular inflammation. Immune complex deposition can lead to myocarditis and pericarditis in indolent infections, whereas acute endocarditis more commonly results in intramyocardial abscesses and pericarditis occurring from bacteremia or direct extension from an abscess. Annular abscesses, associated with aortic valve infection, are characterized by valve regurgitation, pericarditis, high-degree A-V block, and death or severe disability soon after development of symptoms. The most significant extracardiac complications result from bland and septic emboli (especially to the brain, spleen, kidneys, and myocardium), mycotic aneurysms, metastatic infection, sepsis and immune complex glomerulonephritis [*1,2,4,6,7,15*]. Complications in our cases included perivalvular aortic abscesses in three cases, evidence of spread of infection (including abscesses and septic emboli) in five, valve orifice obstruction in two, and coronary artery emboli in two.

Pneumococcal endocarditis, present in Case 2, is distinctly unusual. Missri and Rohatgi [*16*] found no cases in a search of the literature for the decade preceding the publication of their single case, a 34-year-old man who developed aortic endocarditis 13 years after splenectomy. Strauss and Hamburger [*12*] reported 15 cases of pneumococcal endocarditis and found that the portal of entry for infection was pneumonia in 7, the sinuses in 3, and was unknown in 5. Thirteen had concomitant pneumococcal meningitis.

Valvular obstruction is a rare complication of infective endocarditis. Roberts and colleagues reported 2 patients [*17*]. The first was a 21-year-old woman who had acute rheumatic fever at age 10 and who developed Group B beta-hemolytic streptococcal endocarditis 3 months following a term pregnancy with normal labor. She died 1 month after onset of her disease, and at autopsy her mitral valve was obstructed by vegetations. Her immediate cause of death was a large intracerebral hemorrhage. The other patient, a 26-year-old narcotic addict who died following an 11-month illness was found to have aortic valve occlusion caused by *Candida parapsilosis* endocarditis. In neither patient was there an antemortem diagnosis of valve obstruction by vegetations. There is one report of a prosthetic aortic valve occlusion by IE [*2*] (vida supra). In our Case 3 a vegetation obstructed a mitral valve with post-rheumatic scarring, and in Case 7 there was occlusion of a porcine tricuspid valve.

Ten to fifteen percent of cases of IE are culture negative [*3,5,14,18*]. In two of our cases (Cases 3 and 12) blood cultures and tissue gram and GMS stains were negative,

while in the other four cases in which blood cultures were obtained, organisms were isolated. Reasons for culture negative IE include prior administration of antibiotics (the most common reason), anaerobic bacteria, nutritionally deficient streptococci, L-forms, fastidious organisms such as *Hemophilus* and *Brucella,* and nonbacterial causes, such as Chlamydia and fungi [*3,5,6,14,18*]. Pelletier and Petersdorf [*19*] reported that the mean duration of symptoms for culture negative IE was 61 days, for *Streptococcus viridans* 68 days, for *S. aureus* 14 days, and for *Streptococcus pneumoniae* 12 days. Pesanti and Smith [*14*] studied 52 patients with culture negative IE. Twenty-five patients underwent histologic examination of valve tissue. In six no organisms were seen on gram stains or grown in culture, suggesting that the majority of patients with a clinical diagnosis of IE will have an identifiable organism causing the infection in the presence of negative blood cultures [*14*].

Conclusion

In the investigation of death caused by IE, as in all cases coming to the attention of medical examiners, a thorough medical history should be obtained. On external exam the presence of needle tracks, petechiae, Osler's nodes, splinter hemorrhages, infected or colonized indwelling vascular catheters or wires, and infected A-V shunts should alert one to the possibility of IE [*2*]. We recommend culturing blood and the vegetation for bacteria and fungi (these cultures were not performed in all of our cases, and we acknowledge that this should have been done). Underlying cardiac disease should be documented and predisposing factors for IE identified. The results of the death investigation and autopsy should be discussed with the treating physician. Sudden death in IE is rare, but when detected in those undergoing forensic autopsy, it has occurred most commonly in those who did not seek or refused medical attention.

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