Extensive *Salmonella enteritidis* Endocarditis Involving Mitral, Tricuspid Valves, Aortic Root and Right Ventricular Wall

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After conducting a PubMed search, 11 articles describing a total of 12 cases of native valve *Salmonella enteritidis* (*S. enteritidis*) endocarditis were identified in the English literature. Only 13 cases of prosthetic valve endocarditis attributed to *S. enteritidis* have been published in the English literature. Only 1 case involving the myocardium and other valves concomitantly could be located. Transthoracic echocardiography proved inadequate to demonstrate valvular vegetations. Transeosophageal echocardiography was instrumental in establishing the diagnosis of endocarditis by documenting vegetations. *S. enteritidis* endocarditis can cause devastating endovascular infections in immunocompromised patients. Patients who present with multiple vague symptoms with medical histories that include diabetes mellitus, immunocompromise, and prosthetic heart valves should alert clinicians to strongly consider *S. enteritidis* endocarditis in their differential diagnoses. Despite considerable effort, *S. enteritidis* endocarditis poses very high risk for morbidity and mortality. (*J Am Soc Echocardiogr* 2009;22:210.e1–e3.)

Keywords: *Salmonella enteritidis*, Endocarditis, Valves, Myocardium

A 69-year-old African American woman with a history of diabetes mellitus presented to the emergency room with complaints of fever, chills, weakness, and lethargy of 4 to 5 days in duration. She reported urinary frequency and lower back discomfort radiating to the right groin. She denied any other symptoms, remote or recent history of food poisoning, or recent travel. She had not had any recent changes in her medications, other than increasing her insulin on her own because of increasing blood glucose levels. She denied any exposure to pets.

The patient’s history was significant for type 2 diabetes mellitus for 25 years with nephropathy and neuropathy, hypertension, hyperlipidemia, coronary artery disease, 4-vessel coronary artery bypass grafting in October 2003, and aortic valve replacement with a porcine valve secondary to degenerative aortic stenosis. She did not smoke or drink alcohol, and she had no history of intravenous drug abuse. The patient’s medication list included glyburide, gabapentin, esomprazole, trazodone, nortriptyline, aspirin, clopidogrel, metoprolol, furosemide, potassium chloride, and neutral protamine Hagedorn insulin.

Physical examination on admission showed a temperature of 101.5°F; blood pressure of 143/72 mm Hg; a pulse of 72 beats/min, a respiratory rate of 18 breaths/min, and oxygen saturation of 98% on room air. The neck was supple, with a full range of motion and no onadistended, with normal bowel sounds. The patient’s mouth was dry, and her breath had an acrid odor. The chest was clear on auscultation. The abdomen was soft, nonaggravated, and nondistended, with normal bowel sounds. The patient did have some right costovertebral angle tenderness. The results of a neurologic examination were nonfocal.

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Laboratory results on admission were as follows: white blood cell count, $13.1 \times 10^9$/mm$^3$; hemoglobin, 12.8 g/dL; hematocrit, 38.2%; mean corpuscular volume, 88.2 fl; and platelet count, $325 \times 10^9$/μL. Metabolic panel results were as follows: sodium, 133 mEq/L; potassium, 4.1 mEq/L; chloride, 97 mEq/L; bicarbonate, 26 mEq/L; blood urea nitrogen, 12 mg/dL; creatinine, 1.1 mg/dL; glucose, 373 mg/dL; venous lactic acid, 2.3 mmol/L; total bilirubin, 0.6 mg/dL; direct bilirubin, 0.2 mg/dL; aspartate aminotransferase, 33 IU/L; alanine aminotransferase, 47 IU/L; total protein, 7.6 g/L; albumin, 4.0 g/L; alkaline phosphatase, 97 IU/L; total creatine kinase, 210 IU/L; troponin, 0.13 ng/L; prothrombin time, 12.0 seconds; international normalized ratio, 1.1; and partial thromboplastin time, 22 seconds.

Electrocardiography on admission demonstrated first-degree atrioventricular block, but no new changes. A chest x-ray showed cardiomegaly but no active disease. Urinalysis and microscopy revealed 2+ leukocyte esterase, 11 to 50 white blood cells, and 11 to 50 red blood cells. The results of lumbar puncture culture were negative.

An initial diagnosis of a urinary tract infection was made, and intravenous levofloxacin 500 mg/day was started. The patient’s blood cultures drawn at the time of admission revealed gram-negative rods, and cultures grew *Salmonella* species. The diagnosis of possible prosthetic valve endocarditis was made. It was recommended that the patient be treated with intravenous ceftriaxone 2 g/day. The final microbiology report revealed *Salmonella enteritidis* (*S. enteritidis*), resistant to ampicillin and sensitive to ceftriaxone.

Transthracic echocardiography (TTE) revealed an ejection fraction of 60% but failed to demonstrate any echocardiographic evidence of endocarditis. Transeosophageal echocardiographic findings are demonstrated in Videos 1-3. The patient underwent further imaging to evaluate for possible other organ involvement. The patient underwent open heart surgery, including replacement of the mitral
DISCUSSION

_Salmonellae_ are gram negative, flagellated, facultatively anaerobic bacilli. Nontyphoidal salmonellosis is a worldwide disease in humans and animals. In the past 20 years, an estimated 1 million to 3 million total cases have been reported yearly worldwide.\(^1\) Approximately 45,000 cases and 400 to 600 deaths have been reported annually to the Centers for Disease Control and Prevention over the past decade. _S. enteritidis_ endocarditis without _S. typhimurium_ constituted 42% of all cases of _Salmonella_ infection in the United States. More than 95% of cases of _Salmonella_ poisoning are foodborne.\(^2,3\) _Salmonella_ species infection may take several clinical forms, the most common being gastroenteritis, which typically presents with fever, diarrhea, and cramping abdominal pain, and most patients have self-limiting infections without complications. However, transient bacteremia may be present in up to 10% of patients and may lead to metastatic infection at a number of sites.\(^4\) Other infections include enteric fever, bacteremia without localized infection, localized infection, and a chronic carrier state.\(^5\) Bacteremia is more common in young, elderly, and immunocompromised patients.

After ingestion (mostly in contaminated food), _Salmonellae_ colonize the ileum and colon, invade the intestinal epithelium, and proliferate within the epithelium and lymphoid follicles. The mechanism by which _Salmonellae_ invade the intestinal epithelium is partially understood and involves an initial binding to specific receptors on the epithelial cell surface, followed by invasion. After invading the epithelium, the organisms multiply intracellularly and then spread to mesenteric lymph nodes and throughout the body via the systemic circulation; they are taken up by the reticuloendothelial cells. The reticuloendothelial system confines and controls the spread of the organism. However, depending on the serotype and the effectiveness of the host defenses against that serotype, some organisms may infect the liver, spleen, gallbladder, bones, meninges, heart valves, myocardium, and other organs. Nontyphoid _Salmonella_ is reported to invade normal arterial intima, causing endothelial infection in the presence of atherosclerosis.\(^4\)

Endocarditis, a rare complication of salmonellosis with an incidence of 0.2% to 0.4%, occurs mostly during or after a concomitant _Salmonella_ infection, such as gastroenteritis. The predisposed patients include those infected with the human immunodeficiency virus and those with underlying heart diseases, such as prosthetic valves (15%), congenital heart disease (5%), and less frequently other valve abnormalities.\(^6\) _Salmonella_ species have also been reported to cause endocarditis in native heart valves.\(^7\) Particular serovars show a strong propensity to produce particular syndromes: _S. typhi_, _S. paratyphi A_, and _S. choleraesuis_ produce enteric fever; _S. choleraesuis_ produces septicaemia or focal infections; and _S. typhimurium_ and _S. enteritidis_ produce gastroenteritis. However, on occasion, any serotype can produce any of these syndromes. In general, more serious infections occur in infants, in adults aged >50 years,\(^4\) and in 46,936 patients with debilitating illnesses.\(^8\) The risk for nontyphoid _Salmonella_ bacteremia leading to endovascular focal infections in patients aged ≥50 years has been reported to be between 7%\(^9\) and 23%.\(^10\) whereas according to a large population-based study by Nielsen et al,\(^4\) the risk is 9%.

_Salmonella_ infection leading to aortitis has a strong propensity to form an aneurysm and rupture.\(^11\) Prosthetic valve endocarditis constitutes a small but devastating segment of infective endocarditis cases and is likely to increase as >100,000 heart valves are implanted annually in the United States.\(^12\) Prosthetic valve endocarditis develops in 1% to 4% of valve recipients during the first year following valve replacement and in approximately 1% per year thereafter.\(^12,13\) The type of prosthetic valve does not have an impact on the development of _Salmonella_ valve endocarditis.\(^14\)

_Salmonella_ endocarditis is an invasive and destructive process, with valve ring abscess, valve perforation, and rupture of the cusps occurring in a significant number of patients.\(^8\) Mortality associated with aortitis and endocarditis caused by nontyphoidal _Salmonella_ remains exceedingly high, between 40% and 45%.\(^10\) In a case series of 7 patients, 5 died perioperatively despite aggressive medical and surgical treatment.\(^15\) New or changing murmurs, cardiac failure, or peripheral embolic manifestations appear during the course of endocarditis in most patients.\(^4\) Normal leukocyte levels should be interpreted carefully in selected patients. Elevated leukocyte counts occur in a minority of patients who are actively infected with _Salmonella_. Patients aged >50 years who have had blood cultures positive for _Salmonella_ along with fever and back and/or abdominal pain should undergo extensive workup for aortitis due to nontyphoid _Salmonella_ aneurysm formation or vascular infection.\(^4\)

The diagnosis of vascular infection due to _Salmonella_ may be hampered by the absence of uniform diagnostic criteria\(^16\) and requires a high degree of suspicion. Third-generation cephalosporins and fluoroquinolones are often effective after blood cultures are obtained. The first target of echocardiography is the identification, characterization, and localization of valvular vegetations, the pathologic hallmark of endocarditis as well as of any potential complications of the infectious process. TTE is the first choice and is easily available, followed by emergent transesophageal echocardiography if TTE is inconclusive. In a case series by Fukushima et al,\(^15\) TTE was not diagnostic in 5 of 7 patients, and transesophageal echocardiography was conclusive in all patients reported. Computed tomography and magnetic resonance imaging should be performed to look for organ involvement, including the aorta, myocardium, lungs, brain, and bones. Early surgical intervention is described as having greatly increased survival and is therefore the treatment of choice in many patients.\(^17\)

CONCLUSION

The diagnosis of _Salmonella_ endocarditis requires a high level of suspicion. TTE is inadequate for diagnosis, and transesophageal echocardiography is usually required to diagnose and evaluate involvement. Most patients do experience multisystem compromise perioperatively. Treated cases are highly likely to recur. Patients who present with multiple vague symptoms, with histories including diabetes mellitus, immunocompromise, renal failure, and prosthetic heart valves, should alert clinicians to strongly consider _Salmonella_ endocarditis in their differential diagnoses.

REFERENCES


