Cardiovascular complications of *Salmonella enteritidis* infection

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Salmonella has the ability to adhere to damaged endothelium, predisposing individuals to complications rarely seen with other Gram-negative organisms. Potential complications include endocarditis, infected atheroma or aneurysms, myocarditis and pericarditis. The present report describes two cases of *Salmonella enteritidis*-associated cardiovascular disease. Patient 1 is a young adult who presented with myopericarditis complicated by recurrent cardiac arrests following return from a tropical climate. This patient was successfully treated with a 14-day course of ciprofloxacin. Patient 2 is an elderly man who developed a pseudoaneurysm of the ascending aorta complicating *S enteritidis* bacteremia, and died of this complication. Recognition of potential complications of salmonellosis, especially in individuals with risk factors, is paramount in correctly diagnosing and managing these patients.

Key Words: Cardiovascular; Aortic aneurism; Myocarditis; Pericarditis; *Salmonella*; *Salmonella enteritidis*

Cardiovascular complications of salmonellosis are rare and thought to occur in less than 5% of bacteremias (1). *Salmonella* species have the ability to adhere to damaged endothelium, causing complications not frequently seen with other Gram-negative organisms. Most cases of cardiovascular complications occur due to infection with nontyphoidal species, such as *Salmonella enteritidis*, as a result of their propensity to cause bacteremia (2).

An understanding of the potential cardiovascular complications that can arise in *Salmonella* infection is important for both correctly diagnosing affected patients and instituting appropriate management. Herein, we report two cases of cardiovascular complications arising from *S enteritidis* infections.

Les complications cardiovasculaires d'une infection par la *Salmonella enteritidis*

La *Salmonella* peut adhérer à l'endothélium endommagé, ce qui prédispose les individus à des complications rarement observées dans le cas d'autres organismes Gram négatif. Les complications potentielles incluent l'endocardite, l'athérome infecté ou les anévrismes, la myocardite et la péricardite. Le présent rapport décrit deux cas de maladie cardiovasculaire associée à la *Salmonella enteritidis*. Le patient 1 est un jeune adulte qui a consulté à cause d'une myopéricardite compliquée par des arrêts cardiaques récurrents après son retour d'un pays tropical. Ce patient a été traité avec succès au moyen de ciprofloxacine pendant 14 jours. Le patient 2 est un homme âgé qui a développé un pseudoanévrisme de l'aorte ascendante compliquant une bactériémie à *S enteritidis* et qui est décédé de cette complication. Le dépistage de ces complications potentielles de la salmonellose, surtout chez des personnes qui présentent des facteurs de risque, est essentiel pour bien diagnostiquer ces patients et les prendre en charge.

CASE PRESENTATIONS

Patient 1

Patient 1 was referred to a tertiary care centre with suspected ST elevation myocardial infarction. This 25-year-old man developed sudden-onset, severe retrosternal chest pain radiating to both arms, prompting his presentation to a peripheral hospital. The initial electrocardiogram showed ST elevations in leads II, III, aVF, V5 and V6 (Figure 1A), and the patient was consequently transferred to the University of Ottawa Heart Institute (Ottawa, Ontario) for urgent angiography.

On presentation, he was hemodynamically stable and the initial assessment noted no pericardial friction rub, no pleuritic or positional nature to the pain, and no murmurs or extra heart sounds. He had no

Figure 1 *Salmonella enteritidis* infection causing myopericarditis. **A** Presenting electrocardiogram demonstrates focal ST segment elevation. **B** Magnetic resonance image of the heart demonstrates pathological delayed gadolinium enhancement (as indicated by arrows)

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Figure 2) Pseudoaneurysm formation caused by rupture of a penetrating ulcer infected with *Salmonella enteritidis*. **A** Intravenous contrast-enhanced axial images demonstrate a small penetrating atherosclerotic ulcer (arrow). **B** Intravenous contrast-enhanced axial images demonstrate the interval development of a pseudoaneurysm arising from the ascending aorta (arrow). **C** Three-dimensional volume-rendered reformations demonstrate the extent of the pseudoaneurysm formation. **D** Transesophageal echocardiogram shows an echolucent space anterior to the aorta with flow noted in the lumen on colour Doppler echocardiogram

significant medical history, but note was made of his return from the Dominican Republic 48 h before presentation, where he had contracted a diarrheal illness. This was accompanied by subjective fevers, chills and sweats.

Given the lack of convincing features for pericarditis and the focal nature of the ST elevations, patient 1 was taken for coronary angiography, which revealed normal coronary arteries and left ventricular function. Laboratory investigations yielded a creatine kinase level of 1159 U/L and a troponin T level of 2.59 µg/L. He was thus diagnosed with myopericarditis and started on acetylsalicylic acid 650 mg four times a day.

Twenty-four hours following admission, the patient had recurrent ventricular fibrillation arrests for which he was successfully treated each time with defibrillation. He was maintained on an intravenous amiodarone infusion and no further arrhythmias occurred. Cardiac magnetic resonance imaging revealed pathological delayed gadolinium enhancement of the left ventricle in a mid myocardial and subepicardial

distribution (Figure 1B). Due to persistent fevers higher than 38°C and diarrhea, blood cultures and stool specimens were sent for microbiological analysis. Empirical oral ciprofloxacin 500 mg twice a day was started 48 h after admission. Blood cultures subsequently grew *S enteritidis*, for which the patient completed a 14-day course of ciprofloxacin.

Patient 2

Patient 2 was an 88-year-old man who was seen in the emergency department for assessment of a refractory pneumonia. The patient had a medical history significant for hypertension and atrial fibrillation, which were managed with hydrochlorothiazide, valsartan and coumadin therapy. He had returned from an uneventful trip to Belarus four weeks before presentation. On his return, he developed a productive cough and recurrent spiking fevers greater than 39°C. He had completed a seven-day course of clarithromycin started by his family doctor, with no resolution of symptoms. Furthermore, there was no history of any gastrointestinal symptoms at any time.

Initial laboratory investigations revealed a neutrophilia with toxic changes but a normal chest x-ray. He was admitted and started empirically on intravenous cefotaxime. During his stay, he developed pleuritic chest pain; a computed tomography scan of the chest was performed to rule out pulmonary embolism. While negative for pulmonary embolus, note was made of a small penetrating ulcer of his ascending aorta (Figure 2A). Blood cultures grew *S enteritidis*, and the patient completed a four-week course of cefotaxime.

Patient 2 returned two months later with recurrent fevers. Repeat cultures were again positive for *S enteritidis* and a computed tomography scan of the chest was performed to rule out endovascular complications. Imaging revealed a 2.8 cm pseudoaneurysm at the site of the previously noted penetrating ulcer (Figures 2B and 2C). A transesophageal echocardiogram also revealed an echolucent space anterior to the aorta with flow demonstrated on colour Doppler echocardiography (Figure 2D). The patient proceeded to surgical repair of the aneurysm, but he remained dependent on inotropes postoperatively and died three days later.

DISCUSSION

Salmonella are flagellated Gram-negative bacilli that can be broadly classified into typhoidal and nontyphoidal forms. Typhoidal *Salmonella* consists of *Salmonella typhi* and *Salmonella paratyphi*, and is spread through fecally contaminated food or water, producing systemic illness with little or no diarrhea. Nontyphoidal *Salmonella* infections, such as *S enteritidis*, also result from contaminated foods but have a greater propensity to cause gastrointestinal symptoms.

Salmonella species use different epithelial cell receptors for translocation into the gastrointestinal submucosa, which may account for the difference in disease symptoms among hosts. For example, the type IVb pilus of the *S typhi* is a major adhesion factor used during entry into gastrointestinal epithelial cells. Its target is a series of 10 residues from the first extracellular domain of the cystic fibrosis transmembrane conductance regulator, whose expression is induced by *Salmonella* infection leading to enhanced bacterial ingestion (3). In contrast, the mechanism by which *Salmonella* species infect endothelial-lined vessels remains less clearly defined. It is, however, well described that *Salmonella* toxins enhance macrophage adhesion and translocation through endothelial cells while also promoting phagocytosis of the bacteria itself into the macrophage – thus shuttling the bacteria into the subendothelial space (4). This unique virulence mechanism may in part explain the predilection for *Salmonella* species to infect endothelial-lined structures.

Cardiovascular involvement is most commonly endocarditis, both valvular and nonvalvular, with pre-existing valve abnormalities being the strongest predisposing factor for development. Following

endocarditis, other endovascular infections such as infected aneurysms or atheromas are the next most common complications. The largest series to date noted that HIV infection, cancer, cirrhosis and lupus significantly increased the risk of bacteremia, but the only predictor of endovascular infection was atherosclerosis (5). Notably, 47 of the 373 patients with nontyphoidal *Salmonella* developed endovascular infections, suggesting a significantly high rate of complications with nontyphoidal *Salmonella*. Finally, myocarditis and pericarditis are extremely uncommon presentations of salmonellosis, with only a few cases reported. Diagnosis of *Salmonella*-associated endovascular infection is generally confirmed when organisms are visualized on stained cardiovascular tissue on pathological examination.

Management for cardiovascular complications may require medical and/or surgical interventions. In cases of myopericarditis, such as in patient 1, standard therapies for pericarditis and management of myocarditis-associated arrhythmias are indicated. Due to multidrug resistance, fluoroquinolones and third-generation cephalosporins are first-line empirical agents. Relapsing bacteremia following a therapeutic course should prompt investigations to rule out endocarditis or other endovascular infections such as in the case of patient 2. In such instances, surgical intervention is mandated.

The present report highlights two cases of cardiovascular involvement from nontyphoid salmonellosis. Although neither patient had cardiac or vascular tissue available to demonstrate *Salmonella* species invasion on pathology, their presentations are consistent with previous reports in the literature. Cardiologists should be aware of the ability of *Salmonella* to infect atherosclerotic vessels, especially in individuals with risk factors for atherosclerosis, and of cardiac complications such as pericarditis and myocarditis – even in patients without predisposing risk factors. This awareness may allow for the appropriate investigation, diagnosis and management of rare but preventable complications.

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