Multidrug-Resistant Salmonella Endocarditis of a Native Valve: A Rare Case Presentation

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Abstract
Salmonella spp. is a rare cause of infective endocarditis that commonly involves a prosthetic or a previously damaged heart valve. We present a case of a 25-year-old young man with a one-and-a-half-month history of cough, fever, shortness of breath, and hemoptysis. Clinical examination revealed bilateral mid-zone crackles, palpable tip of the spleen, and an early diastolic murmur in the aortic (A2) area. Initial lab results indicated anemia with leukocytosis, raised inflammatory markers, and low serum albumin. Blood cultures showed the growth of multi-drug-resistant salmonella typhi. A radiological workup showed multiple aortic valve vegetation.

Salmonella endocarditis was diagnosed based on Duke’s Criteria. The patient was treated with culture-sensitive antibiotics and subsequently showed significant clinical recovery. This case highlights a rare native valve, multi-drug resistant salmonella endocarditis. It also emphasizes the difficulties in making a diagnosis and the benefit of using a multidisciplinary strategy to manage challenging clinical manifestations.

Categories: Internal Medicine, Cardiology, Infectious Disease

Keywords: native valve disease, salmonella complications, para enteric salmonella, multidrug resistant (mdr), salmonella typhi endocarditis

Introduction
Infective endocarditis (IE) is a cardiac endothelial infection with an annual incidence of 3-10/100,000 people [1]. Salmonella species are responsible for more than 1.2 million illnesses each year [2]. It typically presents with mild gastroenteritis but can be more severe, especially in infants, the elderly, and immunocompromised hosts [3]. The most prevalent cause of IE in most studies is Staphylococcus aureus (∼ 26.6%), followed by viridans group streptococci (18.7%), other streptococci (17.5%), and enterococci (10.5%). These organisms are responsible for 80-90% of all endocarditis cases [4]. Salmonella spp. was discovered to be a rare cause of infective endocarditis. Furthermore, previous studies have focused more on non-typhoidal infections, owing to their increased relative prevalence [5]. Patients with an underlying cardiac pathology, most notably rheumatic heart disease or prosthetic valve replacement, have been involved in the bulk of documented Salmonella cases with cardiac involvement. Additionally, studies have indicated that the mitral valve is the valve that is most likely to be impacted [5].

If not treated properly it carries a high mortality rate. This emphasizes the importance of selecting an appropriate antibiotic regimen with timely administration of antibiotics to achieve a cure for this disease [6]. Previously reported cases of Salmonella endocarditis have been traditionally treated with fluoroquinolones and third-generation cephalosporins. Studies on Salmonella endocarditis due to multiple drug-resistant Salmonella typhi are scarce. Here, we present a rare case of infective endocarditis, with an atypical presentation due to multidrug-resistant Salmonella typhi.

Case Presentation
A 25-year-old Male of South Asian descent with no previous comorbidities, working in the TB center as a porter, presented with a cough for 45 days, fever for 30 days, shortness of breath for 30 days, and hemoptysis for 3 days. The cough was associated with sputum initially whitish in color, which later changed into red color. The fever was high grade (102-104°F) and associated with rigor, chills, and night sweats which were relieved with over-the-counter medications, there was shortness of breath initially with exertion which later worsened. The past medical and family history was unremarkable. The patient was an ex-smoker with 5-pack years.

Upon examination, the patient was active, alert, and oriented. He was stable with a pulse of 76/min, BP 110/70, and SpO2 of 95% on room air. On chest examination, there was an equal expansion on bilateral palpatation, dullness to percussion in the right mid-zone, auscultation of the bilateral upper zone.
revealed wheezes, bilateral mid-zone crackles, soft and non-tender abdomen, and a palpable spleen tip. Cardiovascular examination revealed an early diastolic murmur in the aortic (A2) area.

His detailed workup to identify the underlying cause consisted of a baseline investigation which included a Chest X-ray, Sputum AFB, Gene Xpert, Blood Culture, Echocardiography, High-resolution CT scan, and inflammatory markers. After sending a blood culture and other investigations the patient was started empirically on antibiotics according to the local guidelines. thus ceftriaxone 2 gm (BID) and Meropenem 2 gm (BID) were started.

The sputum AFB and X-pert genes were negative for acid-fast bacilli therefore excluding pulmonary tuberculosis which was our initial suspected diagnosis, the rest of the labs are presented in Table 1 below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>On Admission</th>
<th>After 48 hours</th>
<th>On discharge</th>
<th>Reference Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Blood Count</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cells</td>
<td>20.4 * 10³/uL</td>
<td>15.4 * 10³/uL</td>
<td>12.4 * 10³/uL</td>
<td>4 – 11 * 10³/uL</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>3.92 * 10⁶/uL</td>
<td>3.75 * 10⁶/uL</td>
<td>3.62 * 10⁶/uL</td>
<td>4 – 6 10⁶/uL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>10.9 g/dl</td>
<td>9.92 g/dl</td>
<td>10.8 g/dl</td>
<td>11.5 – 17.5 g/dl</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>35.3 %</td>
<td>33.7%</td>
<td>35.9%</td>
<td>36 – 54%</td>
</tr>
<tr>
<td>Platelets count</td>
<td>521 * 10³/uL</td>
<td>411 * 10³/uL</td>
<td>299 * 10³/uL</td>
<td>150 – 450 * 10³/uL</td>
</tr>
<tr>
<td>% Neutrophils</td>
<td>88</td>
<td>82</td>
<td>70</td>
<td>40 – 70</td>
</tr>
<tr>
<td>% Lymphocytes</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>20 – 45</td>
</tr>
<tr>
<td>% Monocytes</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>0.9 – 5.2</td>
</tr>
<tr>
<td>Inflammatory Markers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-Reactive protein (mg/dl)</td>
<td>11.6</td>
<td>6.4</td>
<td>3.5</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/1^st hr.)</td>
<td>110</td>
<td>122</td>
<td>105</td>
<td>0 – 15</td>
</tr>
<tr>
<td>Lactate dehydrogenase (U/L)</td>
<td>303</td>
<td>297</td>
<td>240-280</td>
<td></td>
</tr>
<tr>
<td>Procalcitonin (ng/ml)</td>
<td>0.72</td>
<td>0.6</td>
<td>&lt;0.5</td>
<td></td>
</tr>
<tr>
<td>Serum Electrolytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>130.4</td>
<td>136</td>
<td>141</td>
<td>135 – 150</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.78</td>
<td>4.39</td>
<td>4.21</td>
<td>3.5 – 5.1</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>99.4</td>
<td>97</td>
<td>102.3</td>
<td>96 - 112</td>
</tr>
<tr>
<td>Liver Function Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Bilirubin(mg/dl)</td>
<td>0.6</td>
<td>0.5</td>
<td>0.52</td>
<td>0.1 – 1.0</td>
</tr>
<tr>
<td>Alkaline transferase (U/L)</td>
<td>160</td>
<td>532</td>
<td>302</td>
<td>10 – 50</td>
</tr>
<tr>
<td>Serum Albumin (g/dl)</td>
<td>2.6</td>
<td>2.9</td>
<td>3.3</td>
<td>3.5 – 5.5</td>
</tr>
<tr>
<td>Renal Function Tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>36.36</td>
<td>64.76</td>
<td>59.28</td>
<td>18 – 45</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.81</td>
<td>1.04</td>
<td>1.12</td>
<td>0.64 – 1.2</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>4.6</td>
<td>5.2</td>
<td>3.4 – 7.0</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 1: Basic laboratory investigations and inflammatory markers**
On Echocardiogram there were multiple aortic valve vegetation and severe AR (non-co-optative aortic valve) and moderate MR. Vegetation is shown in Figure 1.

![Echocardiogram showing multiple small aortic valve vegetations](image)

**FIGURE 1: Echocardiogram showing multiple small aortic valve vegetations**

Red arrows: indicate small multiple aortic vegetations

Chest HRCT showed bilateral dense multi-lobular shadowing on the background of ground-glass opacification with interlobular and intra-lobular septal thickening and multiple sub-centimeter mediastinal lymph nodes suggestive of an infectious disease process, as shown in Figure 2 & 3.
FIGURE 2: High-resolution CT scan showing bilateral dense multi-lobular shadowing on the background of ground-glass opacification with interlobular and intra-lobular septal thickening.

Black arrow: showing ground glass opacities.

Red arrow: consolidation in the background of ground glass opacities.
FIGURE 3: High-resolution CT Scan showing bilateral ground-glass opacification, small cavitations and multiple sub-centimeter mediastinal lymph nodes

*Black arrows: indicating ground glass opacities*

After 7 days, the blood culture was positive for heavy growth of Salmonella Typhi sensitive to imipenem, meropenem, ceftriaxone, and cefixime, and resistant to ciprofloxacin, co-trimoxazole, chloramphenicol, ampicillin, and intermediate to azithromycin. By applying the Duke’s criteria for infective endocarditis he fulfilled 2 of the major criteria (positive blood culture and vegetation on echocardiography) and 2 minor criteria (temperature > 38°C, Embolic phenomenon) therefore diagnosed as definitive endocarditis as it fulfilled 2 major criteria.

He continued the same treatment with ceftriaxone (2 gm BID) and meropenem (2 gm BID for two weeks. During this period, the patient showed significant clinical recovery and was counseled about further treatment and prevention in special circumstances, such as dental and surgical procedures. He is currently healthy and regularly attends follow-up OPD.

**Discussion**

Salmonella endocarditis is one of the rarest causes of infective endocarditis worldwide [5]. In studies conducted from 1976 to date, fewer than 90 cases have been reported in the literature, mainly composed of case reports and case series. The total burden of salmonella endocarditis (0.01 - 2.9%) of bacterial endocarditis cases. Most often, the affected population is in their 6th decade of life, with the most common valve affecting the mitral valve [5,7].

In most reported cases, the patient had either a previously damaged or prosthetic valve replacement. Contrary to the reported literature, our patient was in the 3rd decade of life and had native valve Salmonella endocarditis of the Aortic valve, which is a rare presentation of a rare etiology of bacterial endocarditis.

Unfortunately, salmonella Endocarditis is a fatal condition with mortality ranging from (42%-69%) [5,7,8,9,10]. Our patient however responded well to medical therapy and survived the event to complete resolution with only medical therapy directed by the culture and sensitivity report.
Salmonella infections most often present with gastrointestinal symptoms; however, extra-intestinal manifestations are possible [7]. The optimal treatment of Salmonella enterica is clearly defined and subject to the culture and sensitivity of the bacteria involved, drastically changing from country to country. Therefore local guidelines based on AntiBrogram reports are ideal for consulting when initiating empirical therapy, however, the treatment for valvular or mural endocarditis as an extraintestinal manifestation of salmonella endocarditis is not yet defined, we started our patient empirically on Meropenem 2 gram BID and Ceftriaxone 2 Gram BID as the burden of XDR salmonella is high in our community. As suggested by Fernandez et al suggest potent antimicrobial with or without surgical intervention to deal with the cardiovascular complications [8,9].

S choleraesuis, S Typhimurium, and S enteritidis are commonly known serotypes among the cases while S Thompsons and S Derby times have also been reported [9,11,12,13]. Infection with multi-drug resistance is associated with a dismal prognosis, however, our patient recovered without incident, as did the case reported by Khan G.Q Et al.

Salmonella endocarditis may be a rare etiology, but in the context of multidrug resistance and extreme drug-resistant pathogens that are prevalent in our province; therefore, it should be a cause for concern as virulent strains like the one reported have the capacity to infect native valves, could wreak havoc on the already existing and growing number of patients with previously damaged valves, and patients with prosthetic valves due to rheumatic fever. Therefore, clinicians should be vigilant when treating Salmonella infections.

Conclusions
In summary, this case presented with initial ambiguity in diagnosis, because of the patient’s significant exposure to TB. Hence this 25-year-old young man with symptoms of fever, cough, and hemoptysis was initially investigated for pulmonary TB. Further workup revealed native valve salmonella infective endocarditis, confirmed by echo and positive blood cultures. The patient responded well to the empirical antibiotic regimen according to local guidelines i.e. combination of ceftriaxone and meropenem. The blood cultures report later on showed sensitivity to the same regimen. While the patient presented with an unusual native valve endocarditis, the blood cultures revealed drug-resistant bacteria of Salmonella typhi.

In conclusion, this case report underscores several critical points regarding Salmonella endocarditis. First and foremost, it highlights the alarming trend of Salmonella strains exhibiting extreme drug resistance, posing a formidable challenge in clinical management. Furthermore, the involvement of the native valve, particularly the aortic valve, instead of the more commonly affected mitral valve, accentuates the variability of this condition and the need for a comprehensive diagnostic approach. Equally important, early detection of complications arising from Salmonella infection, such as endocarditis, assumes paramount significance. Therefore, our findings underscore the necessity for heightened vigilance in screening patients for such complications, enabling timely intervention and better outcomes in the management of Salmonella-related endocarditis. This case serves as a reminder of the evolving clinical landscape of Salmonella infections and the importance of tailored and vigilant clinical strategies.

Additional Information

Author Contributions
All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Mahnosh Saleh, Kamran Ahmad

Drafting of the manuscript: Mahnosh Saleh, Memoona Zahoorn, Musa Kakakhel, Mohammad Sayyar, Yasir Ali

Concept and design: Memoona Zahoorn, Musa Kakakhel, Aima Yousaf, Mohammad Sayyar, Yasir Ali

Supervision: Memoona Zahoorn, Kamran Ahmad

Critical review of the manuscript for important intellectual content: Kamran Ahmad, Musa Kakakhel, Aima Yousaf, Mohammad Sayyar, Yasir Ali

Disclosures
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References