Salmonella-Associated with Deep Vein Thrombosis: Report of a Case and Review of the Literature

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(Received: January 29, 1992)
(Accepted: May 10, 1992)

Key words: salmonellosis, deep vein thrombosis

Introduction

While Salmonella infection may produce a variety of clinical pictures, deep vein thrombosis (DVT) is a rare manifestation. To our knowledge, there have been only two reported cases dealing with Salmonella-associated DVT. In this study, we describe a case recently encountered in our hospital and review the literature.

Case Report

A 68-year-old housewife with no past history of significant systemic illness was admitted to National Cheng Kung University Hospital on August 7, 1989, with the chief complaint of an erythematous swelling on the left lower extremity which was associated with chills and fever. About one week before admission, she became aware of an erythematous swelling over the left lower leg. On the next day, headache, anorexia, chills and mild fever occurred. She was placed on some undefined oral medicine for three days by a physician with no discernible improvement. As the painful swelling of the lower extremity was worsening, she called on our emergency service.

On admission, physical examination revealed a well nourished woman with a blood pressure of 120/90 mmHg, pulse rate 98/min, and temperature 37.3°C. The left lower extremity was diffusely swollen with associated local heat and mild erythema. This lesion was tender, especially in the calf region. Otherwise physical examination revealed nothing remarkable.

The initial hemogram showed the white count 9.700/mm³ with 3% myelocyte, 2% metamyelocyte, 6% band form, 49% segmented neutrophil, 13% monocyte and 24% lymphocyte. The hemoglobin level was 12.1 gm/dl; the prothrombin time, 11.6 sec (control 11.4 sec) and the activated partial thrombin time, 30.2% (control 26.2 sec). A blood chemistry study revealed total serum protein of 6.4 gm/dl with albumin 3.1 gm/dl, globulin 3.3 gm/dl; AST 37.0 μ/l; ALT 60 μ/l; LDH 280 μ/l. The following studies were normal: serum total bilirubin, serum alkaline phosphatase, blood urea nitrogen, serum creatinine, serum electrolytes, fasting blood sugar, serum alpha-fetoprotein, carcinoembryonic antigen, antithrombin III and protein C.

The chest X-ray on admission showed a wedge-shaped patchy density in the right lower lung field.
Venogram of the lower extremities demonstrated extensive DVT from the left calf, popliteal and femoral veins to the external iliac vein with abundant collateral circulation in the left thigh and pelvic wall (Fig. 1). Lung perfusion scan revealed two perfusion defects in the superior and anterior basal segments of right lower lobe. (Fig. 2).

Blood culture on admission was negative, but when repeated one week later grew Salmonella enteritidis group C1, which was sensitive to ampicillin, chloramphenicol, cephalothin, cefamandol, ceftazidime, gentamicin and tobramycin. Urine and stool cultures were negative. The agglutinin titer for typhoid “H” antigen was reactive at 1:40 while that for typhoid “O” antigen titer was reactive at 1:20.

Under the impression of DVT with probable pulmonary embolism, heparinization therapy was initiated on admission with a loading dose of 5,000 units as a bolus injection and followed by about 1,000 units/hour intravenous infusion. As the result the swelling in the left lower extremity improved dramatically.

Antibiotic regimen initially consisted of cephalothin and tobramycin, but fever persisted. After Salmonella infection was disclosed in a repeated blood culture, antibiotics were changed to ampicillin 1 gm intravenously every 6 hours. The fever subsided gradually and she made a steady progress.

The anticoagulant was switched to warfarin on day 12 and dose regulated to maintain the prothrombin time at 1.5—2.5 times the control. On day 23, the patient was discharged with almost completely resolved swelling of the left lower extremity. She received regular follow-up at our outpatient clinic thereafter with continuation of warfarin therapy at the maintenance dose for additional 3 months. No fever or leg swelling has reoccurred ever since.

Discussion

Genus Salmonella consists of three species i.e. Salmonella typhi, Salmonella choleraesuis and Salmonella enteritidis which include more than 1,700 different serotypes differentiated by O (somatic) and H (flagella) antigens. These pathogens may produce asymptomatic infection of the intestinal tract or
Salmonella-associated deep vein thrombosis

Table 1 Summary of Clinical Data of Three Reported Cases with Salmonella-Associated DVT

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Age &amp; sex</th>
<th>Underlying disease</th>
<th>Lesion site</th>
<th>organism</th>
<th>specimen</th>
<th>associated lesions</th>
<th>Treatment antibiotics</th>
<th>anticoagulant and/or thrombolytic therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veliv P, 1987(5)</td>
<td>11-day-old, neonate</td>
<td>no bilateral renal veins</td>
<td></td>
<td>Salmonella ibadan</td>
<td>blood</td>
<td>none</td>
<td>ampicillin</td>
<td>urokinase, then heparin</td>
<td>recovery</td>
</tr>
<tr>
<td>Omer AH, 1988(10)</td>
<td>25-year-old, M</td>
<td>no right popliteal &amp; femoral veins</td>
<td></td>
<td>Salmonella enteritidis group D1</td>
<td>blood, stool</td>
<td>intestinal perforation of the lower ileum</td>
<td>chloramphenicol</td>
<td>heparin</td>
<td>recovery</td>
</tr>
<tr>
<td>Ping-I Hsu, 1989</td>
<td>68-year-old, F</td>
<td>no left calf, popliteal, femoral &amp; iliac veins</td>
<td></td>
<td>Salmonella enteritidis group C1</td>
<td>blood</td>
<td>pulmonary embolism</td>
<td>ampicillin</td>
<td>heparin</td>
<td>recovery</td>
</tr>
</tbody>
</table>

several different clinical syndromes in humans, such as gastroenteritis, enteric fever, bacteremia, and localized infections[1]. The cardiovascular complications of Salmonella infection ranged from endocarditis[2,3], myocardial abscess[4], pericarditis[5], mycotic aneurysm[6,7], superficial and deep vein thrombosis[8,9,10]. According to the observation of Manson et al.[8], minor thromboses of the calf veins appears commonly in salmonellosis. Major thrombosis in the femoral and subclavian veins rarely occur. In reviewing the literature, there were only two reports dealing with Salmonella-associated DVT. Verlin et al.[9] described the first case in 1987 in an 11-day-old neonate who presented a bilateral renal vein thrombosis in the course of Salmonella ibadan infection. The second case reported by Omer et al.[10] in 1988 was a 25-year-old male, who was afflicted by Salmonella enteritidis group D1 infection and presented with intestinal perforation and right popliteal and femoral vein thrombosis. The case here presented was a 68-year-old female who developed left lower extremity DVT with probable pulmonary embolism during a Salmonella enteritidis group C1 infection. The clinical data of these three cases are summarized in Table 1.

We are uncertain that the coincidence of Salmonella sepsis and DVT indicates that the former causes the latter. However, similar to the case reported by Omer, the patient mentioned in our study presented with no obvious predisposing factors of DVT, such as oral contraceptive use, malignant neoplasm, immobilization, intrinsic anticoagulant deficits or previous surgeries. Therefore, we reserve a high index of suspicion that DVT may be triggered by Salmonella sepsis. In our speculation, Salmonella endotoxin or the presence of severe dehydration associated with salmonellosis may be responsible. More reported cases and further investigations are necessary to render this assumption more convincing.

In the past, hundreds of mycotic aneurysms associated with Salmonella infection have been reported and Paul et al.[11] summarized the pathogenesis of this complication as intravascular or extravascular origin. Those intravascular sources may arise from (i) the vegetations of endocarditis or (ii) bloodstream dissemination of bacteria to the intima surface of the artery or the vasa vasorum. Without surgical intervention, mycotic aneurysms in Salmonella infection almost all resulted in rupture of involved vessels[1,12]: in view of the good clinical response in all these 3 cases with antibiotics, anticoagulant and/or thrombolytic therapy alone, we speculate the venous thrombosis is likely to be non-suppurative.

Because DVT is sometimes present in the absence of clinical symptoms and signs, the true incidence of this complication in Salmonella sepsis remains to be determined.

In the treatment of DVT in Salmonella infection, anticoagulant therapy with or without thrombolytic agents seemed effective and usually could yield satisfactory initial results, but the recurrence rate of DVT is unknown still.

In summary, Salmonella-associated DVT may be present in previously healthy persons. It usually responds well to anticoagulant and antibiotic therapy. The true incidence and exact pathogenesis of this serious condition have not yet been established. To clarify these issues, more case reports and further
investigations are necessary.

References