

[CASE REPORT]

Cerebral Venous Thrombosis due to Nontyphoidal *Salmonella* Bacteremia

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Abstract:

A 19-year-old previously healthy man presented with convulsions, fever, headache, diarrhea, and vomiting. Brain magnetic resonance imaging revealed cerebral hemorrhaging in the right parietal lobe and thrombotic occlusion of the right great cerebral vein. Blood cultures were positive for nontyphoidal *Salmonella*. The patient was successfully treated with antibiotics and anticoagulants. Nontyphoidal *Salmonella* bacteremia can cause cerebral venous thrombosis and physicians therefore need to consider nontyphoidal *Salmonella* bacteremia as a potential cause of cerebral venous thrombosis.

Key words: bacteremia, nontyphoidal *Salmonella*, venous thrombosis, MERS

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Introduction

Cerebral venous thrombosis (CVT) is a rare disorder with a reported incidence of 0.5% to 1% of all strokes, but it is potentially life-threatening. The risk factors for CVT include inherited thrombophilia, pregnancy, antiphospholipid syndrome, and cancer. Infection is also a major cause of this disorder (1). *Salmonella* is a genus of rod-shaped Gram-negative bacteria. *Salmonella* species are food and waterborne pathogens, and infection results in a variety of presentations, including enteritis, fever, and bacteremia and it may spread to any site in the body, including the brain. We herein report a rare case of CVT due to *Salmonella* infection.

Case Report

A 19-year-old previously healthy man was admitted to our hospital with convulsions, fever, headache, diarrhea, and vomiting. He had no pets and had eaten noodles with boiled eggs at a restaurant 7 days before admission. He had developed abdominal pain and diarrhea a couple of days thereafter and had visited a nearby hospital to receive antidiarrheals, after which his abdominal symptoms had improved

immediately. Several days later, his mother had found him in a state of tonic seizure and requested an ambulance. His body temperature was 37.2°C. Physical examination revealed convulsions, headache, diarrhea, and vomiting, with increased bowel sounds. The cardiovascular and respiratory findings were unremarkable, meningeal signs were absent, and no Osler's node and Janeway lesions were observed. No neurological abnormalities other than the seizure were found. An initial hematological investigation revealed a white blood cell count of $13.7 \times 10^3/\mu\text{L}$, with 86% neutrophils with no renal dysfunction or hypocomplementemia.

The D-dimer level was slightly elevated (3.3 $\mu\text{g/mL}$), but antithrombin III was 90%, protein C activity was 144% and protein S activity was 101%, so there was no evidence of inherited thrombophilia, and anti-cardiolipin antibody was not elevated. Two sets of blood cultures performed at the same time were positive for *Salmonella* spp. with O4 and Ha antigens. Brain computed tomography (CT) and magnetic resonance imaging revealed spotty cerebral hemorrhaging in the right parietal lobe and thrombosis of the right parietal cortical vein (Fig. 1). Magnetic resonance venography showed no occlusion of the superior sagittal sinus, right transverse sinus, and right sigmoid sinus (Fig. 2A). A transient high-intensity area was seen in the splenium of the corpus callosum on diffusion-weighted images (Fig. 2B), so-

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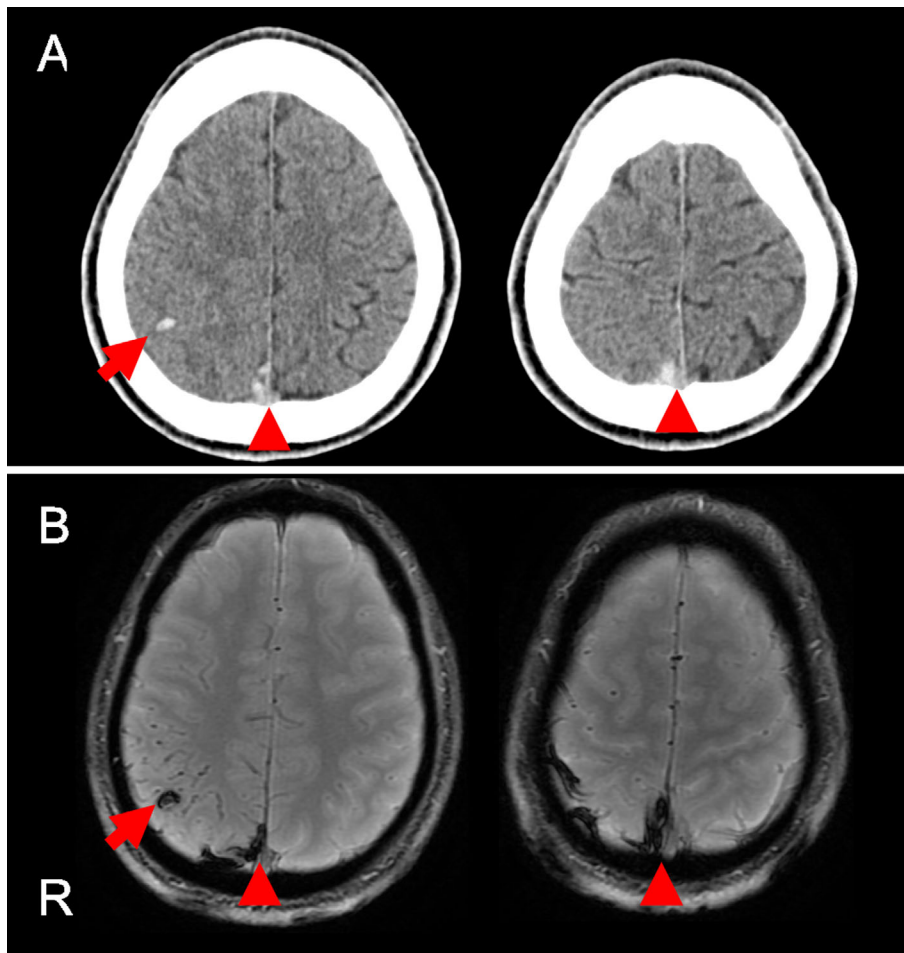


Figure 1. Brain computed tomography (CT) and magnetic resonance imaging (MRI) findings in our patient. Brain CT (A) and MRI T2* weighted images (B) showed right parietal hemorrhaging (arrows) and a thrombus in the suprasagittal sinus (arrowheads).

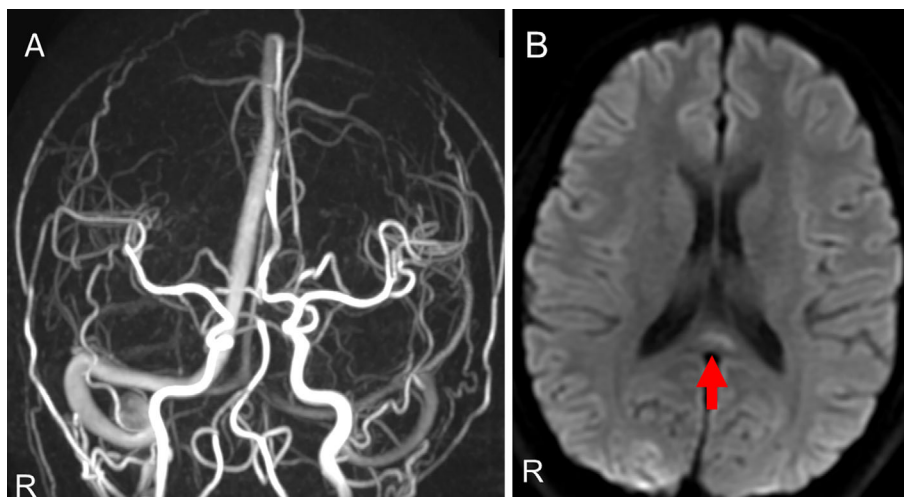


Figure 2. Magnetic resonance (MR) venography and diffusion-weighted imaging (DWI) findings. MR venography showed no occlusion of the major cerebral veins (A). The splenium of the corpus callosum demonstrated hyperintensity on DWI (B; arrow).

called clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) (2). Electroencephalography was normal. No other focus of infection was detected on systemic CT scans.

Tonic clonic convulsion was successfully treated by intravenous diazepam, and fosphenytoin was administered to prevent a recurrence of the seizure. Anticoagulant therapy was initiated with heparin 10,000 units/day, and warfarin was

gradually substituted for the heparin. Empiric antimicrobial therapy with intravenous ceftriaxone (2 g every 24 hours) was started for the *Salmonella* bacteremia. Ceftriaxone was used for four days, and then it was replaced by intravenous levofloxacin for twelve days because of an elevation of liver enzymes. Stool cultures after the end of antibiotic administration were positive for *Candida glabrata*, but *Salmonella* was not detected, and blood cultures were negative after antibiotic therapy. Twenty-two days after admission, the patient was discharged with no neurological impairment. He was thereafter administered warfarin and levetiracetam for three months and had no recurrence of thrombosis or convulsion. Moreover, the thrombosis of the right great cerebral vein was found to have disappeared.

Discussion

This case is unique in two aspects. First, it is rare for nontyphoidal *Salmonella* bacteremia to occur in a previously healthy subject. *Salmonella* is a genus of rod-shaped Gram-negative bacteria. *Salmonella* species can be found in the gastrointestinal tracts of humans and animals—especially reptiles and birds. Infection is spread by contaminated food and water, and the incubation period varies from 4 to 72 hours. *Salmonella* serotypes can be divided into typhoidal and nontyphoidal. Nontyphoidal serotypes are the most common and cause self-limiting gastrointestinal disease, but bacteremia occurs in 5% to 10% of all infected persons (3). The risk of bloodstream infection depends on the host's immune system and the degree of bacterial virulence; infancy, immune deficiency, malnutrition, malaria, and anemia are well-known risk factors (4-6). Most adults who develop nontyphoidal *Salmonella* bacteremia have predisposing diseases and are usually already receiving medications, particularly immunosuppressive agents (6). Some types of salmonella that can easily enter the blood have been identified and include serotype Heidelberg (7). Our patient was a 19-year-old male with no medical history of note, but the use of antidiarrheals may have prolonged the infection or led to the onset of bacteremia (8).

Second, it is rare that nontyphoidal *Salmonella* bacteremia caused CVT. Usually, this bacteria often affects young patients and can cause variable neurological symptoms, such as headache, papilledema, diplopia, and other focal neurological deficits. These clinical symptoms are related to increased intracranial pressure and focal brain injury. However, in our case, there was no focal injury and MRI showed MERS, so the clinical symptoms of our case are therefore considered to have been caused by CVT. Inherited thrombophilia, pregnancy, antiphospholipid syndrome, cancer, and other uncommon causes are associated with CVT (9). Parameningeal infection has predominated in previous cases of infectious CVT (1), and there are only a limited number of reported cases of CVT due to *Salmonella* bacteremia (10-12). Initial treatment with anticoagulants is effective for preventing further thrombus development and facilitating

recanalization. In this case, no underlying cause of CVT except for the *Salmonella* bacteremia was detected. In a mouse model, systemic *Salmonella typhimurium* infection was reported to induce thrombosis via the ligation of C-type lectin-like receptor-2 on platelets (13), and a similar mechanism likely operates in humans. Moreover, adults with nontyphoidal *Salmonella* bacteremia are at risk for developing infected aortic aneurysms (14). Taken together, these results suggest that nontyphoidal *Salmonella* has a high affinity for the vascular system. Our patient was successfully treated with appropriate antibiotic and anticoagulant therapy. Both CVT and *Salmonella* bacteremia are uncommon, but life-threatening conditions. Clinicians should therefore consider *Salmonella* bacteremia as a potential cause of CVT.

The authors state that they have no Conflict of Interest (COI).

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