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Case report

Strongyloides Hyperinfection Syndrome causing fatal meningitis and septicemia by Citrobacter koseri

Felix Reyes[a,b,c], Navneet Singh[a,*], Nigar Anjuman-Khurram[b], Jihae Lee[a], Lillian Chow[c]

[a] Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY, USA
[b] Department of Pathology, SUNY Downstate Medical Center, Brooklyn, NY, USA
[c] Department of Pulmonary and Critical Care Medicine, SUNY Downstate Medical Center, Brooklyn, NY, USA

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ABSTRACT

Citrobacter koseri is a gram-negative bacillius that belongs to the Enterobacteriaceae family. It is an uncommon pathogen that typically causes meningitis and brain abscesses in children, however central nervous system (CNS) infections are rarely found in adults. We present a case of C. koseri meningitis in an immunocompetent adult secondary to intestinal micro-perforation caused by *Strongyloides* A 76-year-old man admitted for asthma exacerbation developed septic shock. A lumbar puncture revealed bacterial meningitis. Blood and CSF cultures grew *Citrobacter koseri* with identical susceptibilities, suggesting infection by one strain. Despite broad-spectrum antibiotics, the patient expired of multi-organ failure. Autopsy identified diffuse alveolar hemorrhage as the immedi ate cause of death with a heavy burden of *Strongyloides stercoralis* in his gastrointestinal system, lungs, and meninges.

Citrobacter koseri is a gram-negative bacillus of the *Enterobacteriaceae* family. It is an uncommon pathogen that typically causes meningitis and brain abscesses in children. Infections in adults occur in immunocompromised hosts or instances where an insult creates a port of entry. This is the first documented case of *C.koseri* sepsis in an immunocompetent host associated with Strongyloides Hyperinfection Syndrome (SHS), where massive parasitic intestinal invasion reaches pulmonary circulation and perforates the alveolar membrane. This case highlights that presence of rare enterobacterial infections should prompt consideration of differentials including SHS.

Introduction

Citrobacter koseri is a gram-negative bacillus that belongs to the *Enterobacteriaceae* family. It is an uncommon pathogen that typically causes meningitis and brain abscesses in children. Central nervous system (CNS) infections caused by *Citrobacter koseri* are rarely found in adults with thirteen cases reported. Most cases have been related to head trauma, facial fractures, post neurosurgical procedures, or found in immunocompromised patients. We present a case of *Citrobacter koseri* meningitis in an immunocompetent adult secondary to intestinal micro-perforation caused by *Strongyloides*.

Case Presentation

A 76-year-old man with history of diabetes mellitus, hypertension, hyperlipidemia, multiple myeloma in remission, hypothyroidism, ischemic stroke, asthma, benign prostatic hyperplasia, and recent deep vein thrombosis on warfarin presented with shortness of breath. He reported failure of his nebulizers in achieving symptomatic relief. On admission, vitals were stable and the patient was in no distress with a baseline neurological exam. Labs were significant for baseline anemia and supratherapeutic INR > 8 with no signs of bleeding. Chest X-Ray showed no airway opacity. He was treated with nebulizers, oral corticosteroids, and admitted for an exacerbation of asthma. By day 5, the patient was noted with progressively worsening altered mental status, fever with hypotension, tachycardia, and progressive tachypnea causing hypoxic respiratory failure. Despite noninvasive positive pressure ventilation and fluid resuscitation, the patient progressively declined, requiring intubation and admission to the ICU where vasopressor and ventilator support was initiated.

The patient was treated with standard therapy for septic shock, including vancomycin with piperacillin/tazobactam for empiric broad-spectrum coverage of sepsis. Labs were significant for WBC 6,060 cell/mm3 with 34% band forms, acidemia with bicarbonate of 15 mmol/L and acute kidney injury with creatinine 3.28 mg/dL from 1.35 mg/dL on admission. Arterial blood gas prior to intubation showed metabolic acidosis with respiratory compensation. A lumbar puncture was performed with results consistent with bacterial meningitis (Table 1).

* Corresponding author at: 450 Clarkson Ave, Box 1262, Brooklyn, NY, 11203, USA.
E-mail address: Navneet.singh@downstate.edu (N. Singh).

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Table 1
Comparison of lumbar punctures.

	Initial Lumbar Puncture	Repeat Lumbar Puncture
Gram Stain	Gram Negative Rod	Gram Negative Rod
Organism	Citrobacter koserii	
Appearance	Cloudy	Cloudy
Color	Xanthochromic	Colorless
WBC	4289	19325
RBC	2733	611
Segs	85	89
Bands	8	2
Lymphs	3	5
Monos	4	4
Bacteria Extracellular	Present	Present
Bacteria Intracellular	Present	Present
Smudge Cells	Present	Present

Gram stain showed gram-negative rods. Given clinical suspicion for bacterial meningitis, ceftriaxone, metronidazole, ampicillin, and acyclovir were started after dexamethasone. Blood cultures grew gram-negative rods and ceftriaxone was changed to cefepime.

On ICU day 3, the blood and CSF cultures grew *Citrobacter koseri* with pansensitivity except for ciprofloxacin and tetracycline. All antimicrobials except for cefepime were discontinued. The next day, the patient's vasopressor requirement increased and he was noted to have increasing leukocytosis. Chest X-ray showed worsening bilateral opacities. A bronchoscopy with bronchoalveolar lavage (BAL) was performed with no significant findings on visual inspection and preliminary BAL resulting negative. A repeat LP showed downtrending glucose and protein with uptrending WBC. CSF culture grew the same initial organism and antimicrobials were escalated to meropenem and levofloxacin. On ICU day 6, the patient suffered a cardiac arrest and expired despite several attempts at resuscitation. Autopsy revealed diffuse alveolar hemorrhage as the immediate cause of death with *Enterobacteriaceae* in pulmonary cultures. Further analysis revealed a heavy burden of *Strongyloides* throughout the gastrointestinal tract. *Strongyloides* was also evidenced in the respiratory tract with parasites visualized in the meninges and choroid plexus (Fig. 1). This corresponded to the post-mortem result of *Strongyloides* in the sputum from BAL.

Discussion

Citrobacter, a member of the *Enterobacteriaceae* family, comprises a group of aerobic, gram-negative bacilli that are frequently found in water, soil, food, and animal and human intestines. *C.koseri* infection has been reported to cause lung abscess and brain abscesses in neonates [1,2], acute rhinosinusitis, intraorbital abscesses [3], retroperitoneal abscesses [4,5], brain abscesses [1]. Immunocompromised hosts, such as diabetics, transplant recipients, and cirrhotics, are known to be at increased risk of *C.koseri* infection [4]. In immunocompetent hosts, a port of entry is typically described.

In our case, post-mortem analysis of the bronchoalveolar lavage (BAL) revealed *Strongyloides* in the sputum and provided a clue towards the unifying diagnosis [6]. Autopsy revealed the port of entry of *C. koseri* was intestinal microperforation by *Strongyloides*. Strongyloides Hyperinfection Syndrome (SHS) is caused by massive intestinal invasion by parasites, which reach the pulmonary circulation and perforate the alveolar membrane[6]. SHS carries a high mortality which increases with bacterial superinfection. The overwhelming majority of cases of SHS are in immunocompromised patients, including those with HIV/AIDS (13%), active hematological malignancies (27%), and autoimmune disease (33%) [6]. While cases of strongyloidiasis have been documented in immunocompetent patients such as ours, this patient population typically has lower parasite burden and develops a chronic or asymptomatic infection [6–8]. Our patient had a history of multiple myeloma treated with levalidomide, however on presentation he was in remission and on no therapy. To our knowledge, our patient had no evidence of being immunocompromised prior to admission.

One notable risk factor for SHS in the immunocompetent patient is systemic corticosteroid therapy [6,9], however our patient was not taking steroids on admission. Another well accepted notion is that co-infection with HTLV in an otherwise immunocompetent patients plays an important role to dampen T-cell response to the parasite and allows for higher parasite burdens and more widespread infection [7,8,10,11]. Given that HTLV infection often remains subacute, one could speculate that while we believed our patient was immunocompetent he may have had a deficiency in his cellular immunity caused by a prior HTLV infection that predisposed him to the development of SHS.

In a case series of 133 patients with SHS, 38% of patients presented with bacterial infections, with bacteremia as the most frequent manifestation and meningitis the least frequent [6]. The culprit organisms of bacteremia in SHS commonly belong to the *Enterobacteriaceae* family but no cases of *Citrobacter koseri* infection have been documented. Bacterial seeding of the meninges through hematological spread was confirmed in our case by the repeated blood cultures and CSF cultures showing *C.koseri*. Corresponding with our case, *Citrobacter* is reported to be resistant to ampicillin and susceptible to ciprofloxacin and gentamicin [3,4].

This case underscores the severity of SHS associated with a bacterial superinfection and the urgency of considering less common causes of intestinal bacterial translocation into the blood and other organs. Another important point is the consideration of unusual infections in patients who are thought to be immunocompetent. Considering factors interfering with cellular immunity such as co-infection with HTLV in this case may prompt more timely consideration of alternative

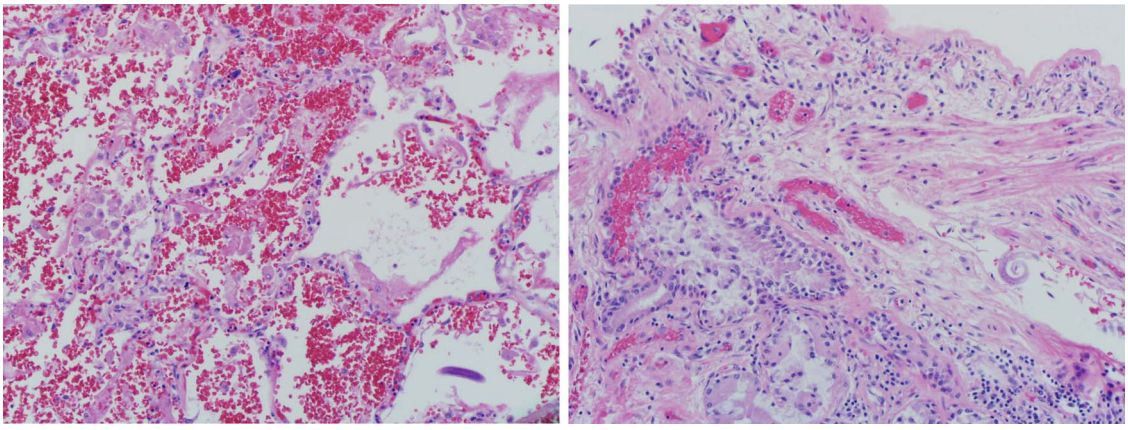

Fig. 1. Autopsy slides showing extensive pulmonary hemorrhage, diffuse alveolar damage, and *Strongyloides* larvae.

diagnoses and therapies.

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