CASE REPORT

Shiga toxin producing *E coli* bloodstream infection secondary to *Strongyloides* penetration through intestinal mucosa

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SUMMARY

A 51-year-old woman with diabetes, who immigrated to the USA 22 years ago from Laos, was admitted to the hospital for evaluation of fever, abdominal pain, vomiting and diarrhoea. A workup for acute gastroenteritis revealed a positive stool PCR for Shiga toxin-producing *Escherichia coli*. Two sets of blood cultures drawn at admission were positive for *E coli*. A review of her previous medical records revealed the presence of eosinophilia, up to 20%, 14 years prior to that was never investigated. Therefore, stool samples were examined and two of three specimens were positive for *Strongyloides stercoralis* larvae, confirming the diagnosis of *Strongyloides* hyperinfection syndrome.

BACKGROUND

Strongyloides stercoralis is an endemic parasitic infection that can cause an asymptomatic infection which can persist for years due to an autoinfection cycle. It has a tendency to cause hyperinfection, especially in immunocompromised patients.¹ *Strongyloides* larvae penetrate through intestinal mucosa to enter the bloodstream, which can result in bacteraemia with gastrointestinal flora. Occasionally, this bloodstream infection can be further complicated by meningitis with enteric organisms. The diagnosis of *Strongyloides* enteric infection can be easily missed in the absence of a clinical suspicion. An undiagnosed infection with *Strongyloides* can result in recurrent secondary bloodstream infections that are associated with high morbidity and mortality.

CASE PRESENTATION

A 51-year-old woman with underlying type 2 diabetes mellitus presented to the emergency room of an outside hospital in December 2012 with abdominal cramping associated with nausea, multiple non-bloody emesis, abdominal pain and diarrhoea of 2 days duration. She was found to have a temperature of 39°C. Her abdominal examination was significant for generalised tenderness to palpation, but without any guarding or rigidity to suggest peritonitis. Her bowel sounds were normal. The remainder of the examination was unremarkable.

Besides diabetes, her medical history was significant for hypertension, hyperlipidaemia and gastroesophageal reflux disease. She had an appendectomy 7 years prior to her presentation.

She had immigrated to the USA from Laos 22 years prior and had not travelled back since that

time. She was living with her husband and had no pets. She had not travelled outside the country in the past many months. She had been drinking city water and had not eaten outside her home during 1 week prior to getting sick. The only raw food she had eaten was a papaya (*Carica papaya*) 2 days prior to the onset of her current illness. She did not know of anyone else who had similar symptoms.

INVESTIGATIONS

CT of the abdomen and pelvis was performed per renal stone protocol due to an initial clinical suspicion of nephrolithiasis. There was no evidence of nephrolithiasis but she was found to have caecal wall thickening and surrounding fat stranding suggestive of right-sided colitis. Simultaneous laboratory investigations revealed anaemia with a haemoglobin 9.3 g/dL (normal: 12–15.5 g/dL), white cell count $9.3 \times 10^9/L$ (normal: $3.5\text{--}10.5 \times 10^9/L$) with 87% neutrophils and platelets $90 \times 10^9/L$ (normal: $150\text{--}450 \times 10^9/L$). She was also found to be in acute renal failure with creatine 2.2 mg/dL (normal 0.6–1.1 mg/dL). A previously noted creatine 5 years ago was 0.5 mg/dL. Blood cultures, urine cultures and stool studies for enteric pathogens were sent and the patient was admitted to the hospital for intravenous fluids and antibiotics. She was started on piperacillin/tazobactam pending further investigations. The next day *E coli* was reported to be growing from both sets of blood cultures. *E coli* growth was also observed on the urine culture plates. Later a PCR performed on stools was also revealing for Shiga toxin producing *E coli* O157.

Given her symptoms including diarrhoea and fever along with the positive stool examination for Shiga toxin producing *E coli*, acute renal failure as well as anaemia and thrombocytopenia, haemolytic uraemic syndrome was suspected and a peripheral smear was checked. However, no schistocytes or other evidence of haemolysis was seen. Later, due to the ongoing diarrhoea, she underwent a colonoscopy, which revealed multiple small punctate lesions with raised yellowish exudates in the ascending colon (figure 1).

Infectious diseases service was consulted to assist with management of her blood stream infection. A review of her electronic medical record revealed the presence of eosinophilia about 14 years ago on a routine complete blood cell count. She did not recall any knowledge of this or any follow-up in this regard.

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Figure 1 Colonoscopy showing xanthomatous lesions.

Given her history of immigration from Laos, a previously documented eosinophilia, the current episode of sepsis related to her *E coli* blood stream infection and presence of xanthoma-like lesions on colonoscopy, presence of an underlying *Strongyloides* infection was suspected and stool studies were advised to confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS

- ▶ Inflammatory bowel disease
- ▶ *Clostridium difficile* colitis
- ▶ Mesenteric adenitis
- ▶ Intestinal parasitic infection
- ▶ Urosepsis

TREATMENT

The patient continued to receive piperacillin/tazobactam for the next few days. Blood cultures were repeated to document clearance of her bacteraemia. The growth of *E coli* from urine cultures was attributed to secondary haematogenous seeding of the urine. She was transitioned to intravenous ceftriaxone and metronidazole on discharge to complete a 2-week treatment course. Stool examination during her hospitalisation did confirm the presence of *S stercoralis* larvae (figure 2) and the patient was treated with two doses of ivermectin (200 mcg/kg/day orally for 2 days).

Figure 2 *Strongyloides stercoralis* larvae in stool (×40 magnification).

OUTCOME AND FOLLOW-UP

The patient was followed up a month later in the outpatient clinic after having completed her 2 weeks course of intravenous antibiotics. All her symptoms and her eosinophilia had resolved as well.

Final diagnosis: Acute gastroenteritis due to Shiga toxin producing *E coli* complicated by *E coli* blood stream infection secondary to underlying *Strongyloides* hyperinfection syndrome.

DISCUSSION

S stercoralis is a helminth commonly found in tropical and sub-tropical regions such as sub-Saharan Africa and Southeast Asia. A seroprevalence rate of greater than 50% has been reported from Canada among Laotian immigrants.² It is found in moist soil and is transmitted by direct penetration of skin by the infective stage of the larvae known as filariform larvae. After penetrating the skin, the infective larvae can cause extremely pruritic urticarial linear rashes termed larva currens. They ultimately reach the vasculature from the site of penetration. They then migrate to the lungs potentially causing an eosinophilic pneumonia after penetrating into alveolar sacs. Thereafter, they are coughed up and swallowed to reach the intestines where they mature into adults. The adults release eggs which hatch into rhabditiform larvae. These are shed in stools and later transformed into the infective filariform larvae after coming in contact with moist soil thereby completing the life cycle. Unlike many other parasites, *Strongyloides* can complete its life cycle within the host by transformation of rhabditiform larvae into filariform larvae which can then reinfect the host by either penetrating the intestinal mucosa or the perianal skin thereby completing an autoinfection cycle. This can lead to persistence of infection within the host for decades following the initial infection.

During their penetration through the intestinal mucosa, the infective larvae can carry gastrointestinal bacteria on their surface into the blood stream causing bacteraemias, pneumonitis or in extreme cases even meningitis. The high-grade bacteraemia in our patient triggered the diagnostic possibility of underlying *Strongyloides* infection, as acute gastroenteritis syndromes are generally not associated with blood stream infections. In general, patients with underlying defects in their cellular immunity like those with haematological malignancy, malnutrition, AIDS or those taking long-term high-dose steroids are at high-risk of disseminated disease with *Strongyloides*.¹ Our patient did not have any of these underlying conditions but did have diabetes which has been reported to be associated with *Strongyloides* hyperinfection syndrome in a few other case reports.^{3–6}

Diagnosis of *Strongyloides* hyperinfection syndrome requires a high degree of clinical suspicion since the most common laboratory finding of an established infection, eosinophilia, may be masked secondary to neutrophilic leukocytosis that usually accompanies an acute sepsis syndrome as was the case in our patient. Review of a patient's medical record may be helpful if they have had a previously documented eosinophilia. Standard stool examination can be insensitive for the diagnosis of Strongyloidiasis as the larvae are shed only intermittently. Multiple stool examinations (up to 7) may be required if clinical suspicion is high. Use of special procedure like Baermann technique or agar plate culture can increase diagnostic sensitivity.⁷ Serology using ELISA can be helpful if multiple stool examinations remain unrevealing. It has a sensitivity of 83–89% and specificity of 97%,⁸ but is only available at reference laboratories. Endoscopy is usually not required for diagnosis but if performed for another indication, it can reveal mucosal erosions, serpiginous ulcerations or xanthoma-like lesions.

Treatment primarily consists of ivermectin 200 mcg/kg administered either daily for 2 days or 2 weeks apart. In a study from Spain, the efficacy of two doses of ivermectin was reported to be 100%.⁹ Alternative treatment can be considered with multiple doses of albendazole.

Prevention measures consist of avoiding walking barefoot on moist soil, adequate food and water hygiene, sanitary disposal of excreta as well as avoiding night soil for farming. According to WHO, control programmes utilising ivermectin for control of lymphatic filariasis may have an impact on incidence of *Strongyloides* as well.¹⁰

A number of cases of *Strongyloides* hyperinfection syndrome occur annually and can easily be overlooked if a practicing clinician is not familiar with the syndrome. Examination of a single stool specimen may miss the adult or larval form of the parasite and thus repeat examination is mandatory in the appropriate clinical setting. A serological test is available but may be falsely negative in immunosuppressed hosts. There may also be high rates of false positives in endemic region where they can represent a prior exposure.

Learning points

- ▶ Strongyloidiasis is endemic in tropical and subtropical regions.
- ▶ Autoinfection cycle can result in persistence of asymptomatic infection for decades.
- ▶ Asymptomatic eosinophilia is the most common manifestation in an immunocompetent host.
- ▶ Disseminated infection can result from heavy parasite burden especially following immunosuppression.
- ▶ Blood stream infections or meningitis with gastrointestinal flora in an individual from an endemic area should prompt clinicians to consider presence of an undetected *Strongyloides* hyperinfection syndrome.

Contributors All authors participated equally in conception and design of the paper. Initial draft was prepared by SS. All authors contributed to the collection, assembly, analysis and interpretation of the data, critical revisions and final approval.

Competing interests None.

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