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Case report

Is Shigella an under-recognized pathogen? A case of pyogenic cervical spondylitis caused by *Escherichia coli* and *Shigella flexneri* infection

Jiafeng Zhang [1], Yaoting Liu [1], Hongkun Wu [1], Lin Zhou [*]

Department of Laboratory Medicine, Shanghai Changzheng Hospital, Naval Medical University, 415 Fengyang Road, Shanghai 200003, PR China

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ABSTRACT

Shigella typically causes gastrointestinal infections, and extra-intestinal manifestations are rare. We report the first known case of pyogenic cervical spondylitis co-infected with *Escherichia coli* and *Shigella flexneri*, highlighting the diagnostic challenges and clinical implications. A 53-year-old woman presented with neck pain for one month. MRI revealed C6 and C7 vertebrae abscesses. The patient underwent anterior cervical debridement and bone-graft fusion. Intraoperative pus culture grew *Escherichia coli*, while metagenomic next-generation sequencing detected both *Escherichia coli* and *Shigella* species. Intravenous imipenem 500 mg every 6 h was administered, leading to full wound healing at a 6-month follow-up. This case emphasizes the importance of considering *Shigella* infection in the differential diagnosis of pyogenic spondylitis and demonstrates the utility of a multi-pronged diagnostic approach.

Introduction

Shigella is a short, gram-negative, non-spore-forming, facultative anaerobic pathogenic bacterium that is a member of the *Enterobacteriaceae* family. It is among the leading causes of diarrhea deaths, with approximately 160,000 deaths per year in all age groups worldwide [3]. *Shigella* generally causes infections of the gastrointestinal tract and induces a diarrheal syndrome. Clinical symptoms of shigellosis include abdominal pain, tenesmus, watery diarrhea, fever, and gastrointestinal inflammation. In some cases, *Shigella* infection is also associated with extra-intestinal manifestations, including involvement of the eyes, skin, bones, urinary tract, and nervous and cardiac systems [1,6]. However, isolated extra-intestinal manifestations without *Shigella* enteritis are rare.

Here, we report the use of multi-pronged approach to detecting *Escherichia coli* (*E.coli*) and *Shigella flexneri* (*S.flexneri*) as the causative pathogens for a case of pyogenic cervical spondylitis. We also present a comprehensive literature review informing this case discussion.

Case report

A 53-year-old woman in previously good health presented with neck pain since 1 month. She lived in rural Jiangsu Province, China, and gave no history of diarrhea, gastrointestinal illness, travel, or insect bite. A physical examination revealed limited cervical flexion and extension, and pressure-induced pain in the gap between the C6 and C7 spinous processes and the paraspinal region. The patient did not have fever. Laboratory examinations showed the following: white blood cell count, 12×10^9/L; C-reactive protein, 15.78 mg/L; and erythrocyte sedimentation rate, 30 mm/h. Magnetic resonance imaging (MRI) showed abnormal signals of the C6 and C7 vertebrae, suggestive of infectious abscess (Fig. 1A). The patient was diagnosed with pyogenic cervical spondylitis, but the cause was unknown. She underwent anterior cervical debridement and spinal fusion with autologous bone graft. Intraoperative cervical-pus samples were sent for culture and mNGS. Two days later, the culture results showed *E. coli*. The isolate was susceptible to piperacillin/tazobactam, cefoperazone/sulbactam, ceftazidime, imipenem, meropenem, and amikacin; moderately susceptible to ciprofloxacin and levofloxacin; and resistant to first- and second-generation cephalosporins. However, mNGS showed 12 sequence reads of *E. coli* and only 2 sequence reads of *Shigella boydii* (*S.boydii*).

Timeline

Timepoint	Event Description
1 month prior	Patient experiences neck pain

(*continued on next page*)

* Corresponding author.
E-mail address: lynnzhou36@126.com (L. Zhou).
[1] These authors contributed equally: Jiafeng Zhang, Yaoting Liu, Hongkun Wu

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Fig. 1. (A) Magnetic resonance imaging on admission shows a reduction in T1-weighted signals in the C6 and C7 vertebral bodies (arrows), paravertebral soft-tissue swelling in the spinal canal, secondary stenosis of the spinal canal, and localized dural sac and spinal cord compression secondary to narrowing. (B) Columbia blood agar plate showing round white colonies of two sizes; MacConkey agar plates with lactose-fermenting (middle) and non-fermenting (right) bacterial growth. (C) Agglutination test shows that the isolate strongly agglutinates in *Shigella* group B (*S. flexneri*) antiserum.

(*continued*)

Timepoint	Event Description
Initial visit	Patient presents with neck pain; undergoes lab tests and MRI, diagnosed with pyogenic cervical spondylitis
Pre-surgery	Patient undergoes anterior cervical debridement and spinal fusion with autologous bone graft
2 days post-surgery	Culture results show *E. coli* infection; mNGS reveals *E. coli* and *Shigella* infection
2 weeks post-surgery	Patient's wound develops swelling and redness, pus drained; culture results show *E. coli* and *S. flexneri* infection
Post-surgery treatment	Patient starts intravenous imipenem 500 mg every 6 h for 8 weeks

The patient did not have gastrointestinal symptoms, and stool cultures did not grow *Shigella*. Given the above findings and the apparent rarity of *Shigella* infections, we considered that *E. coli* was the primary cause of the infection. The patient was empirically treated with intravenous cefoperazone sodium, sulbactam sodium, and moxifloxacin. After 2 weeks of treatment, the patient's wound developed swelling and redness, and 5 mL pus was drained from the wound. The purulent liquid was cultured for bacteria, fungi, and mycobacteria. After incubation for 24 h, Columbia blood agar plates showed round white colonies measuring 1–2 mm in diameter, and MacConkey agar plates showed two types of bacterial growth: lactose-fermenting and non-fermenting bacteria (Fig. 1B). No fungal or mycobacterial growth was seen. The two strains were identified as *E. coli* and *Shigella* group by using Vitek2 Compact®. A 16S rRNA gene polymerase chain reaction (16 S PCR) test revealed that the sequence was identical to *S. flexneri*. The *Shigella* strain was susceptible to imipenem and meropenem; moderately susceptible to ciprofloxacin and cefoperazone/sulbactam; and resistant to ampicillin, ampicillin/sulbactam, ceftriaxone, and sulfonamides. Stool culture was repeated, but *Shigella* was not isolated from the feces. A specimen was sent to the Shanghai Center for Disease Control and Prevention for agglutination testing with *Shigella* immune serum. The isolate strongly agglutinated in *Shigella* Group B (*S. flexneri*) antiserum but not in Group A, C, or D antisera (Fig. 1C).

The patient was diagnosed with pyogenic cervical spondylitis caused by *E. coli* and *S. flexneri*, and started on imipenem 500 mg every 6 h for 8 weeks. At a follow-up visit 6 months later, she claimed gradually resolved symptoms, and she had complete clinical and microbiological recovery.

Discussion

Our case report contributes to the limited knowledge on extra-intestinal Shigella infections, particularly in the context of pyogenic cervical spondylitis. By presenting a rare case of concurrent E. coli and S. flexneri infection, we aim to raise awareness among clinicians about the importance of considering Shigella as a potential causative agent and to emphasize the need for appropriate diagnostic and therapeutic approaches.

Our patient was diagnosed with pyogenic cervical spondylitis due to *E. coli* and *S. flexneri* infection. Extra-intestinal manifestations of shigellosis are rare, possibly because *Shigella* infection is usually a self-limiting disease. Only 5 cases of *Shigella* infection of the bones or joints have been described in the literature (Table 1) [5,7–9]. Of the 5 patients, 4 had no gastrointestinal symptoms before onset. Consistent with our case, in the above 5 cases, the clinical symptoms of the patients were usually nonspecific. *Shigella* was not isolated from the stools of any of these patients. The absence of preceding gastrointestinal symptoms in almost all patients may mean that *Shigella* infection of the bones or joints is an occult infection. Little is known about the association between bone or joint infections and *Shigella* species, and the pathway by which *Shigella* infected the bones or joints was unknown in all of the above cases, except one [8].

Definitive diagnosis of *Shigella* infection can only be made by

Table 1
Clinical characteristics of patients with bone or joint infections caused by *Shigella* species.

Year	Age, sex	Job	Risk factors	Clinical features	Body parts	Species	Specimen	Identification method	Treatment/duration	Outcome	Reference
1996	69, M	Hunter	Trip to Mexico	Back pain, weakness, and sensory loss	9th and 10th thoracic vertebral bodies	*Shigella boydii*	Intraoperative tissue	Culture	Cefazolin/6 weeks	Symptom improvement	[4]
1994	19 mo, M	NA	None	Coryza, diarrhea, left leg pain, refusal to walk, irritability, fever	Hip joint	*Shigella sonnei*	Synovial fluid	Culture	Cefuroxime/21 days, Gentamicin/7 days	Asymptomatic with normal gait and good serological evolution	[2]
1968	23 months, F	NA	None	Fever, chills, painful swelling of hands and feet	Right ankle, left tibia, and radius	*Shigella sonnei*	Blood, pus	Culture	Chloramphenicol/ intravenously 3 weeks, orally 1 week; Ampicillin/ 1 week	Completely normal	[5]
2001	34, F	No	None	Right arm pain	Proximal humerus	*Shigella* spp., *Flavobacterium* spp.	Diaphysis of right humerus	Culture	Ciprofloxacin/6 weeks	Complete resolution of symptoms, complete recovery	[6]
1993	24, M	No	Incision and drainage of right tibia without antibiotics 1 year ago	Painful swelling of right tibia for 1 week	Right tibia	*Shigella flexneri*	Soft tissue and medullary canal	Culture	Ampicillin/8 weeks	Wound well healed, good serological evolution	[7]
2021	53, F	Farmer	No	Neck pain	C6 and C7 vertebrae	*Shigella flexneri*, *Escherichia coli*	Pus	mNGS, 16 S PCR, culture	Imipenem/8 weeks	Disappearance of pain and scan anomalies, good serological evolution	Present case report

isolation of the microorganism from a specimen and serological typing of the isolate. In this case, we performed mNGS and culture of the intraoperative pus sample for optimal sensitivity. However, a limitation of this technique is that its sensitivity is heavily dependent on host background levels [2]. In our case, 12 sequences were detected for *E. coli* and 2 sequences were detected for *S. boydii*. The reason for this difference may be the influence of the human host background, which leads to a reduction in the number and proportion of microbial read lengths. Additionally, when the results of 16 S PCR test and mNGS are inconsistent, it is not clear which one should be believed. It is necessary to consider mNGS results in combination with the clinical manifestations and conventional methods to reach a conclusion.

The widespread application of antibiotics has led to increasing resistance of *Shigella* to fluoroquinolones. The use of fluoroquinolone antibiotics to treat *Shigella* infections, which carry quinolone-resistant strains, may increase the risk of individuals developing a more severe clinical course. The US Centers for Disease Control and Prevention recommends that ciprofloxacin not be used at a minimum inhibitory concentration (MIC) $>$ 0.12 μg/mL to treat *Shigella*, even if the isolate is susceptible to fluoroquinolones. Therefore, it is important to test the initial *Shigella* isolate for drug sensitivity, especially for quinolones, and to note the MIC.

In our case, the patient never had diarrhea, and stool cultures showed no evidence of the presence of *Shigella.* The intraoperative pus sample did not grow *Shigella* cultures, but the mNGS did show *E. coli* and *S. boydii*. Considering the homology of the two species combined with the culture results and the rarity of *Shigella* in spondylitis cases, we initially excluded *Shigella* infection. During anti-infective treatment against *E. coli*, the patient developed purulent discharge from the incision site. Repeat culture of the wound secretion did grow *Shigella*. The reasons for the initial negative cultures (with the exception of *E. coli*) of the pus obtained via anterior cervical debridement may be varied and related to specimen collection, laboratory operations, bacterial counts, etc. The possibility that the *Shigella* infection was acquired intraoperatively seems unlikely but cannot be excluded.

Conclusion

We describe a potential pathogen causing spondylitis. Our case illustrates the importance of a multi-pronged approach to detecting pathogenic bacteria. In addition, microbiologists and clinicians should recognize the need for drug-susceptibility testing of the initial *Shigella* isolate, and pay attention to the MIC of quinolones.

Ethics approval

Informed consent was obtained for the publication of this article.

Consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethics approval and consent to participate

Design of the work has been approved by the local ethical committee.

Statement of independence of researchers from funders

The authors are free of any financial incentives or involvement in the promoting of this study.

Authors' contributions

JZ and YL collected data and wrote the original draft; HW re-collected the data and revised the manuscript. LZ conceived the manuscript and made a revision of it. All authors read, edited, and approved the final version of the manuscript.

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Declaration of Generative AI and AI-assisted technologies in the writing process

All authors confirm that no generative AI tools or software were used in the writing, editing, or revision of this manuscript.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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