CASE REPORT

Rare case of *Streptococcal enteritis* in HIV patient

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Abstract

Only a small number of cases of *Streptococcus pneumoniae* bacteremia with gastrointestinal tract involvement have been reported in the literature, even in immunocompromised patients.

This case report describes an immunosuppressed forty-year old human immunodeficiency virus (HIV)-positive patient with *S. pneumoniae* bacteremia presenting as acute enteritis. The patient suffered from fever, severe watery diarrhea, and acute abdomen. Laboratory tests showed elevation of inflammatory markers and acute kidney injury. Stool examination was positive for fecal leucocytes, while radiology studies were indicative of respiratory involvement. The patient was rehydrated and initially treated with IV ciproflocaxin and metronidazole, but after positive blood culture result for *S. pneumoniae*, the treatment was changed to IV ceftriaxone. The patient responded to the treatment and was discharged on 7th day with oral moxifloxacin prescribed. Ten days after finishing the treatment, there was a lower respiratory tract recurrence with negative blood cultures for *S. pneumoniae*, which responded to meropenem without another recurrence until today.

In the last 26 years (1993-2019), a few cases have been described, two of which in HIV-positive patients. To our knowledge, this is the first case of concurrent severe *S. pneumoniae* pneumonia and enteritis without any complaints from the respiratory system in a severely immunosuppressed patient.

Key words: HIV, immunosuppression, diarrhea, enteritis, *Streptococcus pneumoniae*.

Introduction

Streptococcus pneumoniae bacteremia involving the gastrointestinal tract is rarely reported in literature, even in immunosuppressed patients. In the last 26 years (1993-2019), a few cases have been described, two of which in human immunodeficiency virus (HIV)-positive patients (Table 1). In this case report, we describe a severely immunocompromised HIV-positive patient with *S. pneumoniae* bacteremia presenting as acute enteritis. Moreover, we present a review of the literature.

Case presentation

A severely immunocompromised forty-year-old HIV-positive male presented with fever, severe watery diarrhea (> 6 bowel movements per day), and diffuse abdominal pain without vomiting for three days. He was a heavy smoker with chronic pulmonary disease and a former intravenous drug user diagnosed with HIV five years ago, and complicated in the past with mycobacterium avium complex disease. He was under antiretroviral treatment with raltegravir, emtricitabine, and tenofovir disoproxil fumarate, with poor

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Table 1. Cases of pneumococcal enteritis reported between 1993-2018

Author(s), year of publication	Age (years)	Site of infection	Evidence of *S. pneumoniae*	Radiologic findings	Treatment	Predisposing factors
Argemi *et al.*, 2016	35	Appendix	Blood culture	CT: dilated, thick-walled, blind-ending tubular structure with an 8 mm diameter	Surgery, antibiotics	–
Caiero *et al.*, 2015	43	Appendix	Culture of drained purulent secretions	CT: thickened appendix (filled with liquid)	Surgery, antibiotics	HIV+ (CD4+ 239 cells/µl)
Clark *et al.*, 1993	28	Appendix	Intraoperative cultures	US: free fluid in the abdomen	Surgery, antibiotics	HIV+ (CD4+ 390 cells/µl), hemophilia A
Petti *et al.*, 2002	33	Terminal ileum	Blood culture	CT: thickening of the cecal wall	Surgery, antibiotics	–
	29	Cecum	Swab of cecal wall	–	Surgery	–
Ronnachit *et al.*, 2017	37	Peritoneum fallopian tube	Blood culture, pelvic pus PCR, urine Ag, ascites Ag	–	Surgery, antibiotics	SLE, orogonitis
	40	Sigmoid colon, lungs	Blood culture	–	Antibiotics	ITP
	41	Gastrointestinal peritoneum	Blood culture, urine A, blood Ag, stool Ag, ascites Ag, stool microscopy	–	Antibiotics, drainage	–
	49	Gastrointestinal	Blood culture, urine Ag, stool Ag	–	Antibiotics	–
Soman *et al.*, 2009	77	Gastrointestinal	Blood culture	–	Antibiotics	–

CT – computed tomography, DM – diabetes mellitus, ITP – idiopathic thrombocytopenia, IUCD – intrauterine contraceptive device, PID – pneumococcal invasive disease, SLE – systemic lupus erythematosus, US – ultrasound

compliance and last CD4 count of 15 cells/mm³. On admission, he was in mild distress due to abdominal pain and high fever. He did not report other symptoms, such as headache, dyspnea, cough, or chest pain. Clinical examination indicated dehydration (tachycardia, mean blood pressure of 70 mm Hg, dry mucous membranes), revealing abdominal guarding and rebound tenderness with hypoactive bowel sounds. Obturator and psoas signs were negative. Lung auscultation showed scarce crackles and wheezing bilaterally without hypoxemia. Laboratory tests resulted in elevation of white blood cell count, C-reactive protein, urea, and creatine, as shown in Table 2. Normochromic normocytic anemia and thrombocytopenia were preexisting and attributed to severe acquired immunodeficiency syndrome (AIDS) disease. The quick sequential organ failure assessment (qSOFA) score indicated zero, while the sequential organ failure assessment (SOFA) score was regarded as inaccurate, since the patient's only pathological value was thrombocytopenia, which was a chronic finding. Further investigation with chest and abdominal X-rays identified a hazy infiltration in the left lower lobe and dilatation of bowel loops. In the meantime, stool examination was positive for fecal leucocytes. Rigorous intravenous rehydration and empirical combination of ciprofloxacin and metronidazole were initiated. Due to the severity of clinical symptoms, an abdominal and chest computed tomography (CT) scanning were performed, revealing mild thickness of terminal ileum wall (the finding consistent with acute enteritis) and bilateral consolidation in the lower lobe with ground glass in the middle and upper left lobe, respectively. During the next two days, the patient's clinical condition quickly ameliorated with recession of his symptoms. On the third hospital day, penicillin sensitive *S. pneumoniae* was isolated from the blood culture drown on admission day and antibiotic treatment was switched to ceftriaxone. On the other hand, the stool culture for common enteropathogens (*Salmonella, Shigella, Campylobacter, Vibrio*, and *Yersinia*) and testing for *Clostridium difficile* (antigen and toxin) remained negative. Additionally, serology and PCR testing for CMV, HSV-1, HSV-2, and blood-sputum cultures for *Mycobacterium tuberculosis* were negative. The patient was

Table 2. Laboratory tests values

Laboratory test	Values	Normal range
Hemoglobin (Hb)	11.8 mg/dl	13-17 mg/dl
Hematocrit (HCT)	33.6%	40-52%
Mean corpuscular volume (MCV)	92.6 fl	80-100 fl
White blood cells (WBC)	$8.73 \times 10^9/l$	$4\text{-}10 \times 10^9/l$
Neutrophils (PMN)	94.8%	40-80%
Platelets (Plt)	$59 \times 10^9/l$	$150\text{-}400 \times 10^9/l$
Glucose (Glu)	87 mg/dl	65-110 mg/dl
Urea (Ur)	116 mg/dl	17-43 mg/dl
Creatinine (Cr)	1.9 mg/dl	0.8-1.3 mg/dl
Aspartate aminotransferase (AST)	36 IU/l	5-30 U/l
Alanine aminotransferase (ALT)	20 IU/l	5-30 U/l
C-reactive protein (CRP)	276 mg/l	< 5 mg/l
Gamma glutamyl transferase (γGT)	14 IU/l	6-50 U/l
Alkaline phosphatase (ALP)	43 IU/l	50-100 U/l
Lactate dehydrogenase (LDH)	333 IU/l	50-150 U/l
Creatine kinase (CK)	947 IU/l	25-200 U/l

discharged on the 7th hospital day, with a recommendation to take moxifloxacin orally for a total of fourteen days. Ten days after the end of antibiotic treatment, there was a recurrence of fever accompanied with severe pain in right hemithorax, worsening in deep inspiration, and the patient was re-admitted to the hospital. No pathological findings, either from physical examination or chest X-ray, were observed. Meropenem was administered empirically due to the recent use of third generation cephalosporin. Another chest CT-scanning showed an ill-defined infiltration in the right lower lobe, with a very small pleural effusion in the same side consistent with recurrent pneumonia. However, it was not confirmed to be due to *S. pneumoniae*, because two pairs of blood cultures drown before the initiation of antibiotics were negative and a rapid urine antigen test for *S. pneumoniae* was not available. The patient presented a quick clinical improvement, and was discharged on the 7th hospital day, without any rebound of his symptom until today.

Discussion

S. pneumoniae is the most common cause of community-acquired pneumonia. The burden of pneumococcal disease in HIV-seropositive patients is higher than that of the general population, with a 100-fold risk for coexistence of pneumococcal pneumonia and bacteremia [1]. Among 9,283 adults aged 15-44 years old with a diagnosis of invasive pneumococcal disease (IPD), 2.4% were living with undiagnosed HIV.

The incidence of IPD in any population is affected by geographic location, time of year, age, and vaccination status. Other predisposing factors include immunosuppression (e.g., HIV with low CD4 count and high levels of HIV RNA, syste-

mic lupus erythematosus, multiple myeloma), social factors (e.g., alcohol abuse, injection drug use, homelessness, smoking), chronic conditions (e.g., cirrhosis, hypoalbuminemia, COPD, asthma, splenectomy, hyposplenism), previous episodes of pneumonia or influenza infection, and pregnancy [3-22].

Particularly in HIV patients, multiple immunity defects have been recognized, including T cells, B cells, low levels of IgG globulins against pneumococcal polysaccharide, and impairment of proinflammatory cytokines [23, 24]. Also, the pneumococcal serotypes may differ between HIV and non-HIV patients as highly invasive ones, such as 1, 5, and 7F, which have been shown to cause IPD to a much lower proportion to HIV patients than those with unknown HIV status [2]. The introduction of antiretroviral treatment (ART) has dramatically reduced the incidence of pneumococcal disease, with a further reduction attributed to the prophylaxis with trimethoprim-sulfamethoxazole against *Pneumocystis jiroveci*.

Although common sites of infection in the setting of *S. pneumoniae* bacteremia are the respiratory and/or central nervous system, alternative rare locations have also been described, as the gastrointestinal system [2].

The pathophysiology of streptococcal invasion to the gastrointestinal system have been attributed to: 1) direct invasion of the gut wall via hematogenous seeding; 2) direct infection via mucosal translocation; 3) enterotoxin production from *S. pneumoniae* strains stimulating a secretory diarrhea; 4) ascending invasion through the fallopian tubes in females [25].

To our knowledge (Table 1), this is the first case report on concurrent severe *S. pneumoniae* pneumonia and enteritis without any complaints from the respiratory system in a severely immunosuppressed patient in the last 26 years (1993-2018) [24-28], for the reasons discussed below.

Due to the patient's CD4+ count < 100 cells/ml, he was vulnerable to a plenty of causes, including opportunistic infections. There was no biopsy confirmation because he responded quickly to conservative treatment. Also, stool cultures lacked sensitivity for *S. pneumoniae* due to inhibitory culture media. Nevertheless, the patient's history, duration of symptoms, frequency, and the rest of laboratory tests were valuable in differential diagnosis.

It is evident that our patient suffered from bacteremic pneumonia and enteritis for the following reasons:

1. Pneumococcal bacteremia was documented in admission and symptoms of enteritis were prominent.

2. According to the duration of symptoms (less than four weeks), all the causes of chronic diarrhea (e.g., ART and HIV-related diarrhea) were excluded.

3. Fecal leucocytes in stool microscopy are not reported in pneumonia presenting with extrapulmonary symptoms [29].

4. No other pathogen was isolated from three stool samples (including parasites), and blood tests for CMV, HSV-1, HSV-2, and *M. tuberculosis* were negative.

5. Abdomen CT was consistent with enteritis.

6. The patient's symptoms were related to the gastrointestinal (GI) system and resolved after the initiation of a short duration antibiotic treatment.

7. Disseminated atypical mycobacterial disease in a severely immunocompromised patient is a very serious persisting condition confirmed by positive blood cultures that demands a combination of antibiotics for an extended period of time to prevent recurrence.

8. There was no epidemiologic exposure history (travels, food, anal intercourses, etc.) leading to another diagnosis, but there are risk factors for streptococcal infection (smoking, immune defect) [25]. It is also noticeable that the patient was not vaccinated against pneumococcal bacteria as recommended, due to poor compliance. The importance of primary prophylaxis is emphasized by the fact that 61% of IPD episodes among HIV-positive adults are caused by serotypes covered by pneumococcal conjugate vaccine (PCV13) [30].

Conclusions

Invasive *S. pneumonia* disease may rarely present with predominant gastrointestinal symptoms. As a result, high suspicion for this entity should be held, when a patient with predisposing factors presents with GI symptoms [24, 31].

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