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Ceftriaxone Resistant Salmonella enterica Serovar Kentucky as a Cause of Bacteremia and Gastroenteritis: A Case Report

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Abstract

Salmonella enterica serovar Kentucky is an emerging human pathogen in developed countries and also a concern for public health in developing countries. Although genus Salmonella is usually susceptible to many antimicrobial agents, a recent increase in resistance has become a cause for concern. A case of ceftriaxone resistant Salmonella enterica serovar Kentucky causing bacteremia and acute gastroenteritis is reported in this paper. The Salmonella Kentucky isolate in this case was resistant to most classes of antibiotics. This is the first case report of Salmonella enterica serovar Kentucky resistant to ceftriaxone. Multidrug resistant patterns of Salmonella Kentucky are observed globally. Awareness of various nontyphoid Salmonella causing human infections is of utmost importance, because delayed identification, serotyping, and susceptibility testing may delay the administration of antibiotics leading to worsening outcomes.

Keywords

- bacteremia
- ceftriaxone resistant
- Salmonella Kentucky

Introduction

Salmonella enterica is a gram-negative, intracellular human and animal pathogen. The species Salmonella enterica includes more than 2,600 serovars, which are taxonomically classified into 6 subspecies, sharing high sequence similarity. The subspecies are divided into two clinically relevant groups according to the disease they cause.[1] Infections within humans are restricted, among which Salmonella typhi, S. Paratyphi A, B, and C can cause invasive, life-threatening systemic diseases and are referred to as typhoid or enteric fever. On the other hand, nontyphoidal serovars normally cause self-limited gastroenteritis, associated with intestinal inflammation and diarrhea that lasts for 5 to 7 days. In recent years, the increasing incidence of nontyphoidal Salmonella (NTS) are a leading cause of gastroenteritis globally including tropical countries like India and sometimes it can be fatal.[2]

With the substantial progress made in preventing food-borne diseases, new pathogens have emerged, some of which have spread worldwide. These pathogens include strains of typhoidal Salmonella and NTS.[3] Global spread of NTS, especially Salmonella enterica serotype Kentucky in animals and humans since the 1990s is a good example.[4] Salmonella enterica serovar Kentucky is an emergent human pathogen, even in developed countries and also a worry to public health in developing countries. However, Salmonella species is usually susceptible to many antimicrobial agents, a recent increase in resistance has become a cause for concern.[5] The diagnosis and treatment of Salmonella enterica serovar Kentucky has become more difficult due to the drug

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resistance. Various studies have reported the foodborne infections and outbreaks of gastroenteritis due to Salmonella Kentucky.[6]

The high incidence of Salmonella Kentucky and the emergence of its recent multidrug resistant strains with high level resistance to ciprofloxacin and ceftriaxone indicates this serovar could be a potential threat to public health. Hence, this case is being reported.

Case Report

A 59-year-old male patient presented with fever, vomiting, and loose stools for 2 days with associated generalized weakness, chest pain, and cough. He is a known case of asthma and hypertension. On general physical examination at admission, the patient was febrile (102°F), dehydrated, pulse rate of 140/min, blood pressure 100/70 mm Hg, respiratory rate 24/min, and SPO2 90% at room air. There was no icterus, cyanosis, clubbing, lymphadenopathy, and edema. Respiratory system examination was normal. Abdomen was soft and no organomegaly noted. Cardiovascular system examination revealed normal S1 and S2 sounds and no murmurs. The patient was conscious and oriented. A provisional diagnosis of acute febrile illness with coronavirus disease 2019 (COVID-19) was made as patient was admitted during the COVID-19 pandemic. The patient was further evaluated with laboratory investigations and nasopharyngeal swab was sent for COVID-19 examination. The patient was started on injection piperacillin and tazobactam 4.5 g three times a day, injection doxycycline 100 mg twice daily, and injection metronidazole 100 mg intravenously three times a day.

Complete blood count showed an increase in total leucocyte count of 18,300 cells/cu mm with 93.5% of neutrophils, platelet count of 1.5 lac/cu mm, and normal red blood cell (RBC) count. Random blood sugar was 119 mg/dL. Renal function tests and urine routine were within normal limits. Liver function test showed mild hypoproteinemia with albumin-globulin ratio of 1.8. Lipid profile was normal. Serum electrolytes showed hypokalemia. Arterial blood gas analysis showed high anion gap with metabolic acidosis. His human immunodeficiency virus status was nonreactive and also nonreactive for hepatitis B surface antigen and anti-hepatitis C virus antibodies. The serum sent for fever panel such as Weil–Felix, dengue NS1 and immunoglobulin M (IgM), Leptospira IgM, malarial antigen (lactate dehydrogenase), and Widal test were negative. Urine culture yielded no growth. Feces microscopic examination showed few leucocytes, few RBCs, and no parasitic forms. No intestinal pathogens were grown in feces culture. Two bottles of blood culture samples were collected from different sites before the administration of antibiotics and were loaded to BacT/Alert system (bioMerieux, Inc). The ultrasonogram of the abdomen showed mild segmental circumferential wall thickening (3.2 mm) of the distal ileal loops, ileocecal junction, and cecum with impression of "infective/inflammatory etiology."

Both blood culture bottles flagged positive within 48 hours of incubation. Direct Gram stain smear prepared from positive blood cultures showed gram-negative bacilli. The reports were informed to attending clinician immediately and subculture was done on MacConkey and blood agar plates that were incubated aerobically at 37°C for 24 hours. The next day, nonlactose fermenting colonies were observed on both MacConkey agar plates and grayish translucent colonies on blood agar plates. The organism was motile, oxidase negative, and catalase positive. The isolate was further processed for identification and antibiotic susceptibility testing (AST) by automated Vitek Compact 2. The following day, Vitek Compact 2 systems identified it as Salmonella group, upon which conventional biochemical tests were performed and serotyping was performed using Poly O antisera, HI, O2, O4, and O9 antisera of Salmonella. In serotyping, the isolate showed agglutination with Poly O antisera and negative with HI, O2, O4, and O9 antisera. The conventional biochemical tests showed indole negative, urea not hydrolyzed, and citrate utilized. On triple sugar iron agar, it showed acid butt with alkaline slant with presence of abundant hydrogen sulfide and hence could not be differentiated from Salmonella Paratyphi B and Salmonella typhimurium species. Report was sent as Salmonella species along with the antibiotic susceptibility pattern as shown in ►**Table 1** along with minimum inhibitory concentration values. The isolate was sensitive to ampicillin, cotrimoxazole, amoxiclav, piperacillin-tazobactam, imipenem, meropenem, ertapenem, and tigecycline and resistant to ciprofloxacin and ceftriaxone by Vitek-2 GNB 405 card that had passed quality control (QC) check. This was confirmed by QC-passed discs by Kirby-Bauer disk diffusion method. All our isolates both typhoidal Salmonella and NTS are found to be sensitive to ceftriaxone. This is the first isolate of Salmonella that is ceftriaxone resistant. The isolate was sent to National Institute of Cholera and Enteric Diseases (NICED), Kolkata, West Bengal, India, for speciation and serotyping. Report from NICED showed that the isolate was identified as Salmonella serovar Kentucky with antigenic Eq. 8: i: Z6.

In view of the isolate being resistant to ceftriaxone, it was advised to continue treatment with piperacillin-tazobactam. The case was finally diagnosed as Salmonella bacteremia with acute gastroenteritis. After 4 days of treatment, the patient recovered symptomatically and was afebrile. He was discharged on 5th day with Taxim-O 200 mg twice daily, doxycycline 100 mg twice daily, and metronidazole 400 mg three times a day to be taken orally for 5 days.

Discussion

Salmonella infection is a major public health problem worldwide. Various animals (especially poultry, pigs, cattle, and reptiles) are reservoirs for Salmonella species, and humans generally get infected by eating undercooked or contaminated food. Recently, Salmonella enterica serovar Kentucky has been recognized as the most prominent Salmonella serovar causing human infections. According to the National Antimicrobial Resistance Monitoring System, the prevalence of S. Kentucky isolates has elevated from 25% in 1997 to 50% in 2007.[4]

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Table 1 Antibiotic sensitivity pattern of the isolate

Antibiotics	MIC	Interpretation	Antibiotics	MIC	Interpretation
Ampicillin	> 32	Resistant	Imipenem	< 0.25	Sensitive
Amoxicillin/Clavulanic acid	4	Sensitive	Meropenem	< 0.25	Sensitive
Piperacillin/Tazobactam	< 4	Sensitive	Amikacin	< 2	Resistant
Cefuroxime	> 64	Resistant	Gentamicin	< 1	Resistant
Ceftriaxone	> 64	Resistant	Nalidixic acid	> 32	Resistant
Ertapenem	< 0.5	Sensitive	Ciprofloxacin	> 4	Resistant
Colistin	< 0.5	Intermediate	Tigecycline	–	Sensitive
Cotrimoxazole	< 20	Sensitive			

Abbreviation: MIC, minimum inhibitory concentration.

In Morocco, Salmonella Kentucky was first identified in an 8-month-old child who was admitted at the pediatric department of the University Hospital Centre Ibn Rochd in Casablanca with an acute febrile diarrhea.[5] Many deaths have been reported in various places in India due to nontyphoid Salmonella infections. Salmonella enterica serovar Kentucky is a multidrug resistant organism that has been reported from various parts in the world.[3] Majority of the studies have concentrated on isolation, identification, and drug resistance of Salmonella serovar Kentucky.

In this case reported, the Salmonella Kentucky isolate was resistant to ampicillin and ceftriaxone which is unlike the isolate of Salmonella Kentucky isolated by Neelambike and Shivappa from Mysuru, South India, Karnataka, India, during 2019, that was sensitive to ampicillin and ceftriaxone.[1] While isolates of Salmonella Kentucky and Salmonella Virchow isolated by Sharma et al during 2020 from in and around Delhi, have reported that 72% of the isolates were resistant to ampicillin.[2] Another study by Sudhaharan et al from Hyderabad, South India have reported that the NTS were sensitive to both ampicillin and ceftriaxone during 2020.[3] Mahindroo et al in their study during 2016 have reported Salmonella Kentucky resistant to β lactams from North India.[4] This is the first case report of Salmonella Kentucky infection resistant to ceftriaxone from India.

Hello et al from Europe have reported that their isolates of Salmonella Kentucky were resistant to cefotaxime and ciprofloxacin in the year 2014.[5] Albert et al have reported their isolate of Salmonella Kentucky to be resistant to ampicillin but sensitive to cefotaxime in 2014.[6] Karraouan et al have reported their Salmonella Kentucky isolates from Morocco to be resistant to amoxycillin during 2017.[7] Hello et al have reported their Salmonella Kentucky isolates from France to be sensitive to ceftriaxone during 2022.[8]

According to a study published in the Lancet Infectious Diseases medical journal, Salmonella Kentucky is responsible for foodborne infections and has spread at an astonishing rate throughout Africa and the Middle East in the space of only a few years.[9,10] In this study, the authors note that the bacteria have recently spread to India and Southeast Asia and has acquired new resistance, particularly resistance to antibiotics of "last resort."[11]

Conclusion

There is an increasing incidence of drug resistance among human nontyphoidal Salmonellosis especially Salmonella Kentucky. The identification of Salmonella enterica serovar Kentucky and other nontyphoid Salmonella cannot be done in laboratories by conventional or automated identification systems, they further require typing from the reference centers. It is important to identify the species, subspecies of Salmonella causing human infections, and determine antibiotic sensitivity patterns by using standard AST methods which will help in the effective management of case and epidemiological studies.

Conflict of Interest
None declared.

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