Journal of Advances in Medical and Pharmaceutical Sciences

18(1): 1-5, 2018; Article no.JAMPS.41647
ISSN: 2394-1111

A Case Study of Multi-drug Resistant Surgical Site Infection after Intestinal Perforation Surgery Treated with Antibiotic CSE-1034

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Authors' contributions

This work was carried out in collaboration between all authors. Author SD designed the study, wrote the protocol. Authors MBD and AD managed the analyses of the study. Author AT managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2018/41647
Editor(s):
(1) Dr. Amr Ahmed El-Arabey, Pharmacology & Toxicology Department, Al-Azhar University, Egypt & University of Science and Technology of China (USTC), China.
Reviewers:
(1) Akobi Oliver Adeyemi, Nigeria.
(2) Angel Justiz Vaillant, University of the West Indies at St. Augustine, Trinidad and Tobago.
Complete Peer review History: http://www.sciencedomain.org/review-history/26372

Case Study

Received 02 April 2018
Accepted 14 June 2018
Published 24 September 2018

ABSTRACT

Background: Surgical site infections (SSIs) are one of the most frequent complications associated with surgeries and contribute significantly to morbidity and mortality if not treated promptly. Poor prognosis associated with SSIs could be partly attributed to the increase in antimicrobial resistance among the causative agents.
Case Presentation: This is a case of SSI due to multi-drug resistant (MDR) *E. coli* associated with intestinal perforation surgery treated successfully with CSE-1034.
Conclusions: CSE-1034 can be effectively used for the treatment of MDR SSIs. Utilizing CSE-1034 as an empiric therapy for SSIs could save time, the spread of resistance and can help to cut hospital-associated costs.

Keywords: Gastro-intestinal perforations; surgical site infections; CSE-1034.

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1. INTRODUCTION

Gastrointestinal tract perforations are usually emergency conditions that can occur at any site along the alimentary tract and require timely recognition and prompt treatment [1]. The mainstay of treatment that is usually recommended for intestinal perforations is immediate surgical intervention [1]. Nosocomial infections like SSIs ranging from minor wound infections to necrotizing tissues is the biggest risk associated with surgeries worldwide and accounts for around 15% of nosocomial infections in surgical patients globally [2]. The problem is much more grave in developing countries like India compared to west, struggling with poor infection control measures, poor hospital hygiene, over-crowded hospitals and most importantly irrational prescription of antibiotics [3,4]. The successful treatment of patients depends on timely identification of pathogen type and selection of an appropriate antimicrobial agent against the microorganism. Antibiotics form an important part of modern medical care and play an important role in the treatment and prophylaxis of bacterial infections. However, the emergence of antimicrobial resistance among hospital pathogens presents a big challenge in the provision of good quality inpatient care [5,6].

The etiological agents causing SSIs vary between different geographical locales and hospitals. One of the common gram-negative pathogen involved in SSIs is *E. coli*. *E. coli* is usually a commensal bacterium of humans and its pathogenic variants cause various infections including SSIs [3]. Over the past few years, the emergence of multi-drug resistance to most antimicrobial agents including cephalosporins, beta lactam/beta lactam inhibitors (BL/BLIs) and last resort drug carbapenems has complicated the treatment for *E. coli* infections [5]. Infections with drug-resistant pathogens result in extended and expensive hospital stays, and could more likely result in patient death [5,6]. If the drug of choice used in empirical therapy for treating the infection fails, the treatment with second or third-choice drugs with resistance breaking mechanisms is required as a failure of empirical therapy often leads to spread of resistance and acquisition of newer resistance mechanisms. Thus MDR infections could result in more sufferings and increased healthcare cost for the patient. Here, we present a case of post-surgical infection by MDR *E. coli* resistant to various classes of drugs and successfully treated with CSE-1034.

2. CASE REPORT

A 35-year-old female presented to the emergency department with chief complaint of loose motion since last 8 days accompanied with abdominal pain and vomiting. On general examination, she was conscious, oriented and was feeling weakness. Her vital signs were blood pressure: 120/80 mm Hg, pulse rate: 104/min, respiratory rate: 22/min and was afebrile (98.4°F). Systemic examination revealed non-distended abdomen, abdominal tenderness and bowel sounds were absent. The patient also complained of being constipated and did not pass stools for last 3 days. Hematology tests done immediately on 1st day revealed deranged TLC count (19500/cu mm) with elevated neutrophils (82%), Lymphocytes (14%), Eosinophils (3%), Monocytes (1%), Basophils (0); normocytic anemia with a hemoglobin level of 5.9 g/dL; raised ESR (148 mm/h) and platelet count of 5.5/cu mm. The patient was started immediately with an intravenous dose of monocef (ceftriaxone) and other supportive treatment including metrogyl (100ml IV TDS), pantoperazole (40 mg IV OD), tramadol (in 100 ml normal saline IV BD). She was suspected of intestinal perforation and decision was made for exploratory laparotomy. As the patient was anemic, she was transfused with two units of blood. Moreover, routine medical fitness tests were done before proceeding for surgery.

In postoperative period, the patient was reported to be febrile and suffered from wound infection. As the patient did not respond to ongoing antibiotic prophylaxis for wound infection, the antibiotic course was changed and piperacillin/tazobactam (pip/taz) was started. Meanwhile, wound swab was sent for culture/sensitivity (c/s) testing. After 48h, it was noticed that the patient did not respond to pip/taz also and continued to be febril with no decrease in wound discharge. The wound specimen c/s report has confirmed the presence of MDR *E. coli* resistant to ceftriaxone, meropenem, ciprofloxacin, amikacin and sensitive to pip/taz, imipenem, CSE-1034 and netillin. Although, c/s report revealed the pathogen isolate was sensitive to pip/taz but as mentioned before also, no clinical improvement was observed with pip/taz. Hence based on c/s report, the patient was started with CSE-1034 3g B.D on first day and then reduced to 1.5g B.D from second day. After 48 h, it was observed that patient responded to treatment and her condition started improving. CSE-1034 was continued at the same

Table 1. Various laboratory parameters of the patients captured at the time of admission and discharge

Parameters	Baseline (Day of admission)	End of treatment
Hb (g/dl)	5.9	8.5
TLC (/cu mm)	19,500	8,500
Platelet count (/cu.mm)	5,50,000	3,46,000
Lymphocytes	14%	25%
Eosinophils	3%	2%
Monocytes	1%	3%
ESR (mm/hr)	148	18

dose for next 5 days. After completion of treatment, the patient was afebrile. Hematological reports (TLC: 8500) and other parameters also confirmed patient's improvement. Repeat sterile wound culture report indicated complete eradication of bacterial pathogen. The wound was healed completely and patient was discharged from the hospital.

3. DISCUSSION

Despite significant advances achieved in infection control and surgical practices, SSIs still continue to be one of the most common health care-associated infections globally and even more in developing countries [2]. The care in surgical patients with post surgical infections cost around threefold higher compared to surgical cases without infections [7]. SSIs are associated with delayed wound healing and recovery, increased antibiotic consumption, extended length of hospital stay and increased health-care costs [2]. Thus prevention of such infections should be the key priority, particularly in developing countries. The incidence of SSIs is influenced by both patient-related and procedure-related factors including pre-existing infection, co-morbidities, old age, poor surgical technique, prolonged surgery duration, improper pre-operative part preparation and most importantly inadequate sterilization of surgical instruments [8]. In addition to these risk factors, the immune response of host is also important predictors of SSIs [8]. Although the overall SSI risk is influenced by numerous patient and procedure specific factors, the effective antibiotic prophylaxis constitutes an important part of polymodal approach to post-operative wound infections as it reduces the risk of resident bacteria overcoming the immune system in the immediate post-operative period [9]. However, the rising emergence of anti-microbial resistance among hospital pathogens worsens the prognosis for SSIs [5,6] .

Here, we present a case of wound infection by multi-drug resistant *E. coli* resistant to many classes of antibiotics including penems, aminoglycosides, quinolones and sensitive to pipercillin-tazobactam and CSE-1034. As the sensitivity test has shown the pathogen sensitive to pipercillin-tazobactam but the patient was not observed to respond.

Frequently, the bacteria responsible for SSIs are members of normal, usually commensal bacterial flora that has co-evolved with their hosts. However, under certain conditions, they are able to overcome protective host responses and become pathogenic particularly when they get a chance to multiply in normally sterile sites [10]. These commensals could be either exogenous microorganisms which include the native flora of patient's skin or endogenous microorganisms that reside on mucous membrane or hollow viscera [2]. Moreover, the microbial population circulating in hospital set up can also enter the operative site either during or after surgery and can lead to SSIs. Though, most of SSIs are caused by *Staphylococcus aureus*, recent years have witnessed a growing number of post-operative wound infections by Gram-negative organisms mainly *E. coli* and *P. aeruginosa* [11]. *E. coli* consists of versatile bacterial strains comprising from harmless commensals to pathogenic strains. Although, based on genome content and phenotypic traits, pathogenic *E. coli* strains can be identified and isolated from non-pathogenic commensals [10]. However, various strains with the ability to cause infections belong to the normal flora of many healthy individuals [10]. These strains become pathogenic taking advantage of immuno-compromised state and the presence of co-morbidities, make a certain individual more vulnerable to them. Over the past few years, the rapid evolution of antimicrobial resistance has drastically reduced the treatment options for infections caused by this pathogen [5]. Because of frequent resistance

was shown to various classes of drugs including fluoroquinolones, aminoglycosides and third-generation cephalosporins, carbapenems are considered as last resort drugs for managing *E. coli* infection [5]. However, carbapenem-resistant *E. coli* infections have been reported in hospitals settings worldwide [12,13]. Various surveillance studies conducted across globe and in India has reported about the rising trend of carbapenem resistance in *E. coli* [12,13,14].

Hence, based on the susceptibility test report and literature survey, the antibiotic chosen for the present case was CSE-1034. The patient responded well to CSE-1034 and showed clinical improvement. Her repeat TLC count done after 5 days of CSE-1034 treatment showed improvement. Moreover, the repeat culture done after the completion of treatment showed absence of the pathogen. Thus the patient was discharged from hospital on the 10^{th} day after admission. This case report clearly signifies that CSE-1034 can be effective empiric option for treating SSIs as 50% treatment time could be saved and development and spread of resistance could be easily prevented. Additionally, a significant reduction in hospital-associated costs can be achieved if CSE-1034 is used empirically. Moreover, various studies have reported CSE-1034 as an effective treatment option for MDR infections as monotherapy or in combination with other drugs [15,16,17].

4. CONCLUSION

From the above study it can be concluded that the susceptibility to CSE-1034 can be attributed to the synergistic effect of Ceftriaxone, Sulbactam and EDTA. In addition to the known anti-microbial activity of Ceftriaxone and Sulbactam, EDTA mediates various anti-microbial effects by chelating metal ions present in the outer membrane causing its destabilization, chelating zinc ions and de-activates carbapenemases and chelates Mg^{2+}ions required for conjugation process [18]. Moreover, CSE-1034 also down-regulates the expression of various efflux pumps [19,20].

CONSENT

It was not required as it is a retrospective case report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Li Y, Wu JH, Meng Y, Zhang Q, Gong W, Liu SD. New devices and techniques for endoscopic closure of gastrointestinal perforations. World J Gastroenterol. 2016; 22:7453–7462.
2. Reichman DE, Greenberg JA. Reducing surgical site infections: A review. Rev Obstet Gynecol. 2009;2:212–221.
3. Tadesse DA, Zhao S, Tong E, Ayers S, Singh A, Bartholomew MJ, McDermott PF. Antimicrobial drug resistance in *Escherichia coli* from humans and food animals. United States, 1950-2002. Emerg Infect Dis. 2012;18:741–749.
4. Kumar GS, Adithan C, Harish BN, Sujatha S, Roy G, Malini A. Antimicrobial resistance in India: A review. J. Nat. Sci. Biol. Med. 2013;4:286–291.
5. Mundhada AS, Tenpe S. A study of organisms causing surgical site infections and their antimicrobial susceptibility in a tertiary care government hospital. Indian J Pathol Microbiol. 2015;58:195–200.
6. Ali SA, Tahir SM, Memon AS, Shaikh NA. Pattern of pathogens and their sensitivity isolated from superficial surgical site infections in a tertiary care hospital. J Ayub Med Coll Abbottabad JAMC. 2009;21:80–82.
7. Salkind AR, Rao KC. Antiobiotic prophylaxis to prevent surgical site infections. Am Fam Physician. 2011;83: 585–590.
8. Korol E, Johnston K, Waser N, Sifakis F, Jafri HS, Lo M, Kyaw MH. A systematic review of risk factors associated with surgical site infections among surgical patients. Plos One. 2013;8.
9. Hawn MT, Richman JS, Vick CC, Deierhoi RJ, Graham LA, Henderson WG, Itani KMF. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. JAMA Surg. 2013;148:649–657.
10. Leimbach A, Hacker J, Dobrindt U. *E. coli* as an all-rounder: The thin line between commensalism and pathogenicity. Curr Top Microbiol Immunol. 2013;358:3–32.
11. Giridhar T, Priya PP, Gowtham P. Surgical site infection (SSI), nosocomial infection, antimicrobial susceptibility. Surg Site Infect

Study Incid Risk Factors Antimicrob Sensit RIMS. Kadapa P; 2015.

12. Nagaraj S, Chandran SP, Shamanna P, Macaden R. Carbapenem resistance among *Escherichia coli* and *Klebsiella pneumoniae* in a tertiary care hospital in south India. Indian J Med Microbiol. 2012; 30:93.
13. Datta S, Wattal C, Goel N, Oberoi JK, Raveendran R, Prasad KJ. A ten year analysis of multi-drug resistant blood stream infections caused by *Escherichia coli* & *Klebsiella pneumoniae* in a tertiary care hospital. Indian J Med Res. 2012; 135:907–912.
14. Shannon A, Wagner K, Cheeptham N, Stephens G. A pilot survey of carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* mediated by K pneumoniae serine carbapenemases in a regional referral hospital in British Columbia. Can J Infect Dis Med Microbiol. 2011;22:61–63.
15. Chaudhary M, Mir MA, Ayub SG. Safety and efficacy of a novel drug elores (ceftriaxone + sulbactam + disodium edetate) in the management of multi-drug resistant bacterial infections in tertiary care centers: A post-marketing surveillance study. Braz J Infect Dis. 2017;21:408–417.
16. Sathe P, Maddani S, Kulkarni S, Munshi N. Management of ventilator associated pneumonia with a new antibiotic adjuvant entity (ceftriaxone + sulbactam + disodium edetate) - A novel approach to spare carbapenems. J Crit Care. 2017;41:145–149.
17. Chaudhary M, Ayub SG, Mir MA. Comparative efficacy and safety analysis of CSE-1034: An open labeled phase III study in community acquired pneumonia. J Infect Public Health; 2018.
18. Chaudhary M, Kumar S, Payasi A. A novel approach to combat acquired multiple resistance in *Escherichia coli* by using EDTA as efflux pump inhibitor. J Microb Biochem Technol. 2012;4.
19. Chaudhary M, Payasi A. Role of EDTA and CSE1034 in curli formation and biofilm eradication of Klebsiella pneumoniae: A comparison with other drugs. J Antibiot (Tokyo). 2012;65:631–633.
20. Chaudhary M, Payasi A. Comparative efficacy of antibiotics in biofilms eradication formed by ESBL and non ESBL producing micro-organisms. Int J Drug Dev Res. 2012;4.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/26372