Case Report

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Internal Medicine Section

Successful Management of Urosepsis with Ceftriaxone+Sulbactam+EDTA: A Case Report of Penem Sparing Approach

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ABSTRACT

Over the past decade, the Anti-Microbial Resistance (AMR) among members of Enterobacteriaceae family is on rise mainly due to rapid spread of strains producing Extended-Spectrum Beta-Lactamases (ESBLs) and Metallo Beta-Lactamases (MBLs). Hence, the choice of drugs available for these resistant strains is diminishing and their treatment is becoming more challenging. This is a case of complicated Urinary Tract Infection (cUTI) due to ESBL producing *E. coli* leading to septic shock which was successfully managed with Antibiotic Adjuvant Entity (AAE), a combination of ceftriaxone+sulbactam+EDTA.

Keywords: Antibiotic adjuvant entity, Multi-drug resistance, Sepsis, Urinary tract infection

CASE REPORT

A 64-year-old male patient presented to the emergency department in an unresponsive state with altered sensorium since last two hours. The review of the patient revealed that he was suffering from continuous high-grade fever associated with chills since 7-8 days. However, the patient did not complain of any rash or diurnal variation. Decreased urine output and dysuria were noted for the past 5-6 days. The patient also reported of breathlessness since past 5 days which increased on lying down and was associated with coughing. However, no sputum or expectoration was reported. Past medical history was significant and included type 2 diabetes mellitus for 25 years with diabetic nephropathy, hypertension since last 6 years (with no regular treatment) and high baseline serum creatinine equivalent to 3mg/dl. No history of urinary instrumentation or surgery in past. Before presenting to the hospital, the patient was having oral antibiotic Cefixime (200mg every 12h) for last 4 days.

Physical examination revealed that the patient was afebrile with a respiratory rate of 20 breaths/minute, heart rate of 64 beats/minute, bp of 90/60mmHg, oxygen saturation of 94% on room air. Blood and urine samples were collected and were sent for basic laboratory investigations and culture sensitivity (c/s) testing. In view of the provisional diagnosis of UTI with septic shock complicated by acute kidney injury or underlying chronic kidney disease, the patient was started with broad spectrum antibiotics including Inj. Piperacillin+Tazobactam (pip/taz) (2.25gm IV 8 hrly) with Teicoplanin (IV 400mg stat) along with inotrophic support. Central line was inserted for CVP measurement and fluid management, and the patient was shifted to ICU. Haematology report showed deranged TLC count (15.8), high ESR and DLC values were 92/3.6/3.9/0.4/0.1. Urine analysis revealed presence of pus cells (30-35/hpf), RBC (70-80/hpf), protein (2+), blood (3+). Chest X-Ray PA view taken revealed cardiomegaly with B/L pulmonary embolus (PE) and prominent broncho-vascular margins. USG of kidney revealed decreased B/L kidney size with increased echo texture, mild ascitis, mild B/L PE and cortico-medullary differentiation. A 2D echocardiography done revealed normal ejection fraction (60%) and concentric left ventricular hypertrophy. After 48 hour, it was observed that the condition of the patient deteriorated further instead of improving with the ongoing treatment. Urine c/s report has confirmed *E. coli* as the causative agent resistant to Pip/Taz and sensitive to AAE and Penems. Hence, based on c/s report, Pip/Taz was discontinued and the patient was started with Inj. Ceftriaxone+sulbactam+EDTA ({1000mg+500mg+37mg} 1.5g, 12h), and Teicoplanin was discontinued. After 3 days, the patient responded to the treatment and his condition started improving, hence was continued on AAE 1.5gm, every 12hour, for 11 more days. Additional peripheral support was given for metabolic acidosis, insulin infusion was also given to maintain steady glucose levels and norepinephrine was gradually tapered off. After the completion of treatment, the patient showed tremendous improvement clinically. Repeat haematological report available on day 16th (TLC: 6040) and other parameters confirmed patient's improvement. Repeat X-ray done showed improvement and effusion was reported to be cleared. Moreover, physical examination revealed normal heart rate and BP: heart rate was 85/min and BP: 110/70 mm Hg. On the 17h day after admission, patient was discharged from hospital with follow up advice after 7 days.

DISCUSSION

UTI occurs more frequently in diabetics as compared to general population. Impaired immune system, in addition to poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy may all contribute to the pathogenesis of UTI in diabetic patients [1]. Most of these infections are community acquired and usually caused by antibiotic susceptible bacteria; however diabetic patients are more prone to get infected with Multi-Drug Resistant (MDR) bacteria [2]. In our case of cUTI caused by MDR bacteria which is difficult to treat, there was no significant hospital contact history or any urological instrumentation or surgery in patient. This probably indicates that the gap in susceptibility profiles of hospital strains and community acquired strains is getting bridged, leading to a spread of resistant bugs in community. Similar findings have been reported worldwide and we might have tough time tackling them [3].

In Indian subcontinent, a very high prevalence of AMR in Gram Negative Bacteria (GNB) is reported compared to western world and it is increasing day by day [4]. This is rendering all our present treatment options ineffective, and very few options are in pipeline which is active against MDR GNB. If we can reduce the use of our last resort antibiotics such as Carbapenems and preserve them for future use, this can help us in having better hospital as well as community ecology and antibiotic susceptibility profiles [5]. In this

case study, the pathogen isolated *E. coli* was resistant to Pip+Taz and other betalactam+betalactam (BL+BLI) inhibitors but sensitive to novel AAE and Penems. Although a wide range of organisms can cause UTI, *E. coli* is the most common organism isolated [6,7]. Moreover, the *E. coli* strains isolated from patients with cUTI are less likely to originate from uropathogenic strains isolated from patients with simple UTIs. Thus the likelihood of treatment failure and serious complications, particularly the development of AMR, is more common in *E. coli* causing cUTI compared to strains leading to uncomplicated cases [7]. The early recognition of risk factors and appropriate selection of broad spectrum antibiotics for treatment may significantly improve the chances of positive outcome. We used AAE in spite of Penems being sensitive, and started getting good clinical response by day 3 and continued the same. Patient recovered successfully after completing 2 weeks of treatment. This indicates, if antibiotic sensitivity test reveals susceptibility of pathogen to AAE, we can use it before Penems so as to reduce Carbapenem use and preserve them for future use. Similarly AAE can also be used as combination therapy with Colistin instead of Penems as reported in the previous studies [8,9].

CONCLUSION

One of the prime causes of UTI is E coli. In view of growing resistance of Enterobacteriaceae towards available antibiotics, newer therapies should be evaluated. In the present case of cUTI due to ESBL E coli resistant to other BL+BLI, the patient was managed successfully with AAE. There are case reports of AAE being used as combination therapy for treating Carbapenem-resistant infections, but our case report shows different aspect of carbapenem sparing utility, we can use it before carbapenems to reduce selection pressure on Carbapenems and preserve them for future use without compromising clinical outcome.

REFERENCES

[1] Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes Metab Syndr Obes Targets Ther. 2015;8:129–36. https://www.dovepress.com/urinary-tract-infections-in-patients-with-type-2-diabetes-mellitus-rev-peer-reviewed-article-DMSO (accessed March 18, 2017).

[2] Venmans LMAJ, Hak E, Gorter KJ, Rutten GEHM. Incidence and antibiotic prescription rates for common infections in patients with diabetes in primary care over the years 1995 to 2003. Int J Infect Dis. 2009;13(6):e344–51.

[3] Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Gurung G, et al. Community acquired multi-drug resistant clinical isolates of Escherichia coli in a tertiary care center of Nepal. Antimicrob Resist Infect Control. 2015;4:15.

[4] Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. Lancet Infect Dis. 2010;10(9):597–602.

[5] Trivedi M, Patel V, Soman R, Rodriguez C, Singhal T. The outcome of treating ESBL infections with carbapenems vs. non carbapenem antimicrobials. J Assoc Physicians India 2012;60:28–30.

[6] Pallett A, Hand K. Complicated urinary tract infections: practical solutions for the treatment of multiresistant Gram-negative bacteria. J Antimicrob Chemother. 2010;65:iii25-33.

[7] Ejrnæs K. Bacterial characteristics of importance for recurrent urinary tract infections caused by Escherichia coli. Dan Med Bull. 2011;58(4):B4187.

[8] Patil UN, Jambulingappa KL. A combination strategy of ceftriaxone, sulbactam and disodium edetate for the treatment of Multi-Drug Resistant (MDR) septicaemia: a retrospective, observational study in Indian tertiary care hospital. J Clin Diagn Res. 2015;9(11):FC29-32.

[9] Chaudhary M, Mir MA, Ayub SG, Protocol 06 Group. 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 off Publ Braz Soc Infect Dis. 2017;21(4):408-17.

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