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Research Paper

Catheter associated multi drug resistant Klebsiella pneumoniae infection management with Elores in complicated neurogenic bladder case

Medical Science

KEYWORDS : Neurogenic bladder, multi-drug resistance, Klebsiella pneumoniae

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ABSTRACT

Neurogenic bladder leads to urological complications like urinary incontinence, vesicourethral reflux and recurrent urinary tract infections (UTIs). High prevalence of resistant Gram negative pathogen induced catheter-associated bacteriuria with increased morbidity and mortality are reported in patients of neurogenic bladder caused by spinal cord injury. Predominant reason for rising resistance is prolonged or repeated exposure to antimicrobial agents causing selection pressure. The common multi drug resistant (MDR) Gram negative pathogens are E. coli, Pseudomonas spp., A. baumannii, K. pneumoniae and Enterococcus. Here we are discussing a case of MDR Klebsiella pneumoniae induced cUTI in a patient with neurogenic bladder successfully treated with Elores (ceftriaxone+sulbactam+disodium edetate) an Antibiotic Adjuvant Entity.

INTRODUCTION

Neurogenic bladder is abnormal function of urinary bladder caused due to the damage of nervous system involved in the control of micturition (Edokpolo et al., 2012). Spinal cord injury (SCI) can lead to alteration in the function of the lower urinary tract causing urologic complications. SCIs are major cause of neurogenic lower urinary tract dysfunction. Major complication of neurogenic bladder are, urinary incontinence, vesicourethral reflux and recurrent urinary tract infections (UTIs) (Pannek, 2011). Elevated bladder pressures that develop from neurogenic bladders can cause hydronephrosis (Vaidyanathan et al., 2012).

Apart from hydronephrosis, cUTI is the most common urological hindrance in neurogenic bladder patients with increased incidence of UTI or bacteriuria reported up to 60% (Balsara et al., 2013). UTI in these patients is the leading cause for septicemia, associated with a significantly increased mortality (Pannek, 2011). The major reasons for increased risk of UTI in SCI patients are bladder overdistention, outlet obstruction, detrusor-sphincter dyssynergia, increased intravesical pressure, vesicourethral reflux, and large postvoid residuals (Edokpolo et al., 2012).

Catheter-associated bacteriuria is the most common source of bacteremia in hospitalized neurogenic bladder patients with prevalence reported up to 40% caused by Gram-negative bacilli (Nicolle, 2005). *Klebsiella spp* are more predominant in these patients along with *E.coli, Pseudomonas spp., and Enterococcus*. Prolonged or repeated exposure to antimicrobial agents and antibiotic pressure increases the risk antibiotic resistance bacteria (García et al., 2003). Khorvash et al. (2009) reported incidence of *Klebsiella spp*, induced UTI to be more severe in neurogenic bladder patients as compared to nosocomial UTI.

Here, we report a patient with neurogenic bladder post spinal injury, on clean intermittent self-catheterization (CISC) suffering with MDR *K. pneumoniae* induced cUTI

Case presentation

A 40 year male patient was admitted in our hospital with chief complaints of fever with chills, profuse sweating and urinary retention since 2 to 3 days. Patient was asymptomatic 2- 3 days back. No history of rash, joint pains, cough, loose motions, vomiting, breathlessness, chest pain, headache, weight loss, any bleeding diasthesis, any other gastrointestinal tract (GIT), respiratory or cardiac symptoms. Patient was a known case of neurogenic bladder sustained after fracture of L-S spine, after alleged history of fall from a height seven months back and was presently on CISC. Patient was recently admitted and treated for chief complaints of UTI with acute kidney injury (AKI) in a tertiary care hospital. No history of diabetes mellitus (DM), hypertension, tuberculosis, coronary artery disease, bronchial asthma, or any other chronic illness or known allergies was there. On admission at our hospital, patient was thoroughly evaluated and relevantly investigated. Patients general condition was fair, conscious oriented, febrile-99.2 ^{0}F, pulse, blood pressure and respiratory rates were within normal limits . No signs of pallor, icterus, clubbing, cynasosis, oedema and lymphadenopathy were noted. Systemic examination was normal. Urologist and nephrologist opinion were taken and advise incorporated in the treatment. At the time of admission his relevant biochemical and hematological parameters were as follows: Haemoglobin (Hb): 9.8 g/dl; Eosinophils: 0; Erythrocyte Sed. rate (ESR): 89 mm/hr; PCV (Haematocrit): 29.9%; Red blood cell (RBC) count: 3.5×10^{12}/L; C-reactive protein (CRP): 196.9mg/l, urine appearance was hazy with WBC- 15-20/HPF. Urine examination for culture and sensitivity was sent. Patient was started on piperacillin plus tazobactam along with injection levofloxacin and other supportive therapy. The culture reports revealed MDR *Klebsiella* showing resistance to piperacillin-tazobactam, meropenem, doripenem and ertapenem, but sensitive to t colistin and Elores (ceftriaxone+sulbactam+disodium edetate). Based on culture and sensitivity report Piperacillin-tazobactam and injection levofloxacin was stopped. Patient was put on Elores 1.5g intravenous infusion in 100ml normal saline with 90 minute infusion, twice daily for next 7 days. Patient condition gradually improved with no-recurrence of symptoms. Patient was discharged in a satisfactory condition with followup advise.

DISCUSSION

Neurogenic bladder refers to bladder dysfunction after disruption of central or peripheral nervous system pathways that regulate bladder storage and emptying (Balsara et al., 2013). SCI, the most common cause of neurogenic bladder, can alter the function of the lower urinary tract (Balsara et al., 2013; Edokpolo et al., 2012). In the current case patient developed neurogenic bladder after spinal injury. Chronic or recurrent episodes of UTI pose a significant risk to all patients with neurogenic bladder. The major factors contributing for UTI in these patients are; urinary stasis due to elevated post-void residual volumes, bladder overdistention, high-pressure voiding, vesicourethral reflux and the use of chronic indwelling catheters (Balsara et al., 2013). It has been reported that, patients with neurogenic bladder develop up to 60% bacteriuria or UTI within the first year post injury (Balsara et al., 2013).

Neurogenic bladder can also *lead to hydronephrosis. In our case patient developed bilateral hydroureteronephrosis, which could be due to the increased intravesical pressure which forces the ureter to pump urine into the bladder at increasingly higher pressures until a state of hydronephrosis is reached (Vaidyanathan et al., 2012). The diagnostic approach in these patients is determined by the patient history, clinical presentation and antibiotic culture sensitivity.*

Bladder management is an essential element in improved outcomes following SCI (Edokpolo et al., 2012). Optimal bladder

management enables emptying of the bladder on a routine, frequent schedule, and allows patients to remain free from urine leakage while storing it at low pressures. CISC is a common bladder catheterization method of choice in bladder emptying following SCI (Edokpolo et al., 2012). Similar to our case, some studies have observed an increased frequency of UTIs in patients with intermittent catheterization (Wyndaele et al., 2012). This might be due to the suitable environment for *bacterial* adhesion, as bacteria attach to the catheter surface and form biofilms (Wyndaele et al., 2012). In biofilm pathogens of inter and intra species colonize to protect themselves from antibiotics, allow more of quorum sensing making pathogens increasingly resistant to antimicrobials. This leads to repeated courses of antimicrobial therapy causing severe cUTI and highlighting a need of antibiotic which is active against biofilm forming MDR pathogens (Nicolle, 2005).

Apart from this, patient with neurogenic bladder frequently have an absence of sensation in the pelvis and identification of potential symptoms of UTI is often difficult. Asymptomatic bacteriuria in neurogenic bladder are common in repeatedly exposed patients to antibiotic therapy, thereby increasing the incidence of multidrug-resistant bacterial infections (Balsara et al., 2013). In the present case, patient developed UTI due to MDR *K. pneumoniae.* Similar to this, in a study by F Khorvash et al, reported more prevalence *Klebsiella spp,* in SCI associated UTI patients compared to nosocomial UTI. The epidemiology of ESBL producing uropathogens is increasing in India. Eshwarappa et al.(2011) reported up to 52.2% ESBL-positive uropathogens. ESBL producers do not respond to the usually prescribed empirical therapy. In the present case, current evidence implicate, asymptomatic bacteriuria in neurogenic bladder frequent exposure to antibiotics, intermittent catheterization, biofilm formation and ESBL production could be the reason for MDR *K. pneumoniae*, showing resistance to piperacillin/tazobactam, meropenem, doripenem, ertapenem. Although, colistin a was sensitive to MDR *K. pneumoniae* in this case, their use was limited in the current case study due to potential risk of neurotoxicity and nephrotoxicity from colistin and minimal urinary concentration of tigecycline (Sabuda et al., 2008; Bates et al., 2012).

Presently, alternative antimicrobial therapy to treat ESBL-positive MDR uropathogens is limited.[9] The use of Elores in treating ESBL-positive UTI has shown promising results in the recent past. Elores an Antibiotic Adjuvant Entity with a novel combination of ceftriaxone/sulbactam/ disodium edetate, can combat antimicrobial resistance produced by bacteria. in vitro studies reported, 4 to 5 fold lower MIC with Elores when compared with other BL BLIs (Chaudhary and Payasi, 2013a). In patients treated with UTI infections, Elores achieved 83.3% (85/102) clinical cure rate and 95% (57/60) bacterial eradication (Chaudhary and Payasi, 2013b). In another, in vitro study done on *K. pneumoniae* strains collected from North India, Elores showed a significant susceptibility against ESBLs and MBLs (Chaudhary and Payasi, 2013c). This is because of Elores activity against down regulation of ESBL/MBL producing genes, increased bacterial cell permeability, down regulation of efflux pump over expression and ability to break bacterial biofilms (Sahu et al., 2014).

In a study on curli formation and biofilm eradication in *K. pneumoniae*, Elores treatment showed significant disorganization of biofilm and formed a honeycomb like structure of disrupted biofilm. Disodium edetate in Elores effectively inhibited curli formation and bacterial adhesion in biofilm formation (Chaudhary and Payasi, 2012). In the present case patient was responded well with Elores antibiotic therapy on MDR *K. pneumoniae.*

CONCLUSION

Treatment of complicated UTIs in patients with neurogenic bladder secondary to SCI remains a challenge. Complications like asymptomatic bacteriuria, DMR due to frequent exposure to antibiotic therapy, catheterisation in neurogenic bladder, increases the incidence of MDR pathogens. With increasing antibiotic resistance for MDR pathogen and limitations of major antibiotics in term of toxicity profile, create a need for an alternative therapy having enhanced safety and efficacy. From the research data available and treatment success of the present case, we recommend newer antibiotic adjuvant therapy Elores for MDR case in terms of safety, efficacy and therapeutic outcome.

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