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Surgery

TREATMENT OF CARBAPENEM RESISTANT ENTEROBACTERIACEAE URINARY TRACT INFECTION WITH COMBINATION OF AMIKACIN AND MEROPENEM

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KEYWORDS :

INTRODUCTION -

Drug resistance of bacteria is biggest challenge humanity is going to face in near future. Bacteria are rapidly developing resistant to multiple drugs and there are not many new drugs in pipeline. Infection because of drug resistant organism is a common cause of morbidity and mortality in intensive care unit. If acquisition of drug resistance by microorganism progresses at this rate, that time is not very far when we will be pushed in to preantibiotic era. We need to develop new strategies to combat drug resistant by microorganism. We report a case of highly drug resistant urinary tract infection caused by Klebsiella. This strain was resistant to both Inj. Meropenem and Inj. Amikacin. This case was successfully treated by combination of Inj. Meropenem and Inj. Amikacin and complete resolution of infection was observed.

Case report -

A 44 yrs old female diabetic and nonhypertensive female had uncontrolled diabetes for 10 years and was insulin along with multiple oral hypoglycaemic agents. She had past history of multiple admissions for diabetes control and management of diabetic ketosis. She was operated 11 years back for percutaneous nephrolithotomy on left side for a left renal staghorn calculus. She had a stone in left renal pelvis for which extracorporeal shock wave lithotripsy was done 2 years back. She was admitted with left renal colic few months back for which left DJ stent insertion followed by removal was done in recent past.

She presented with severe pain in left loin to groin region associated with high grade fever since 2 days. On presentation, her examination showed that she was conscious and oriented. She was febrile with temperature of 99.2 degree farenheit, she did not have pallor or icterus. She had pulse of 120/ min and blood pressure of 121/74 mmHg. Her saturation on room air was -97%. She was admitted for further management. Her RT PCR test was done for diagnosis of COVID 19, it came negative. Her investigation showed, Haemoglobin of 10.9 gm/dl, WBC count – 18160 / cmm, Serum Creatinine 0.7 mg/dl, BUN 11.4 mg/dl, Liver function test was normal, Serum electrolytes were normal. Peripheral smear for malarial parasite was checked and it was not detected. Her Urine routine analysis showed 80 – 100 pus cells / HPF, Urine protein absent and Urine sugar was 3+. Her HbA1c was 9.3 %

Her urine culture analysis showed Klebsiella pneumoniae organism which was Resistant to all and sensitive to Colistin with MIC of 2, Resistant to Inj. Meropenem – MIC – More than 16, Resistant to Inj. Amikacin – MIC – More than 64. She was started on Inj. Meropenem 1 gm three times a day and Inj. Amikacin 750 mg once a day. She showed significant symptomatic improvement after starting antibiotic. Her fever resolved. Her pain from left loin to groin also resolved. Her urine routine microscopy analysis showed only 2- 4 pus cells which was reduced from previous 80 – 100 pus cells. Her WBC count showed reduced from 18,160/cmm to 6000 / cmm.

Her Sonography was done and it showed that there was left sided hydronephrosis with a 14 mms

Sized calculus complex within the dilated left lower renal polar calyceal system with an 7 mms

Calculus complex in the left renal pelvis. Right kidney was normal. She was operated for left percutaneous nephrolithotomy. She recovered from surgery well and was discharged. At the time of discharge she was afebrile and her investigations were in normal limits. At two month of follow up she remains asymptomatic.

DISCUSSION

Klebsiella pneumoniae is becoming increasingly drug resistant and hypervirulent. Therefore, Klebsiella pneumoniae related infections are on rise. Simple urinary tract infection caused by Klebsiella pneumoniae has become difficult to treat because of acquired drug resistance by the organism. As far as urinary tract infection is concerned, Klebsiella pneumoniae is second most common bacteria causing urinary tract infection and E.Coli being the commonest organism causing urinary tract infection. (1)

Yasin et al reported a case of Klebsiella related urinary tract infection treated by combination of Meropenem and Amikacin – however in this case organism was sensitive to both antibiotics. (2) It has been observed that Klebsiella has acquired multiple modes of drugs resistance – such as decreased permeability of cell membrane causing decreased influx of antibiotic and increased efflux mechanism removing antibiotic out of the cells. In addition Klebsiella has acquired multiple types of carbapenemases, such as KPC, OXA 48 and NDM etc. Out of multiple carbapenemases NDM is more prevalent in Indian subcontinent. (3)(4) Carbapenemase resistant Klebsiella Pneumoniae is termed as CRE and it has been a cause of higher morbidity and mortality because of lack of consistently effective modality of treating such infection. (5)

In this case the organism was sensitive to Inj. Colistin, However Colistin has its own problems. It has been found that use of Colistin is associated with increased risk of renal failure in critically ill patients. (6) It has been suggested that Colistin is best to be used as combination therapy and its recommended to be used and is maximally effective when MIC is less than 1. (7) There are few studies which indicates that MIC of 1 should be considered as breakpoint for Colistin sensitivity in order to detect higher cases of drug resistant strains of Klebsiella pneumoniae. (8) In view of these considerations and non-availability of Colistin in hospital stock, it was kept as reserve drug in this case.

All cause Mortality related to carbapenem resistant Klebsiella pneumoniae blood stream infection is reported as 58% in one study. (9) For treatment of Carbapenem resistant Klebsiella pneumoniae infection, combination of antibiotic is more useful than single drug therapy. It is also recommended that in such combination one of the drug can be from carbapenem group even though microorganism is already resistant to carbapenem. (10) Ceftazidime-avibactam is a new combination therapy specifically indicated for carbapenemase producing Klebsiella pneumoniae. (11) However high cost of the Ceftazidime-avibactam combination prohibits is wide spread use. Another therapeutic option for carbapenemase producing Klebsiella pneumoniae infection is use of double carbapenem combination therapy (12) (13)

Combination of Meropenem with Amikacin for treatment of Carbapenemase producing Klebsiella Pneumoniae infection has been described in literature. (14) In vitro analysis of combination of Meropenem with Amikacin against Carbapenemase producing Klebsiella pneumoniae suggested synergistic activity of both antibiotic. (15) In an animal model combination of Meropenem with Amikacin was found to be effective against infection caused by Carbapenemase producing Klebsiella pneumoniae. (16)

In our case, the patient had infection with Klebsiella pneumoniae

organism which was resistant to Meropenem with MIC of more than 16 and it was resistant to Amikacin with MIC of more than 64. However combination of Meropenem with Amikacin showed immediate clinical response with symptoms of urine infection as well as investigation showing complete resolution of urinary tract infection. This complete response to infection helped in carrying out safe surgery of left percutaneous nephrolithotomy. This patient remains asymptomatic 8 weeks after surgery.

Meropenem and Amikacin has synergistic action against bacteria. This synergistic action probably has bactericidal effect on organism which are resistant to both drugs individually. However further study need to be done to find out subgroup of patients who respond to combination of Meropenem and Amikacin in spite of being resistant to both drugs.

CONCLUSION –

Carbapenem resistant enterobacteriaceae infection is major cause of morbidity and mortality in intensive care unit. It is second most common cause of urinary tract infection. Carbapenem resistant Klebsiella pneumoniae infection could be successfully treated by combination of Meropenem with Amikacin in spite of organism being individually resistant to both the drugs. Carbapenem and Amikacin has synergistic antibacterial action which can be used for treatment of resistant infection.

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