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A CASE REPORT ON NECROTIZING SOFT TISSUE INFECTION (NSTI) CAUSED BY CARBAPENEM-RESISTANT *KLEBSIELLA PNEUMONIAE*

Pharmaceutical Science

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ABSTRACT

Necrotizing soft tissue infections (NSTIs) are rare, potentially fatal bacterial infections characterized by a widespread necrosis of skin and subcutaneous tissues. Primary urgent management of NSTIs include broad-spectrum antibiotic therapy and rapid surgical debridement of all infected tissues. It is important to select antibiotics which are sensitive to the particular causative organism for eliminating treatment failure. Multidrug resistant gram-negative strains of bacteria are reporting globally at increasing rates. Carbapenems are considered as last-resort antibiotics for the treatment of infections caused by multidrug-resistant Gram-negative bacteria. With the increasing use of carbapenems in clinical practice, the emergence of carbapenem-resistant enterobacterales (CRE) poses a great threat to human health. A 63-year-old female patient admitted in General surgery department with complaints of painful swelling and discolouration of left foot for 5 months. She underwent amputation of 3rd,4th and 5th toes along with wound debridement with a diagnosis of necrotizing soft tissue infection. The collected material sent for pus culture. Pus culture done using disc diffusion method and the culture was positive for *Klebsiella pneumoniae* ssp *pneumoniae*. Patient was initially treated with Meropenem 1g IV TID and Trimethoprim/sulfamethoxazole per oral BD which did not reduce infection. Soon after the pus culture results obtained, Meropenem and Trimethoprim / sulfamethoxazole discontinued and Inj. Tigecycline 50 mg BD continued for 5 days. The infection was significantly reduced and wound was clean by day 5 of Tigecycline treatment. Necrotizing soft tissue infection (NSTI) caused by Klebsiella pneumonia which was resistant to most of the antibiotics, was successfully treated in our case, in accordance with current therapeutic concepts, and urgent wide surgical debridement to remove devitalized tissue.

KEYWORDS

Necrotizing soft tissue infection, *Klebsiella pneumoniae*, Tigecycline, Carbapenems

INTRODUCTION

Necrotizing soft tissue infections (NSTIs) are rare, potentially fatal bacterial infections characterized by a widespread necrosis of skin and subcutaneous tissues [1]. Primary urgent management of NSTIs includes broad-spectrum antibiotic therapy and rapid surgical debridement of all infected tissues. Antibiotic therapy for NSTI patients involves several challenges and should (1) carry broad-spectrum activity against gram-positive and gram-negative pathogens because of frequent polymicrobial infections, considering extended coverage for multidrug resistant strains. (2) decrease toxin production (3) achieve the best possible tissue diffusion in regard to impaired regional perfusion, tissue necrosis, and pharmacokinetic and pharmacodynamic alterations [1][2][3][4].

Multidrug resistant gram-negative strains of bacteria are reporting globally at increasing rates. Carbapenems are considered as last-resort antibiotics for the treatment of infections caused by multidrug-resistant Gram-negative bacteria [5]. With the increasing use of carbapenems in clinical practice, the emergence of carbapenem-resistant Enterobacterales (CRE) poses a great threat to human health. Antibiotic abuse and misuse have led to a high incidence of isolates encoding extended-spectrum beta-lactamase (ESBL) and carbapenemase enzymes, particularly in developing nations. Among carbapenem-resistant gram-negative bacteria, *Klebsiella pneumoniae* is the most often isolated nosocomial pathogen [5][6]. It is often isolated from patients in intensive care and can result in epidemics with high fatality rates. The complexity of managing carbapenem resistant-*Klebsiella pneumoniae* (CR-Kp) strains is due to the various mechanisms that mediate carbapenem resistance [1]. It is important to select antibiotics which are sensitive to the particular causative organism for eliminating treatment failure.

Here, we present a case of Necrotizing soft tissue infection in which carbapenem resistant *Klebsiella pneumoniae* was the causative agent and was successfully treated with tigecycline monotherapy.

Case Study

A 63-year-old female patient admitted in General surgery department with complaints of painful swelling and discoloration of left foot for 5 months. Patient had known complaints of type 2 DM for past 12 years and was taking T. Metformin 500mg BD. Clinical findings shows that three toes gangrenous, infected soft tissues dorsum and ventrum, slough and pus along tendon sheaths. She underwent amputation of 3rd,4th and 5th toes along with wound debridement with a diagnosis of necrotizing soft tissue infection. The collected material sent for biopsy and pus culture. Pus culture done using disc diffusion method and the culture was positive for *Klebsiella pneumoniae* ssp *pneumoniae.* The isolated organism was resistant to antimicrobials like Amoxicillin/clavulanic acid (MIC >=32), Piperacillin/Tazobactam (MIC>=128), Cefuroxime (MIC >=64), Ceftriaxone (MIC >=64), Cefoperazone/sulbactam (MIC >=64), Cefepime (MIC >=32), Ertapenem (MIC >=8),Imipenem (MIC >=16), Meropenem (MIC >=16), Amikacin (MIC =32), Gentamycin (MIC >=16),Ciprofloxacin (MIC >=4), Trimethoprim/ sulfamethoxazole (MIC >=320).Organism was intermediate sensitive to Fosfomycin and colistin and was susceptible only to Tigecycline. Patient was initially treated with Meropenem 1g IV TID and Trimethoprim/sulfamethoxazole per oral BD which did not reduce the infection significantly. Soon after the pus culture results obtained, Meropenem and Trimethoprim/ sulfamethoxazole discontinued and Tigecycline 100mg IV given as single dose. Then, Inj. Tigecycline 50 mg BD continued for 5 days. Repeated debridement done on 3rd day of surgery

Patient had elevated FBS levels on admission (FBS- 151 mg/dl), oral hypo-glycemic agents added to the treatment plan. Patient was also diagnosed with anemia (Hb- 8 g%). Peripheral blood smear gave an impression of microcytic hypochromic anemia. RBC transfusion done on day 2(Hb- 8.4g%), day 5(Hb- 8.8g%) and day 7(Hb- 10.2g%) and further managed with Ferrous ascorbate and folic acid tablets. Patient had hypoalbuminemia with albumin levels 2.5 g/dl on day 1 which was managed with protein powder and egg whites as dietary supplements.

The infection was significantly reduced and wound was clean by day 5 of Tigecycline treatment. Tigecycline discontinued and patient got discharged. The discharge instructions include Clindamycin 300mg tablet BD to be taken for 5 days along with daily dressing, limb elevation and rest. The general condition of the patient followed up after 1 week and the condition was better with complete heal of infected site.

DISCUSSION

Carbapenem-resistant *K. pneumoniae* (CR-Kp) poses a serious threat to public health, due to its high death rate and widespread distribution. It is believed that CR-Kp development in hospitals is a separate risk

factor for high mortality rate. The development of colonization or infection with multidrug-resistant microorganisms, including CR-Kp, is significantly predisposed by the use of carbapenems and/or broad-spectrum cephalosporins [7]. Conditions that are linked to colonization with a microbe that produces carbapenemase include trauma, diabetes mellitus, cancer, organ transplantation, mechanical ventilation, usage of urinary catheters, and central venous catheters. The most typical CR-Kp infections include bacteremia, urinary tract, and lung infections. There are only few antibiotic alternatives available for treating such resistant strains and remains a lack of clarity surrounding the therapy of CR-Kp infections. These antibiotics consist of Fosfomycin, tigecycline, colistin, and amino glycosides [6][8][9].

Necrotizing soft tissue infections (NSTIs), which are mainly caused by Gram-positive cocci existing on the skin surface, are more common than those caused by Gram-negative bacteria; however, the role of Gram-negative bacteria as emerging pathogens in NSTIs cannot to be ignored. Early diagnosis and treatment are important to avoid mortality as NSTI is a life-threatening condition. Developing an early diagnosis is the primary challenge related to NSTI. Diagnosis should include the identification of causative organism and the treatment should be specific to the organism which invaded.

Necrotizing soft tissue infection (NSTI) caused by *Klebsiella pneumonia* which was resistant to most of the antibiotics, was successfully treated in our case, in accordance with current therapeutic concepts, and urgent wide surgical debridement to remove devitalized tissue. NSTI is an acute, progressive, invasive, and severe infection that producing inflammation and necrosis of the adjacent muscle, subcutaneous fat, and skin. The incidence of NSTI ranges from 0.3 to 15 cases per 100,000 population [10][7]. Necrotizing Fascitis (NF) may be classified according to microbiological aetiology (polymicrobial or monomicrobial), anatomy, and depth of infection. Polymicrobial NF (a mix of aerobic and anaerobic bacteria) mostly occurs in immune compromised individuals. Monomicrobial NF (caused mainly by *Streptococcus pyogenes* but also by *Klebsiella pneumonia*) is less common and may affect healthy individuals who often have a history of trauma, or recent surgical intervention [11][12]. Initial empiric broad-spectrum antibiotic coverage is needed in cases of NF, directed against aerobic Gram-positive cocci, Gram-negative rods, and a variety of anaerobes as recommended by the Infectious Diseases Society of America [12][13].

We started with carbapenem as an initial treatment. We isolated *Klebsiella pneumonia* as a causative agent which was resistant to carbapenem which led to tigecycline treatment where the organism was susceptible. Our patient had a past history of type II diabetes mellitus that had been treated with oral hypo-glycemic agents but had poor blood sugar control. It is thought that diabetes mellitus could cause susceptibility to NSTI via tissue hypoxia resulting from diabetic vascular disease, and also the underlying immunodeficiency associated with poorly controlled disease [13][14]. Several studies have suggested that the most important factors influencing mortality from NSTI are the time to first surgical intervention and adequacy of surgical debridement [15]. Therefore, early recognition and diagnosis of NSTI is essential to facilitate early surgical intervention and thus decrease morbidity and mortality.

CONCLUSION

In conclusion, we hope that our case report highlights on an uncommon instance of NSTI brought on by carbapenem-resistant *Klebsiella pneumonia*, which was well managed with tigecycline monotherapy. We also feel that our report reinforces the need for early and decisive surgical intervention once the diagnosis has been made and the identification of causative agent along with its antibiotic susceptibility to decrease mortality rates in NSTI and to improve patient outcomes.

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