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Case Report

Pancytopenıa and Sepsıs due to Meropenem: A Case Report

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Abstract

Meropenem is one of the most commonly used antibacterial agents with relatively few side effects. Serious adverse reactions reported with meropenem are rare with an incidence of 1 %. Recently we came across two rare adverse effects of meropenem in one patient with acute renal failure. There was pancytopenia and sepsis, respectively. To the best of our knowledge, a only few cases have been reported in the literature that document an association between meropenem administration and pancytopenia, and about half of these cases were sepsis. With the use of meropenem becoming more widespread, these two rare but fatal complications of meropenem should be borne in mind.

Keywords: *Meropenem, Pancytopenia, Sepsis, Fatal complications*

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INTRODUCTION

Meropenem is an ultra-broad spectrum injectable antibiotic used to treat a wide variety of infections, including meningitis and pneumonia [1]. It is a beta-lactam drug and belongs to the subgroup of carbapenem, similar to imipenem and ertapenem. It gained United States Food and Drugs and Administration (FDA) approval in July 1996. It penetrates well into many tissues and body fluids including the cerebrospinal fluid, bile, heart valves, lung and peritoneal fluid. The spectrum of action includes many Gram-positive and Gram-negative bacteria (including *Pseudomonas*) and anaerobic bacteria. The overall spectrum is similar to imipenem although meropenem is more active against *Enterobacteriaceae* and less active against Gram-positive bacteria [2]. The most common adverse effects are diarrhea (4 – 5 %), nausea and vomiting (1 – 4 %), injection-site inflammation (2 %), headache (2 %), rash (2 – 3 %), and thrombophlebitis (1 %). Rarely, it has been associated with pancytopenia, sepsis, septic shock, toxic epidermal necrolysis, renal damage and acute renal failure [3]. We report a case of meropenem induced pancytopenia and sepsis in a 78-year-old woman.

CASE REPORT

Our patient is a 78-year old female with left hip fracture which occurred as a result of a fall. Total hip replacement surgery had been done by an orthopaedic clinic. As a result of the prothesis dislocation, she was sent to the orthopaedic clinic of our hospital. Following evaluation, the

orthopaedic doctors decided to remove the prothesis because there was infection and relaxation in prothesis. After removing the prothesis, she was treated with 3 mg/kg/day dose intravenous (iv) gentamicin, for 10 days. Due to pain, doctors gave her intramuscular diclofenac sodium injection twice a day. The patient presented with a reduction in the amount of urine, intermittent nausea and vomiting, ten days after the intake of gentamicin and non-steroidal antiinflammatory drug. As a result of the elevation of creatinine levels, patient was referred to us. The patient developed acute renal failure because of the nephrotoxic agents which had been used for treatment. Therefore, gentamicin was discontinued and she was placed on ıv piperasilin tazobactam 2.25 mg three times daily, after which we took over management.

There was no other systemic disease in the patient. Her general condition was normal and conscience was clear. There was no problem about orientation and she was cooperative. Her vital signs were normal. Şhe was obese and her conjunctival sac and skin were pale. There were crackles at bilateral basal region of the lung. There was considerable (+++) edema on the left proximal part of the femur due to surgery. There was also pre-tibial pitting edema on bilateral lower extremities. Laboratory test results obtained (along with normal range of values) are shown in Table 1. For her arterial blood parameters, pH was 7.29 whule HCO_3^- was 13 (normal range = 22 - 26). There was no proteinuria. She was given intravenous fluid by close monitoring of blood pressure and peripheral venous pressure. We used gave diüretic when necessary. After a few days, the creatinine levels of the patient began to decline. The patient developed purpuric and itchy lesions all over body six days after the intake of piperacillin tazobactam.

Patient was referred to the dermatology clinic and her antibiotic was changed to iv meropenem 1 g two times daily. We dressed her wound daily and took wound culture everyday. On the 7th day of her admission, *Acinetobacter baumonnii* and methicillin-resistant coagulase-negative *Staphylococci* (MRCNS) were found on her wound cultures. The patient was then referred to the infectious diseases clinic. The patient was kept in isolation with all aseptic precautions. In accordance with the advice of infectious diseases clinic, we began treatment with doripenem, tigesycline and rifampicin. Meropenem treatment was commenced on the second day. One day after the growth of the bacteria, her fever was about 39 ^oC. Her blood pressure was 80/40 mmHg brachial and her pulse was 110/min. Her new laboratory test results showed the following: white blood cells 1000 cell/µl, hemoglobin 6.6 g/dl, platelet count 97000 cell/µl, international normalized ratio (INR) 1.53, blood urea nitrogen (BUN) 74 mg/dl, creatinine 3 mg/dl, sodium 152 mEq/l, potassium 3.6 mEq/l, calcium 5.5 mEq/l, phosphate 6.1 mEq/l, C-reactive protein :159 mg/L. The patient developed pancytopenia and sepsis three days after intake of meropenem. Two days after the growth of the bacteria, she died.

Table 1: Laboratory findings before and after treatment with meropenem

Parameter	Before meropenem administration	After meropenem administration	Normal range
WBC	7600	1000	4300 - 10300 cell/µl
Hb	8.3	6.6	13.6 - 17.2 g/dl
Plt	186000	97000	156000 - 373000 cell/µl
BUN	94	74	5 - 23 mg/dl
Cre	9.2	3	0.81 - 1.44 mg/dl
Na	136	152	135 - 145 mEq/l
K	3.9	3.6	3.5 - 4.5 mEq/l
Ca	6.8	5.5	8.8 - 10.8 mEq/l
P	8.5	6.1	3.0 - 4.5 mEq/l
UA	11	-	2.4 – 7.0 mg/dl
CRP	72	159	0 - 10 mg/L
ESR	50 mm/h	-	0 - 20 mm/h
INR	1.12	1.53	0.9 - 1.2

Abbreviations: WBC = white blood cell, Hb = hemoglobin, Plt = platelet, BUN = blood urine nitrogen, Cre = creatinine, Na = sodium, K potassium, Ca = calcium, P = phosfate, UA = uric acid, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, INR = international normalized ratio.

DISCUSSION

Pancytopenia is a rare life-threatening complication of meropenem [2]. The overall incidence of non-chemotherapy drug-induced agranulocytosis ranges from 2.6 to 10 cases per million patients exposed to the drugs per year [4]. Neutropenia usually leads to severe sepsis, requiring iv broad-spectrum antibiotic therapy, as

in the case of our patient. The severity of neutropenia and its duration may also impact negatively on the outcome. Hemopoietic growth factors have been shown to shorten the duration of neutropenia in drug-induced agranulocytosis. With appropriate management, the mortality rate is around 5 % [4].

In the literature, a study of pancytopenia among people who take meropenem hasbeen reported in eHealthMed based on 87 reports from FDA and user communities [2]. Fifty nine percent of people who had pancytopenia while taking meropenem were male and 38 % of them were > 60 years old. Most of these 87 patients also had *Pseudomonas* infection. Another study of bacterial sepsis among people who take meropenem, also in eHealthMe and based on 7 reports from FDA and user communities reported that 57 % of those who had bacterial sepsis while taking meropenem were female and 28 % of them were over 60 years old. Most co-used drugs for these patients in these studies were vancomycin, tacrolimus, methotrexate and neupogen [2].

In our patient, we came across two rare life-threatening complications of meropenem, namely, pancytopenia and sepsis. There have been reports in the past regarding the fatal outcome of meropenem-induced pancytopenia and sepsis. Our patient died but we do not know exactly whether meropenem was the cause of her death since şhe also had acinetobacter and MRCNS infections. However, the literature, derived mostly from FDA reports, shows that most of the cases involved *Pseudomonas* infection.

CONCLUSION

We believe that with the use of meropenem becoming more widespread, these two rare but fatal complications of meropenem should be borne in mind while using this drug. Clinicians should also take into consideration the important adverse effects mentioned in this report.

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