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MEROPENEM-ASSOCIATED SEVERE HEMATOLOGICAL COMPLICATIONS LEADING TO CARDIOVASCULAR COLLAPSE IN ELDERLY CRITICALLY ILL PATIENTS: A CASE SERIES

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ABSTRACT

Meropenem is a broad-spectrum carbapenem antibiotic widely used in critically ill patients and is generally considered safe. However, rare but serious hematological adverse effects including leukopenia, bone marrow suppression, and hemolytic anemia have been reported. We present a case series of two elderly postoperative patients with multiple comorbidities who developed severe hematological complications during meropenem therapy. The first patient developed profound leukopenia suggestive of acute marrow suppression, followed by rapid cardiovascular collapse. The second patient developed acute hemolytic anemia with associated cytopenias, which partially improved after drug discontinuation but was ultimately followed by sudden cardiac arrest. Although both patients had significant baseline comorbidities, the temporal association between meropenem administration and hematological deterioration suggests probable drug-induced toxicity. These cases highlight the importance of close hematological monitoring in elderly and critically ill patients receiving meropenem.

INTRODUCTION

Meropenem is a broad-spectrum carbapenem antibiotic commonly used in intensive care settings for severe bacterial infections. It is generally well tolerated, and most adverse effects are mild, including gastrointestinal disturbances and hypersensitivity reactions. However, rare hematological complications such as leukopenia, neutropenia, thrombocytopenia, pancytopenia, and immune-mediated hemolytic anemia have been described.

Drug-induced cytopenias may be overlooked in critically ill patients where sepsis, malignancy, nutritional deficiencies, and systemic inflammation are common contributors to bone marrow dysfunction. In elderly individuals with limited physiological reserve, acute hematological derangements can precipitate rapid clinical deterioration. We describe two elderly postoperative patients who developed severe hematological complications during meropenem therapy, both culminating in cardiovascular collapse.

CASE 1: SEVERE LEUKOPENIA FOLLOWING MEROPENEM THERAPY

A 75-year-old woman was admitted with acute pulmonary edema and hypertensive urgency. Her medical history included dilated cardiomyopathy with severe left ventricular dysfunction (ejection fraction 27%), coronary artery disease with paroxysmal atrial fibrillation, type 2 diabetes mellitus, systemic hypertension, bronchial asthma, chronic microcytic hypochromic anemia, prior cerebrovascular infarct, pemphigus vulgaris, and glaucoma.

On admission, she had leukocytosis (19,800 cells/mm^3) and elevated NT-proBNP levels. Echocardiography revealed dilated cardiac chambers with global hypokinesia and moderate systolic dysfunction. She improved with diuretics and oxygen therapy.

During hospitalization, she developed acute abdominal pain and was diagnosed with an irreducible umbilical hernia. Emergency exploratory laparotomy with strangulated omentocolectomy was performed. Histopathology revealed poorly differentiated ovarian carcinoma with elevated CA-125 levels.

Postoperatively, she developed worsening hypoxia and metabolic acidosis. Suspecting infection, intravenous meropenem was initiated. Shortly after initiation, her white blood cell count dropped abruptly to 500 cells/mm^3, and hemoglobin decreased to 8 g/dL, while platelet counts remained normal. Meropenem-induced bone marrow suppression was suspected, and the drug was discontinued.

Despite withdrawal, she developed sudden bradycardia (29 beats/min), followed by unrecordable blood pressure and asystole. Resuscitative efforts were unsuccessful, and she expired shortly thereafter.

CASE 2: MEROPENEM-ASSOCIATED HEMOLYTIC ANEMIA

An 83-year-old woman with triple vessel coronary artery disease, type 2 diabetes mellitus, systemic hypertension, dyslipidemia, chronic kidney disease, chronic obstructive pulmonary disease (COPD), and obstructive sleep apnea sustained an osteoporotic right intertrochanteric femur fracture following a fall. She underwent proximal femoral nail anti-rotation (PFNA2) surgery.

Postoperatively, she developed type 2 respiratory failure secondary to COPD exacerbation requiring BIPAP support. Baseline investigations showed leukocytosis (12,500 cells/mm³) and hemoglobin of 9.6 g/dL. Intravenous meropenem was initiated.

Meropenem was continued for eight days. On day 8, hemoglobin dropped to 7 g/dL, white blood cell count to 3,000 cells/mm³, and platelets to 1.5 lakh/mm³. Reticulocyte count was elevated at 12%, suggesting active hemolysis. Drug-induced hemolytic anemia was suspected, and meropenem was discontinued. Heparin was also withheld. One unit of packed red blood cells was transfused, and hematological parameters showed partial improvement over the next three days.

Despite apparent stabilization, she developed sudden bradycardia (39 beats/min), followed by cardiac arrest and asystole. Resuscitation was unsuccessful.

DISCUSSION

Meropenem is a broad-spectrum carbapenem antibiotic extensively used in critically ill patients because of its excellent activity against gram-positive, gram-negative, and anaerobic organisms and its overall favorable safety profile.[1] Hematological adverse effects are considered uncommon and are usually mild and reversible. However, rare but potentially life-threatening complications such as leukopenia, neutropenia, thrombocytopenia, pancytopenia, and immune-mediated hemolytic anemia have been described in the literature.[5] The two cases presented here illustrate distinct but severe hematologic toxicities temporally associated with meropenem therapy in elderly postoperative patients with multiple comorbidities, both culminating in fatal cardiovascular collapse.

In the first patient, the abrupt decline in white blood cell count to 500 cells/mm³ shortly after initiation of meropenem strongly suggests acute drug-induced marrow suppression or immune-mediated leukocyte destruction. Although critically ill patients frequently develop leukopenia due to sepsis, disseminated intravascular coagulation, nutritional deficiencies, or bone marrow infiltration, the sudden and profound nature of the drop, coupled with previously documented leukocytosis, supports a drug-related effect. Carbapenem-induced leukopenia is believed to occur through either direct toxic suppression of myeloid progenitor cells or immune-mediated peripheral destruction. Beta-lactam antibiotics have been shown in some cases to induce hapten-mediated immune reactions in which drug-dependent antibodies target circulating leukocytes. Another proposed mechanism involves cumulative dose-dependent bone marrow suppression, particularly in patients receiving prolonged therapy, although idiosyncratic reactions can occur even early in the course of treatment. In this patient, the rapid onset after drug initiation favors an immune-mediated or hypersensitivity mechanism rather than purely cumulative toxicity.[2,5]

The clinical consequences of profound leukopenia in an elderly patient with severe left ventricular dysfunction are substantial. Severe neutropenia markedly impairs host defense and predisposes to overwhelming infection and systemic inflammatory responses. Even in the absence of documented bacteremia, profound cytopenia can trigger systemic inflammatory cascades, endothelial dysfunction, and hemodynamic instability. In individuals with advanced cardiomyopathy and limited cardiac reserve, the added stress of systemic inflammation, metabolic acidosis, and hypoxia can precipitate bradyarrhythmias and cardiac arrest. The synergistic interaction between cardiac dysfunction, postoperative physiological stress, metabolic derangements, and severe leukopenia likely contributed to the rapid cardiovascular collapse observed in this case. Although malignancy was diagnosed postoperatively, there was no prior evidence of severe cytopenia to suggest pre-existing marrow failure, making acute drug-induced suppression a plausible contributing factor.[2,5]

The second case demonstrates a different hematologic manifestation, namely acute hemolytic anemia with associated leukopenia and thrombocytopenia. Drug-induced immune hemolytic anemia is rare but well documented with several beta-lactam antibiotics. The pathogenesis typically involves drug-dependent antibodies that bind to red blood cells in the presence of the drug, leading to complement activation and extravascular or intravascular hemolysis. The elevated reticulocyte count in this patient supports active marrow compensation for

peripheral red cell destruction, strengthening the likelihood of hemolysis rather than simple bone marrow suppression. The temporal relationship between meropenem administration and the decline in hemoglobin, along with partial recovery after drug discontinuation, further supports a probable adverse drug reaction. While direct antiglobulin testing was not reported, the clinical pattern is compatible with immune-mediated hemolysis.[3,5]

In elderly patients with significant coronary artery disease, chronic kidney disease, and chronic obstructive pulmonary disease, acute anemia substantially reduces oxygen-carrying capacity and increases myocardial oxygen demand. Even moderate reductions in hemoglobin can destabilize patients with limited cardiopulmonary reserve. Acute hemolysis may also release free hemoglobin and inflammatory mediators, contributing to endothelial dysfunction and hemodynamic instability. In the second patient, despite partial hematologic recovery and transfusion support, the physiological stress of recent anemia superimposed on severe comorbidities may have predisposed to fatal arrhythmia and cardiovascular collapse. The delayed cardiac arrest following apparent stabilization underscores the vulnerability of elderly critically ill patients even after initial correction of laboratory abnormalities.

In both cases, alternative etiologies such as sepsis, postoperative inflammatory response, malignancy-related marrow infiltration, nutritional deficiencies, and hemodilution must be considered. Critically ill patients often experience multifactorial cytopenias, and establishing definitive causality in such settings is inherently challenging. evertheless, the close temporal association between meropenem exposure and hematologic deterioration, along with partial improvement following withdrawal in the second case, suggests a probable relationship. These cases highlight an important clinical principle: medications widely regarded as safe can produce rare but catastrophic adverse effects, particularly in elderly patients with multiple comorbidities. Age-related decline in renal function, altered drug metabolism, polypharmacy, immune dysregulation, and reduced marrow reserve may all increase susceptibility to hematologic toxicity. Furthermore, early warning signs of drug-induced cytopenia may be subtle and easily attributed to underlying illness. Routine and frequent monitoring of complete blood counts during prolonged broad-spectrum antibiotic therapy is therefore essential, especially in high-risk populations. Prompt recognition of unexplained cytopenia and immediate discontinuation of the suspected agent may prevent progression to irreversible systemic decompensation.

In conclusion, this case series emphasizes that meropenem-associated hematologic toxicity, although rare, can be severe and potentially fatal in vulnerable patients. Clinicians should maintain a high index of suspicion when abrupt cytopenias occur during therapy and should carefully balance the benefits of broad-spectrum antimicrobial coverage against the potential risks in elderly critically ill individuals.[4]

CONCLUSION

This case series describes two elderly postoperative patients who developed severe hematological complications temporally associated with meropenem therapy, culminating in fatal cardiovascular collapse. In the first patient, profound leukopenia suggestive of acute bone marrow suppression occurred shortly after initiation of treatment, while in the second, acute hemolytic anemia with associated cytopenias developed during continued therapy and partially improved after drug withdrawal. Although both patients had multiple comorbidities that independently increased their risk of deterioration, the close temporal relationship between meropenem exposure and hematologic decline supports a probable drug-related adverse reaction. In physiologically fragile individuals with significant cardiac and pulmonary disease, even transient but severe cytopenias may critically impair oxygen delivery, immune competence, and hemodynamic stability.

These cases underscore the importance of maintaining a high index of suspicion for drug-induced hematological toxicity during meropenem therapy, particularly in elderly and critically ill patients. Unexplained reductions in blood counts should prompt immediate evaluation and consideration of discontinuing the suspected agent. Regular monitoring of complete blood counts during prolonged or high-risk antibiotic use is essential, as early recognition and timely intervention may prevent rapid clinical deterioration and potentially fatal outcomes.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and alternative names will be used; due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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