J Korean Med Sci 2007; 22: 1082-4
ISSN 1011-8934
DOI: 10.3346/jkms.2007.22.6.1082

Morganella Morganii Sepsis with Massive Hemolysis

Morganella morganii is a facultative gram-negative and anaerobic rod. It may be a cause of devastating infections in neonates and immunocompromised hosts. Some bacterial infections such as *Clostridium* and *Vibrio* are associated with hemolysis. However, massive hemolysis caused by *M. morganii* sepsis has not yet been reported. We observed a 59-yr-old man who had chemotherapy-induced neutropenia and was found to have massive hemolysis and metabolic acidosis due to sepsis. He died 6 hr after admission in spite of aggressive treatment. Two sets of blood cultures revealed the growth of *M. morganii*. We report here that *M. morganii* sepsis can cause fatal massive hemolysis leading to death.

Key Words : *Morganella Morganii; Sepsis; Hemolysis*

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Received : 21 August 2006
Accepted : 1 November 2006

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*This work was supported by a 2004 Inje University Research Grant.

INTRODUCTION

Morganella morganii is a facultative gram-negative and anaerobic rod found in the feces and intestines of humans, dogs, and other mammals. It is known to be a causative organism of opportunistic infections in the respiratory tract, the urinary tract, and in wound infections. It can cause devastating infections in the neonates and postoperative stages, especially in diabetic patients (1). The risk of infection is particulary high when a patient becomes neutropenic as a result of myelosuppressive chemotherapy (2). Massive hemolysis can be associated with bacterial infection and has been reported mainly in cases of *Clostridial* or *Vibrio* sepsis (3, 4). We report here on a case of *M. morganii* sepsis associated with massive hemolysis in a neutropenic patient who underwent chemotherapy.

CASE REPORT

A 59-yr-old-male was admitted to the emergency room (ER) with a 1-day history of jaundice, drowsiness, and a high fever. He had been diagnosed with stage IIIa non-small-cell lung cancer one year earlier. He had undergone a left pneumonectomy followed by 3 courses of adjuvant chemotherapy with gemcitabine and cisplatin. Since the chest computed tomography (CT) scan taken after 3 courses of chemotherapy revealed newly developed mediastinal lymph nodes enlargement, the chemotherapeutic regimen was switched to paclitaxel and carboplatin. He had completed the course of chemotherapy with paclitaxel and carboplatin 10 days before his admission to the ER. Two days prior to admission to the ER, he visited the outpatient department to check the possibility of chemotherapy induced cytopenias. At that time the patient was afebrile, and his blood test showed hemoglobin 11.7 g/dL, hematocrit 34 %, a white blood cell count of $2.12 \times 10^3/\mu L$ (8.4% segmented neutrophils, 81.6% lymphocytes, 5.7% monocytes, 3.8% eosionphils, and 0.5% basophils), and a platelet count of $107 \times 10^3/\mu L$. Granulecyte colony-stimulating factor was administered for the chemotherapy-induced neutropenia. Later that night he experienced fever and chills. The day before his admission, jaundice and dark red-colored urine developed. On admission, he was icteric and lethargic. He was drowsy but there were no focal neurological findings. There was no history of drug overuse. His blood pressure was 180/100 mmHg, the heart rate was 135 beats/min, the respiration rate was 24 breaths/min, and his temperature was 36°C. His arterial acid/base status was as follows: pH 7.04, pCO_2 14 mmHg, pO_2 77 mmHg, HCO_3- 3.8 mM/L, SaO_2 87%. The laboratory findings were

as follows: hemoglobin 4.8 g/dL, hematocrit 6.9%, white blood cell count 2.47 × $10^3/\mu$L (11.8% segmented neutrophils, 77.7 % lymphoctes, 8.5% monocytes, 0.8% eosinophils, 1.2% basophils), platelets 71 × $10^3/\mu$L, reticulocyte count 60.7%, total bilirubin 31 mg/dL, direct bilirubin 5.6 mg/dL, aspartate transferase 9 IU/L, alanine transferase 7 IU/L, blood urea nitrogun 47 mg/dL, and creatinine 1.0 mg/dL. Electrolytes, ionized calcium, and glucose levels were all within normal limits. A peripheral blood smear showed polychromatric and spherocytic red blood cells, toxic vacuolation and toxic granulated neutrophils. Direct and indirect antiglobulin tests were all negative. The level of glucose- 6-phosphate dehydrogenase was within the normal range. Chest radiography and electrocardiogram findings did not show any abnormalities. A CT scan of the abdomen revealed a 3 cm-sized focal parencymal destructive lesion with air in S6 of the liver, mild dilated intrahepatic duct without stones, and periductal edema, indicating a gas-forming abscess in liver. The patient had a history of a left lobectomy of the liver due to a villotubular adenoma and intrahepatic duct stones. His condition deteriorated rapidly in spite of intensive treatment. After sampling blood and urine for microbiological examination, antibiotics composed of ceftazidime 2 gm and amikacin 500 mg were injected intravenously on the basis of suspected neutropenic sepsis. Despite the adequate replacement of sodium bicarbonate and oxygen, severe metabolic acidosis and hypoxemia were not corrected. Cardiac arrest followed, and he died 6 hr after admission. An autopsy was not performed according to the family's decision. Two sets of blood cultures were incubated (VITAL, bioMérieux, Marcy-L'Etoile, France), and both showed the growth of *M. morganii*. Antibiotic susceptibility testing was performed using VITEK 2 (bioMérieux, Marcy-L'Etoile). While the isolate was resistant to ampicillin, cephalothin, and trimethoprim/sulfamethoxazole, it was sensitive to cefotaxime, ceftazidime, aztreonam, gentamicin, amikacin, ciprofloxacin, and imipenem.

DISCUSSION

The case presented here is unique and interesting since *M. morganii* seldom causes sepsis and massive hemolysis associated with this organism in human being has not been previously reported. This patient was in a condition of severe neutopenia that made him susceptible to bacteremia. When cytotoxic chemotherapy is used to treat cancer, it has potent effects on both humoral and cellular immunity. All types of infections are associated with higher rates of morbidity and mortality in patients who receive chemotherapy (5). Within the enterobacteriaceae, the genus *M. morganii* belongs to the tribe Proteeae, which also includes the genera Proteus and Providencia. It resides in human colonic mucosa as a normal flora. It is well known that it may cause an opportunistic infection, especially in an immunocompromised host. The majority of *M. morganii* infections are related to postoperative wound infection and urinary tract infection. Mylotte et al. reported that the risk factors for *M. morganii* infection were old age, the presence of a serious underlying disease, the presence of concomitant bacteremia, hospitalization, recent surgery, and concurrent antibiotic use. *M. morganii* infections do not typically induce bacteremia. However, bacteremia caused by *M. morganii* infection can be associated with a mortality rate of 22-38%. According to a review recently published, *M. morganii* sepsis frequently occurred secondary to urinary tract or hepatobiliary tract infection. It was associated with a high mortality rate, especially for patients with solid tumors, diabetes, polymicrobial bacteremia, and inappropriate antibiotic treatment. The major portals of entry of *M. morganii* bacteremia were the urinary tract, followed by the hepatobiliary tract (6-8). Massive hemolysis, a rare but well-known and characteristic complication of *Clostridium perfringens*, has been reported in cases of postabortion and postpartum infections and gas gangrene (9). In *C. perfringens* infection, alpha-toxin gives rise to lysis of the erythrocytes. Intravascular hemolysis is caused by the alpha toxin, which is a phospholipase C lecithinase. The alpha toxin hydrolyzes sphingomyelin and lecithine to phosphoryl choline and diglyceride and, therefore, can cause the lysis of red blood cells, white blood cells, platelets, and endothelial cells. There are reports that *Bacillus cereus*, *Vibrio vulnificus,* and *Haemophilus influenzae* can also cause intravascular hemolysis (10). Recent studies showed that 56% of *M. morganii* strains could produce the hemolysin and that there is a genetic homology between the hemolysin of *M. morganii* and the alpha hemolysin of *Escherichia coli*. It has been reported that the *M. morganii* hemolysin causes hemolysis by generating a pore in the erythrocyte membrane. *M. morganii* hemolysin might also cause leakage of ATP in human granulocytes, leading to cell death. Production of this hemolysin seems to be lethally virulent. Intranasal application of the hemolytic strains in mice caused death within a short time and hemorrhagic lung edema was found during an autopsy (11).

Chemotherapy-induced side effects can be thought of as the cause of hemolytic anemia and metabolic acidosis in this case. However, it has not been reported that chemotherapeutic agents such as paclitaxel and carboplatin, which were administered to this patient, cause either massive hemolysis or metabolic acidosis. Hemolytic uremic syndrome (HUS) should be ruled out as a possible cause of the massive hemolysis in this case. In HUS, the expected time frame of the clinical course is days to weeks and the urinary function is abnormal. This patient showed a rapid deterioration in the clinical course along with massive hemolysis and normal renal function. Thrombotic thrombocytopenic purpura (TTP) can also be a cause of hemolytic anemia. However, neither HUS nor TTP has been associated with these drugs. Based on these findings, we diagnosed this patient as having sepsis with massive hemolysis due to *M. morganii*. The clinical course of hemolysis provoked by *M. morganii* infection is not well known. As far as we know, this is the first case of *M. morganii* sepsis with massive hemolysis.

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