Emphysematous Pyelonephritis Successfully Treated with Nephrectomy and Granulocyte Colony-Stimulating Factor

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A 58-year-old woman developed diabetic ketoacidosis and emphysematous pyelonephritis caused by Escherichia coli. She was successfully treated with nephrectomy, antibiotics, and recombinant human granulocyte colony-stimulating factor (rhG-CSF). RhG-CSF therapy may be an effective adjunct for diabetic patients with severe infection, even when neutropenia is not present. (Internal Medicine 33: 234–236, 1994)

Key words: diabetic ketoacidosis, Escherichia coli

Introduction

Emphysematous pyelonephritis is a rare and life-threatening bacterial infection associated with gas formation in the renal parenchyma and frequently also in the perirenal space or collecting system (1). We report a case of emphysematous pyelonephritis in a patient with diabetic ketoacidosis that was successfully treated with nephrectomy, antibiotics, and recombinant human granulocyte colony-stimulating factor (rhG-CSF).

Case Report

A 58-year-old woman was admitted to our hospital with lower back pain on January 18, 1993. She had been taking haloperidol, biperiden, flunitrazepam, and triazolam for schizophrenia for 12 years, but had been well until two days before admission. She was not known to have diabetes.

On admission, she had a temperature of 39.7°C and was drowsy. Right costovertebral angle tenderness was present. Urinalysis revealed 3+ glucose, 2+ ketones, 2+ protein, and 15–20 white blood cells per high power field (HPF). The white blood cell (WBC) count was 27,600/mm³, with a shift to the left on the differential count. Plasma glucose was 617 mg/dl, blood urea nitrogen (BUN) was 57 mg/dl, creatinine (Cr) was 1.4 mg/dl, sodium was 139 mEq/1, potassium was 2.4 mEq/1, chloride was 107 mEq/1, and C-reactive protein (CRP) was 45.2 mg/dl.

Arterial blood gases on room air were as follows: pH, 7.38; PaCO₂, 24.5 mmHg; PaO₂, 84.0 mmHg; base excess, -18.0 mmol/l; and HCO₃⁻, 7.2 mmol/l. Escherichia coli (E. coli) was cultured from both blood and urine, and abdominal ultrasound showed diffuse enlargement of the right kidney.

The clinical diagnoses were diabetic ketoacidosis, pyelonephritis, and bacteremia. Continuous intravenous regular insulin, fluid replacement, and administration of piperacillin (6 g on day, and then 3 g/day) were started. The plasma glucose level subsequently fell to 130–220 mg/dl. However, her fever still persisted on the third hospital day and dyspnea developed, with the blood gases worsening to a PaCO₂ of 25.5 mmHg and a PaO₂ of 52.8 mmHg. Renal function also deteriorated, with a BUN of 64 mg/dl and a Cr of 2.6 mg/dl. The urine sediment still contained 10–15 white cells per HPF, but cultures of blood and urine were negative. Ceftazidime (2 g/day) was also administered. The cultured E. coli was sensitive to both drugs, but her fever did not improve. On the eighth hospital day, ultrasound (Fig. 1) showed gas echoes within the parenchyma and perirenal fluid accumulation of the right kidney, as well as slight enlargement of the left kidney. Computerized tomography (CT) scan confirmed these findings (Fig. 2). Right nephrectomy was performed on the 11th hospital day. The resected kidney showed multiple abscesses in the cortex, accumulations of lymphocytes and plasma cells in the medulla, and infiltrations of neutrophils in the renal capsule and perirenal fat.

Her dyspnea improved postoperatively, but low-grade fever still persisted. The urine was 1+ for protein and the sediment contained 5–10 white cells per HPF. Cultures of blood and urine yielded no microorganisms. However, the BUN rose to 95 mg/dl and the Cr to 4.7 mg/dl. From the 24th hospital day, imipenem cilastatin sodium (0.5 g/day) was administered. Ultrasound showed diffuse enlargement of the left kidney. It was suspected
that her low-grade fever was caused by pyelonephritis of the remaining kidney and/or residual infection of the tissues around the site of the resected right kidney. After the commencement of treatment with imipenem cilastatin sodium, the CRP began to fall, but both the CRP and fever increased again on the 36th hospital day. The urine sediment contained 5–10 white cells per HPF, although blood and urine cultures were negative. On the 40th hospital day, although the WBC was 5,500/mm³ (80% neutrophils), rhG-CSF administration was started (125 µg given subcutaneously on two successive days followed by one day off) (Fig. 3). The WBC increased to about 20,000/mm³ (85% neutrophils). Five days after starting rhG-CSF administration, her fever resolved and the CRP and urinalysis findings were normalized. Her renal function also improved (BUN, 16
mg/dl; Cr, 1.2 mg/dl).

Discussion

Ahlering et al. (2) have previously reported 13 patients with emphysematous pyelonephritis the average age was 53 years. There were 10 females (77%), and all the patients had diabetes mellitus. In a different report (1), a very high percentages 92%, of the patients had diabetes. E. coli was the most frequent causative organism (69%), followed by Klebsiella and Proteus. The mortality rate was as high as 42%. Early diagnosis and nephrectomy have been suggested to improve the prognosis. The pathogenesis of gas formation in this condition is not well understood. Huang et at (3) reported that the gas consists of hydrogen, carbon dioxide, nitrogen, and oxygen, and they suggested that it is produced from glucose fermentation by the infecting organisms. Our patient was successfully treated by nephrectomy and the administration of antibiotics and rhG-CSF.

In the diabetic state, chemotaxis, phagocytosis, and intracellular killing by neutrophils are all reduced (4-7) and the serum opsonic activity is also low (8). In addition, cell-mediated immunity is depressed (7), and these changes lead to a decrease in host resistance to infection.

Granulocyte colony-stimulating factor (G-CSF) is a cytokine which causes the proliferation and differentiation of hematopoietic progenitor cells, and is mainly produced by monocytes, macrophages, fibroblasts, and endothelial cells (9). Its production is regulated by a network of other cytokines such as interleukin-1, 3, and 4, tumor necrosis factor-a, and interferon-g(10). Recently, rhG-CSF therapy has been used for neutropenia due to cancer chemotherapy, myelodysplastic syndrome, and primary neutropenic diseases (11). In addition to promoting granulocyte proliferation and differentiation, rhG-CSF also enhances superoxide release by granulocytes (12) and activates neutrophil chemotaxis (13) and phagocytosis (14).

There have been some reports that rhG-CSF is effective for treating experimentally induced infection in mice or rats (15, 16). In addition, Sato and Shimizu (17) reported that rhG-CSF improves the production of oxygen-derived free radicals in diabetic neutrophils. This suggests that even in the absence of neutropenia, administration of rhG-CSF may be effective for treating infection in diabetic patients.

The present patient had persistent fever after nephrectomy, despite the long-term administration of multiple antibiotics. Left renal pyelonephritis and/or residual right perirenal infection was suspected, but the peripheral neutrophil count was inappropriately low for such severe infection. The production or activity of G-CSF may be reduced in diabetes, because the T lymphocytes and macrophages which regulate G-CSF production (10) show various functional abnormalities in patients with this disease (7, 18). After administration of imipenem cilastatin sodium, the CRP was decreased temporarily. However, the CRP and fever both rose again 12 days later, so administration of rhG-CSF was started. After rhG-CSF was initiated, the WBC increased appropriately considering her severe infection and the fever improved immediately, indicating that this therapy was effective for controlling the infection.

Our observations suggest that rhG-CSF may be effective for severe infections associated with diabetes mellitus, even when the neutrophil count is normal. However, further research is necessary to confirm this finding.

References