Coexistence of Emphysematous Pyelonephritis and Cystitis Rarely Seen in an Uncontrolled Diabetes Mellitus Case: Case Report and Review

Kontrolsüz Diyabetes Mellitus Vakasında Nadir Görülen Amfizematöz Piyelonefrit ile Sistit Birlikteliği: Vaka Raporu ve Literatür Derlemesi

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Abstract

Emphysematous pyelonephritis (EP) and emphysematous cystitis (EC) are rare urinary tract infections that are more frequently seen in women. Nearly 90% of the patients have diabetes mellitus (DM). They generally start suddenly and progress rapidly. They develop within a short time following septicemia and acute kidney failure symptoms. The most sensitive radiological test for showing gas accumulation as well as identifying its localization and boundaries is abdominal computed tomography (CT). The current prevailing general opinion favors starting broad spectrum antibiotherapy without waiting for culture results and then performing percutaneous catheter drainage if necessary, depending on the clinical condition of the patient. Nephrectomy is performed in nonresponsive cases. In this case, the approach to unregulated diabetes mellitus induced emphysematous pyelonephritis is discussed.

Key Words: Emphysematous pyelonephritis,emphysematous cystitis,diabetes mellitus

Öz

Amfizematöz piyelonefrit (EP) ve amfizematöz sistit (EC) bayanlarda daha sık olmak üzere nadir görülen bir idrar yolları enfeksiyonu tipidir. Hastaların yaklaşık % 90'nında diabetes mellitus (DM) mevcuttur. Genellikle ani başlar ve hızlı seyirlidir. Septisemi ve akut böbrek yetmezliği semptomlarını takiben kısa sürede ortaya çıkar. Gaz birikimini göstermek, lokalizasyonunu ve sınırlarını belirlemek için en sensitif radyolojik test abdominal bilgisayarlı tomografidir (BT). Güncel hakim genel görüş kültür sonuçları beklenmeksizin geniş etki spektrumlu antibiyoterapi başlanmasını takiben hastanın klinik durumuna göre gerekirse perkütan kateter drenajı yapılmasıdır. Bu vakada kontrolsüz diabetes mellitusa bağlı meydana gelen amfizematöz piyelonefrit vakasına yaklaşım ele alınmıştır.

Anahtar Kelimeler: Amfizematöz piyelonefrit,amfizematöz sistit,diabetes mellitus [tr]

INTRODUCTION

Emphysematous urinary tract infections (EUTI) are associated with gas formation in the upper and lower parts of the urinary tract. EUTI can manifest as cystitis, pyelitis or pyelonephritis. Emphysematous pyelonephritis (EP), a rare suppurative infection characterized by gas formation in perirenal and renal parenchyma with substantially high mortality unless diagnosed quickly and started on effective treatment. Emphysematous cystitis (EC) is characterized by air accumulation within the bladder lumen and wall. Diabetes mellitus (DM) is a major risk factor for EUTI and increases the frequency of cystitis, and renal and perinephric abscess development besides causing asymptomatic bacteriuria (1). Conventional EUTI treatment consists of percutaneous drainage, parenteral antibiotherapy and surgery for the purpose of preventing the infection from spreading (2).

In this article, we discussed a case of emphysematous pyelonephritis and cystitis coexistence in an uncontrolled DM patient that did not exhibit clinical recovery with broad spectrum antibiotherapy and percutaneous catheter drainage and required a nephrectomy in conjunction with reviewing literature data.

A CASE PRESENTATION

A forty four-years old female patient with type 2 DM diagnosis known for 5 years presented to the emergency department with right side pain and dysuria complaints ongoing for the last 7 days, as well as fever, nausea, weakness, dull intermittent pain and burning sensation in the right lumbar region that became distinct within the last 24 hours. The patient was transferred to internal diseases intensive care unit. It was understood that the patient, who received ciprofloxacin 750 mg twice a day for the last five days and had a history of Type 2 DM for 7 years, used metformin, gliclazide and acarbose treatments irregularly. In physical examination, fever was 38.8 °C. Abdominal examination showed tenderness in the epigastric area, tenderness and temperature increase in the right upper quadrant and right costovertebral angle tenderness. The patient's laboratory tests showed: plasma glucose 266 mg/dL, HgbA1C 11.6% (103.3 mmol), leukocyte 5.120/mm3, neutrophil 4.950/mm3, hemoglobin 8 g/dl, hematocrit 25.6%, C-reactive protein 349.22 mg/l, erythrocyte sedimentation rate 82 mm/hour and procalcitonin 18.1 ng/m. Microscopic urinalysis showed leukocyte 1124/hpf, erythrocyte 154/hpf, glucose +1, leukocyte esterase +3 and protein +3 Abdominal

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ultrasonography showed hyperechogenicity that has an 12 cm acoustic shadow on the posterior in the right kidney region and abdominal CT did not show distinct kidney structure in the right kidney region, generalized air densities were seen in the kidney and in the collecting duct system, and right kidney perirenal areas had distinct contamination and were edematous (class 2 EP) (Figure 1). The patient underwent percutaneous catheter drainage. Plenty of foul-smelling air was drained. The patient was started on 500 mg imipenem + 500 mg cilastatin four times a day after collecting blood and urine samples for culturing. Fluconazole 100 mg twice a day was added to the antimicrobial treatment after urine culture showed Klebsiella pneumoniae and Candida (non-Albicans) growth. The patient was started on crystallized insulin for blood glucose regulation and blood glucose was followed up every four hours. After treatment for 12 days, the urology department performed a nephrectomy as a result of consultation due to the continuing generalized air densities within the kidney parenchyma seen in the abdominal control tomography on the patient, who still exhibited increasing acute phase reactants but fine general condition. Nephrectomy material was sent to pathology laboratory (Figure 2). The patient, with a Glasgow coma score of 15 and stable vital signs was conscious, cooperative, oriented in the postop period and she was transferred to the intensive care unit. However, the patient had a cardiac arrest in the third hour due to sudden ventricular fibrillation and passed away. Informed consent form has been taken from the patient's husband.

Figure 1. Generalized air densities within the right kidney

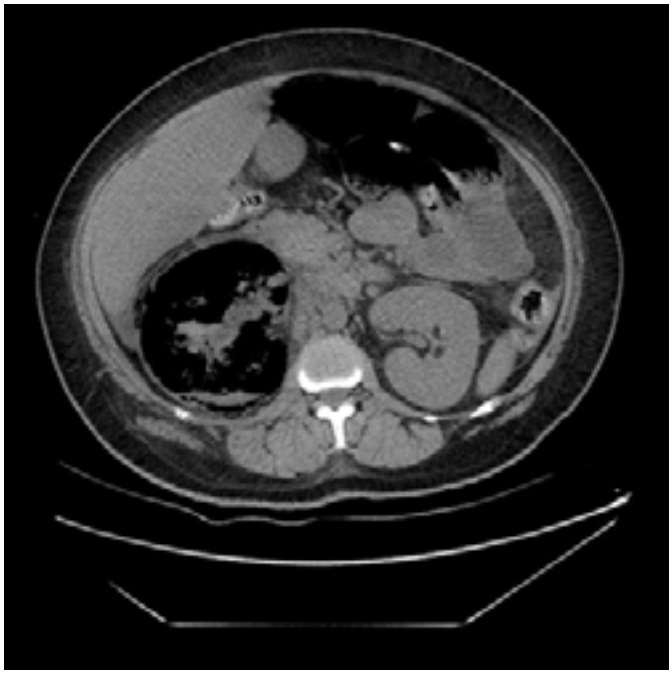

Figure 2. Nephrectomy material

DISCUSSION

DM, which is accepted as one of the greatest threats to health in the last century, is a clinical syndrome associated with a deficiency in insulin activity or secretion. The number of people that will have a DM diagnosis in 2025 is estimated to be nearly 380 million (3). In patients with DM, there is immune response impairment besides the classic complications of the disease. DM is associated with reduced T-cells, neutrophil functions and humoral immunity (4-6). In DM patients, the frequency of infection is increased in comparison to the normal population, hence, rare events such as mucormycosis are seen due to impaired immune response. These events might induce diabetic complications such as hypoglycemia and ketoacidosis in addition to the signs developed depending on their own infectivity level.

Infections in DM patients can be studied under two categories, i.e. host- and organism-specific factors. Host-specific factors consist of negatively affected immune response due to hyperglycemia, vascular insufficiency, peripheral neuropathy, autonomic neuropathy, and skin and mucosa colonization by microorganisms such as Stafilococcus aureus and Candida species. Examples of organism-specific factors include proteins induced by high glucose levels in women with poor glycemic control, facilitating the adhesion of candida factors such as primarily Candida albicans on vulvar and vaginal epithelium, and ketone reductases facilitating the transport of Rhizopus fungus species that lead to mucormycosis, and triggering infection development in patients with ketoacidosis. The main mechanisms of infection pathophysiology in patients with DM consist of reduced T-lymphocyte response, reduced neutrophil function, antioxidant system depression, reduced inflammatory cytokine secretion, gastrointestinal system dysmotility, and increased virulence of infection microorganisms with increased polymorphonuclear cell apoptosis due to hyperglycemia. One of the main mechanisms responsible for humoral immunity is the complement system. The complement system is made up of surface and serum proteins that have the main functions of enabling opsonization of microorganisms and inducing lysis of these microorganism via macrophages and neutrophils. Some studies showed a deficiency in C4 component in patients with DM (7, 8). The decrease in C4 level may be associated with polymorphonuclear cell dysfunction and reduced cytokine response. In patients with DM, mononuclear cells and monocytes may secrete less interleukin-1 (IL-1) and IL-6 in response to lipopolysaccharide stimulation. Reduced interleukin synthesis stems from the intrinsic deficiency in the cells of patients with DM (9). In addition, other studies showed that increased glycation can inhibit both the IL-10 production from myeloid cells and the production of interferon gamma (IFN- γ) and tumor necrosis factor (TNF)- α from T-cells. Furthermore, glycation reduces

the expression of class 1 major histocompatibility complex (MHC) on the surface of myeloid cells damaging cell immunity (10). In uncontrolled DM patients with irregular blood glucose level, mobilization of polymorphonuclear leukocytes, chemotaxis and reduced phagocytic activity can be observed (11, 12). Hyperglycemic tissues may inhibit antimicrobial functions by inhibiting glucose-6-phosphate dehydrogenase (G6PD), increasing polymorphonuclear leukocyte apoptosis and decreasing the migration of polymorphonuclear leukocytes from endothelium. In tissues that do not need insulin to transport glucose, hyperglycemic tissue environment increases intracellular glucose levels that will be metabolized later by using NADPH as a cofactor (13). The decrease in NADPH levels prevents the regeneration of molecules that play a key role in antioxidant protection mechanisms of cells and in turn increases susceptibility to oxidative stress. Regarding lymphocytes, it was shown that when glycosylated hemoglobin (HbA1c) is < 8.0 %, proliferative function of CD T lymphocytes and response to antigens were adequate (6). In patients with DM, immunoglobulin glycosylation occurs in correlation with the increase in HbA1C and this may impair the functionality of antibodies (6).

Pneumonia, urinary tract infections, skin and soft tissue infections are more common in the diabetic population. Although factors causing pneumonia are similar to the factors in the non-diabetic population, gram-negative microorganisms, Stafilococcus aureus and Mycobacterium tuberculosis are seen more frequently. Urinary tract infections (both the lower tract and pyelonephritis) are the result of common bacterial agents such as Escherichia coli; however, many yeast species (Candida and Torulopsis glabrata) are also seen commonly. Complications associated with urinary tract infections consist of EP and EC (14). The main causes of urinary tract infections in DM patients are inadequate glycemic control, duration of the disease, impaired leukocyte functions and anatomical and functional impairments of the urinary tract (15, 16).

EUTI, which is more frequently seen in DM patients as compared to the normal population, can manifest as cystitis, pyelitis or pyelonephritis. EP is a urinary tract infection characterized by the presence of gas in the renal collecting system or perinephric tissues and the presence of necrosis in the renal parenchyma. DM is more prevalent in women as compared to men. Presenting symptoms are fever, shivering, side pain, nausea and vomiting. The benefit of direct urinary system radiography is limited in diagnosis, whereas CT provides the pattern and localization of gas in the urinary tract. EP was first described by Kelly and MacCallum in 1898 and then divided into two groups, i.e. type I and type II, by Wan et al. in 1977 (17). Type I EP is characterized by gas formation and severe clinical course coexisting with renal parenchymal destruction and requires emergency nephrectomy. Type II EP is characterized by gas presence in the collecting system as well as renal or perinephric fluid. The up to date classification of EP was specified by Michaeli et al. in 2000 and revised by Huang and Tseng as CT classification, which is provided in Table 1.

EC affects individuals with DM more frequently than those who are not diabetic. It is characterized by the presence of gas in bladder space and bladder wall infiltration by carbon dioxide-producing microorganisms due to infection (18). The most common causes consist of E.coli, Enterobacter, Proteus, Klebsiella and Candida (19). EC is more frequently seen in women and the standard method for diagnosing EC is CT (19, 20).

Table 1: Emphysematous pyelonephritis classification

EP classification	
Class 1	*Gas in the collecting system only*
Class 2	*Gas in renal parenchyma only*
Class 3A	*Extension of gas or abscess to perinephric space*
Class 3B	*Extension of gas beyond Gerota's fascia*
Class 4	*Bilateral EP or solitary kidney with EP*

Medical therapy is generally enough for the treatment of emphysematous cystitis (20). In addition, bladder irrigation might be required if there are blood clots. If the bladder cannot be emptied adequately, catheter placement is often required. In rare cases, bladder debridement and partial or total cystectomy might be required. The duration of antimicrobial treatment depends on the clinical response. The average antibiotic treatment period was reported as 10 days in the review of 20 emphysematous cystitis cases followed-up throughout the treatment period (20).

The treatment of emphysematous pyelonephritis or pyelitis used to generally consist of nephrectomy and antibiotherapy with open drainage (21). The reports published in recent years recommend successfully treating patients with parenteral antibiotics while performing percutaneous catheter drainage (PCD) of gas and purulent material, and also relieving urinary tract obstructions, if there is any (22-24). Of course, all patients need parenteral antibiotic treatment regardless of the drainage or operation type employed.

The most important way to prevent all complications in patients with DM is the strict regulation of blood glucose levels. Patient self-monitoring of blood glucose (SMBG) and A1C are avaliable to health care providers and patients to assess the effectiveness and safety of the management plan on glycemic control.

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