CASE REPORT
OLGU SUNUMU

A chronic myeloid leukemia case diagnosed following acute kidney injury

Akut böbrek hasarını takiben tanı konan kronik miyeloid lösemi olgusu

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SUMMARY

A chronic myeloid leukemia (CML) case following acute kidney injury (AKI) was reported here.

80 year old man, admitted to the clinic with oliguria and increasing in serum urea and creatinine levels. He was diagnosed as acute kidney injury (AKI) and treated supportively, but recovered partly; no renal replacement therapy was required. Four months later he was referred to the clinic again because of significant, persistent leukocytosis; after peripheral blood smear, bone marrow biopsy and BCR-ABL gene scanning examination, he was diagnosed as chronic myeloid leukemia.

Keywords: Acute kidney injury, chronic myeloid leukemia, BCR-ABL gene, KDIGO criteria

ÖZET

Bu yazıda akut böbrek hasarını (ABH) takiben tanı alan bir kronik myeloid lösemi (KML) vakası bildirilmiştir.

80 yaşında erkek hasta, oligüri ve serum kreatinin düzeylerinde yükselme ile kliniğe başvurdu. Akut böbrek hasarı (ABH) teşhisi kondu ve destekleyici tedavi verildi,kısmen iyileşme sağlandı,renal replasman tedavisi gerekmedi. Dört ay sonra persistan lökositoz nedeniyle tekrar kliniğe başvurdu; periferik yayma,kemik iliği biyopsisi ve BCR-ABL gen tarama incelemesi sonrasında kronik myeloid lösemi tanısı kondu.

Anahtar kelimeler: Akut böbrek hasarı, kronik myeloid lösemi, BCR-ABL geni, KDIGO kriterleri

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INTRODUCTION

Acute kidney injury (AKI) is a syndrome characterized by the rapid loss of kidney function. Recently acute kidney injury was described and classified by KDIGO (Kidney Disease: Improving Global Outcomes) guideline (1). Acute kidney injury is a common complication and causes to increase in mortality rate significantly in hospitalized and critically ill patients (2). It was reported that AKI may be responsible for 2 million deaths per year in the United States, and furthermore, 50% of critically ill patients in intensive care may develop AKI (3).

Chronic myeloid leukemia (CML) is a disease in the class of chronic myeloproliferative diseases defined as chronic, accelerated and blastic phase. In the pathogenesis of the disease; As a result of t (9:22), the BCR gene in the 11q band of the 22nd chromosome and the ABL gene located in the q34 band of the 9th chromosome are combined on the 22nd chromosome (Ph chromosome), and the formation of the BCR-ABL1 fusion gene is responsible. Ph chromosome causes cell clone proliferation and leukocytosis. (4)

Chronic myeloid leukemia accounts for approximately 15% of adult leukemias, with an annual incidence of approximately 1.6 / 100,000(5). Most patients typically present with splenomegaly, anorexia or abdominal pain, but 30-40% of patients are asymptomatic and the diagnosis is made after a routine blood test. (6).

AKI is a common complication in malignancy; the incidence of AKI among cancer patients was reported between 11% and 20%. Hematologic malignancies especially leukemia, lymphoma, and multiple myeloma have higher risks to develop AKI (7). However; malignant cell infiltration and AKI development was not reported as common complication for CML.

We report here an acute on chronic kidney injury case with diabetes, hypertension and previous prostate adenocarcinoma operation. Surprisingly few weeks later he applied to the clinic with persistent leucocytosis and diagnosed as CML.

CASE REPORT

An 80 years old male presented to the outpatient clinic with epigastric pain and anuria. Patient has a history of prostate adenocarcinoma two years ago, also has a history of hypertension and diabetes mellitus.

First day of the admission as shown on the table I, the blood chemistry analyses demonstrated evidence of acute renal failure as follows: Creatinin 7,19 mg/dl, blood urea nitrogen 72 mg/dl, sodium 126 mEq/L, potasium 4,8 mEq/L, phosphate 6,2 mg/dl. Total blood count shows WBC 9,97x 10^3 cells per mm^3, with %77.2 neutrophils, hemoglobin 14,1 g/dl , trombocyte 209 10^3 cells per mm^3. Spot urine analysis revealed proteinuria (+1).

Table 1. Laboratory feature of the patient

	Discharge	*CML Diagnosed*
BUN(mg/dl)	*51*	*25*
Creatinin(mg/dl)	*2.2*	*1.5*
Sodium	*140*	*137*
Potasium	*2.8*	*4.9*
Calcium(mg/dl)	*8.9*	*9.6*
Phosphor(mg/dl)	*3*	*4.8*
Uric acid(mg/dl)	*7.1*	*9.3*
Proteinuria(24-hour urine(mg/day)	*562*	*382*
Leukocyte (K/mm3)	*10.6*	*23.9*
Hemoglobin(g/dL)	*14.6*	*15.3*
Platelet(K/mm3)	*285*	*589*

*BUN: Blood Urea Nitrogen, WBC: White Blood Cell, Hb: Hemoglobin , PLT: Platelet

Urinary system ultrasound showed that the size of the right kidney was measurement was 129x53 mm, and pelvicalyceal ectasia was observed in the middle-lower pole of the right kidney. Renal parenchyma echogenicity increased in both kidneys consistent with grade 1 renal parenchymal disease.

Further examination of rheumatological and oncological markers resulted negative. Rheumatoid factor 14,5 IU/ml(0-18 IU/ml) , ANA(anti nuclear antibody) were negative, Anti ds DNA (anti-double stranded DNA) and ANCA(Anti-neutrophil cytoplasmic antibody) were negative , Complement C3 0,89 g/L(0,75-1,8 g/L) , Complement C4; 0,29 g/L(0,1-0,4 g/L) ,PSA total (prostate specific antigen) 5.13 ng/mL (0-6,5 ng/mL) , PSA free 0,76 ng/mL (0-1,5 ng(mL) , AFP(alpha-fetoprotein) 2,22 ng/mL(0-7 ng/mL) , CEA (carcino embryogenic antigen) 4,92 ng/mL(0-5.5 ng/mL) , CA 125 (cancer antigen) 13,69 U/mL(0-35 U/mL) , CA 15-3 15,01 U/mL (0-25 U/mL) , CA 19-9 22,06 U/ml(0-37 U/mL) ,CA 72-4 1,06 U/mL(0-6,9 U/mL).

After seven days of treatment with hydration and forced diuresis with furosemide (200mg/d), urine amount increased; urea, creatinine levels returned to baseline level. As he needed he was supported with polystyrene sulfonate, calcium carbonate, sodium hydrogen carbonate and allopurinol. Serum creatinine level stabilized between 2,2- 1,5 mg/dl, serum electrolytes level returned to normal level, however kidney function recovered partly (Table I).

During the follow up in the hospital, he had mild leukocytosis (15,000) without an underlying infection. Further laboratory tests; peripheral blood smear, bone marrow biopsy and abdominal CT were recommended but patient refused to do it.

4 months later during the routine control examination, it was noticed that WBC was still increased moderately so a peripheral blood smear was decided to perform.

Peripheral smear results ; band neutrophil :2 , neutrophil :64 (hypersegmented) , lymphocyte :18 , eosinophil : 3 , monocyte : 2 , basophil:6, metamyelocyte :1 ,myelocyte :4 , thrombocyte: increased , morphology of erythrocytes : normochrome, normocyte. This blood smear examination suggested that he might be suffering from chronic myeloid leukemia and patient was referred to the hematology clinic. The results of tests in hematology clinic were as follows:

Bone marrow biopsy performed:
Bone marrow aspiration and biopsy resulted with myeloid hyperplasia without observing blast increase. Bone marrow biopsy was compatible with chronic phase chronic myeloid leukemia. Bone marrow cytogenetic with karyotyping revealed that 46,XY;t(9;22), gene rearrangement of BCR-ABL was 25,1316 IS%(133358 copies/µg RNA) and FISH t(9;22) was detected %100.

He was accepted as Chronic Phase CML.

DISCUSSION

AKI is a frequent complication in oncology (8); In a 7-year Study; the 1-year risk of AKI as defined KDIGO classification was found 17,5% (1). Whereas among the critical ill patient AKI incidence found to be increased up to 54% (2 . AKI in cancer patient is associated with substantial morbidity and mortality. 8 weeks mortality was found 13.6% in AKI with risk category, and 61.7% with AKI in failure category who required dialysis therapy, on the contrary in the same study the patients with no AKI mortality were found 3.8% (7).

There are cancer-related risk factors for the development of AKI in cancer patients (table 2). Invasion of tumor cells to the renal tissue and tumors of the kidney seems to be leading cause of AKI secondary to malignant diseases (1). CML case described here was presented with acute on chronic kidney disease. He had suffered type II Diabetes mellitus for 10 years and prostatic cancer operation two years ago; so he might have previous kidney damage for some degree and the development of malignancy might affect the kidney and cause further damage and ended up anuria and AKI. AKI here may be due to the direct effects of the malignancy, such as with the development of light chain cast nephropathy in patients with multiple myeloma, in addition lysozymuria is another condition causes AKI which rarely may accompany acute promyelocytic leukemia and chronic myelomonocytic leukemia. Lysozymes which are malign cell product, reabsorbed from the proximal tubules and causes cellular damage and AKI (9).

Table 2. Risk factors and etiologies of acute kidney injury in critically ill patients with cancer.

CANCER-RELATED RİSK FACTORS
Neutropenia and resulting sepsis
Hematological cancers
Post-nephrectomy for RCC
Urinary tract obstruction
Post HSCT
Thrombotic microangiopathy
Tumor lysis syndrome
Hypercalcemia
Paraneoplastic glomerular diseases
Chemotherapy toxicities

In the CML-chronic phase, leukemic cells are minimally invasive and their proliferation is largely limited to hematopoietic tissues: mainly blood, bone marrow, spleen and liver. During the blastic phase, not only these areas but also a number of extramedullary tissues, including lymph nodes, skin, soft tissue, and central nervous system, may show leukemic infiltration (10).

However leukemic infiltration of kidney is not unusual finding but in autopsy more often renal dysfunction in CML has been reported to be associated with acute tubular insufficiency or necrosis and hypercalcemic nephropathy (11).

Tumor lysis syndrome (TLS) is an important, frequent cause of AKI, counted among oncologic emergencies, characterized by metabolic abnormalities leading to organ failure (12-15). Furthermore obstructive nephropathy, disseminated intravascular disease, chemotherapy-induced nephrotoxicity were described among the other causes of AKI in malignity's (16).

In this case report, we described the diagnosis of chronic myeloid leukemia of the patient who developed leukocytosis few weeks later following acute kidney injury episode. Patient refused any further examination for example kidney biopsy, otherwise we could have understand better the reason of AKI in this CML cases. But we still found interesting and rare presentation for CML cases, based on the previous reports. As we explained earlier; in this case, all etiological factors for AKI were excluded with some laboratory and radiological tests.

Acute kidney injury preceding leukocytosis was the clinical finding that guided us in this case. We diagnosed CML by peripheral blood smear and bone marrow biopsy. Our case responded quickly to renal support therapy and hydration, within a week we managed the acute kidney injury, but AKI was incompletely recovered because of probable previous kidney damage (diabetes and prostate carsinoma). Unfortunately we could not perform biopsy which might show most accurate result to prove suspected leukemic infiltration.

The mission of this case report is to keep in mind that patients with unexplained etiology presenting with acute kidney injury may have leukemic infiltration of the kidney.

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