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Acute Renal Failure Caused by Blunt Trauma in a Kidney Transplant Recipient

Bulent Unal[1], Uner Kayabas[2], Hulya Taskapan[3], Turgut Piskin[1], Tamer Baysal[4], Basak Kayhan[5]

[1] Division of Kidney Transplantation, Department of General Surgery, Faculty of Medicine, İnönü University, 44100 Malatya, Turkey

[2] Division of Kidney Transplantation, Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, İnönü University, 44100 Malatya, Turkey

[3] Division of Nephrology and Kidney Transplantation, Department of Internal Medicine, Faculty of Medicine, İnönü University, 44100 Malatya, Turkey

[4] Department of Radiology, Dr. Lutfi Kirdar Kartal Education and Research Hospital, 34890 Kartal, İstanbul, Turkey

[5] Department of Medical Biology and Genetics, Faculty of Medicine, İnönü University, 44100 Malatya, Turkey

Abstract

Injuries in renal graft are mostly caused by blunt trauma to the abdomen in any time after transplantation. The response to a trauma depends on the balance between inflammatory and anti-inflammatory mediators. Trauma associated renal failure can be confused with acute humoral/cellular rejection in an allograft recipient. Delay in diagnosis and appropriate treatment can cause loss of graft in those patients. A 27-year-old male patient underwent renal transplantation because of unidentified end-stage renal failure. He was admitted to emergency department with abdominal pain on graft region, hematuria and oliguria. He informed that he fell down on his bottom from tabouret in the bath before onset of the complaints. After observing hematoma in renal pelvis of the transplanted kidney by urinary ultrasonography, an ureteral double J stent was applied. The serum creatinine level continuously increased, anuria was observed and creatinine level rose to 7.9 mg/dL. The patient was treated with pulsed doses of methylprednisolone, anti-thymocyte globulin because of acute allograft rejection with preliminary diagnosis. But both radiological findings of renal allograft and the performed immunological tests excluded the diagnosis of renal acute allograft rejection and confirmed the renal kidney failure due to post-traumatic blood clots in the renal pelvis and ureter of the allograft. Then he was discharged with functional graft through applied medical interventions.The application of basic immunophenotyping protocols together with clinical assessment may help to distinguish rejection from the other situations in renal transplant recipient with acute renal failure following blunt trauma.

Keywords: Kidney injury, kidney transplantation, blunt trauma, immunophenotyping

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Corresponding Author: Basak Kayhan, Department of Medical Biology and Genetics, Faculty of Medicine, İnönü University, 44100 Malatya, Turkey
E-mail: basak.kayhan@inonu.edu.tr **Phone**: +90 4223410660-1264

Introduction

The renal trauma is the cause of 3% of overall admissions to the emergency and as many as 10% of patients who sustain abdominal trauma. Blunt renal trauma is more than penetrating trauma [1]. Renal injuries may be generally divided into 5 groups: contusion or non-expanding subcapsular hematoma, non-expanding peri-renal hematoma, cortical laceration, laceration or vascular injury, shattered kidney [2]. The number of renal transplant recipients is increasingly worldwide. Hence they are admitted to the emergency department for various reasons.

Injury is mostly caused by blunt trauma to the abdomen in any time after renal transplantation. The response to a trauma depends on the balance between inflammatory and anti-inflammatory mediators. The response may be abnormal in patients on immunosuppression. Trauma associated acute allograft rejection suggesting that same inflammatory mediators associated acute traumatic inflammation is usually caused as a result of ischemia due to injury [3-5]. This situation may cause to diagnostic confusion between graft rejection and post renal kidney failure in a traumatized renal transplant recipient.

Unless patients informed the physicians correctly about trauma, post renal kidney failure or allograft rejection caused by trauma can be confused with acute humoral or cellular immune reactions or as inflammatory reactions.

In that report we present the some immunological parameters and clinical assessment of a renal transplant recipient with acute renal failure after blunt trauma with mimicking the clinical features of acute rejection few days after renal transplantation.

Case Report

A 27-year-old male patient underwent renal transplantation 15 days ago because of unidentified end-stage renal failure was admitted to emergency department with abdominal pain on his graft region, hematuria and oliguria. He informed that he fell down on his bottom from tabouret in the bath before onset of the complaints. His previous medical data revealed on dialysis for five months before renal transplantation from living donor with haplotype match in a cold ischemic time of 2h 35 min. The post-operative recovery was completely unremarkable. He was discharged on the fifth day of transplantation surgery with serum

creatinine of 1.8 mg/dL on treatment regimens of tacrolimus, mycophenolate mofetil (MMF), prednisolone, pantoprazole, trimethoprim/sulfamethoxazole, valganciclovir. His temperature was 36.2°C, blood pressure 153/78 mmHg, and pulse rate 92 bpm in emergency department. The patient's physical examination revealed abdominal tenderness on his graft region and pallor of skin and palpebral conjunctiva. Initial laboratory results of the patient were presented in Table 1. Hematoma and a ureteral double J stent were observed in renal pelvis of the transplanted kidney by urinary ultrasonography. The color Doppler ultrasonography of the transplanted kidney demonstrated resistive index more than 1. Then the patient was treated with intravenous pulsed doses of 500 mg of methylprednisolone because of acute allograft rejection for three days and together with hydration and furosemide.

Table 1. Some blood laboratory test results of the patient

Tests	Initial results	Control results*	Normal range
Urea nitrogen (mg/dL)	38	26	8 - 20
Creatinine (mg/dL)	2.08	1.6	0,7 - 1,2
Potassium (mmol/L)	5.2	3.5	3,5 - 5
Hemoglobin (g/dL)	6.3	9.3	13,6 - 17,2
White blood cells (/μL)	13600	5100	4 - 10
IL-1β (pg/mL)	14.7	ND	4.6 ± 0.3**
IL-6 (pg/mL)	12.1	ND	21.1 ± 2.3**
PRA Class-I (%)*	36	0	0
PRA Class-II (%)**	0	0	0
T-Lymphoctye Cross Match**	Negative	ND	Negative
B-Lymphocyte Cross Match**	Negative	ND	Negative

*Two month after the trauma

** The healty controls by the reference 16

ND; Not defined

Although white blood cell count was 34.200/μL at the third day of admission, any source of infection was not detected. Urine and blood culture results were concluded as negative. Moreover double J stent was removed. Following that hypertension observed and immediately perlinganit infusion performed. Since the serum creatinine level continuously

increased, anuria was observed and creatinine level rose to 7.9 mg/dL at fifth day. In order to prevent possible cellular rejection, 150 mg anti-thymocyte globulin (ATG) was given for four days.

Therefore some immunological investigations have been performed to eliminate acute rejection basing on an immunological reaction. Accordingly, class I and class II specific PRAs, T- and B- lymphocyte cross-match tests, serum IL-1β and IL-6 levels have been performed in the fourth day of trauma associated complains (Table 1). Additionally immunophenotyping investigation was performed from peripheral blood lymphocytes in flow cytometer. CD14 positive monocyte (1.5%) population consists 90.3% HLA-DR^+ population. In 0.4% lymphocyte gate none T cells but 70.7% B-cell populations were detected. No detectable amount of activated T cell ($CD3^+$HLA-DR^+) population was observed. Trace amount of Natural killer (NK) ($CD3^-CD16^+56^+$) cell population 1.8% was observed. Beside that there were no detectable amount of NK-T ($CD3^+CD16^+56^+$) cells (Figure 1).

ATG was discontinued for these immunological tests results. Two sessions of plasmapheresis were performed to reduce high serum creatinine level. Human plasma-derived immunoglobulin G has been given 30 g/day at fifth and sixth days. Hemodialysis was firstly performed at sixth day, continued requiring intervals and terminated at sixteenth day. Since hematoma at renal pelvis and ureteric stenosis due to coagulated blood, ultrasonography-guided nephrostomy catheter has been inserted into the pelvis of the transplanted kidney to drain the urine and hematoma at sixth day. Abdominal computed tomography (CT) was performed at eleventh day for persisting hematuria, anuria and hematoma (Figure 2). The antegrade pyelogram revealed incomplete filling of the pelvicalyceal system with contrast material. This was consistent with the presence of blood clots in the pelvicalyceal system and the ureter (Figure 3).

The diuresis began at nineteenth day. Meanwhile surgical site infection occurred at nephrostomy tube insertion site. Therefore meropenem and teicoplanin were administrated for seven days. Nephrostomy was terminated at twentieth day, hematuria was observed shortly after and then ureteral catheter was applied to wash the bladder with saline for four days. Totally 15 unites of leukocyte depleted erythrocyte and 12 unites of fresh frozen plasma were transfused overall hospitalization period. Patient was discharged with no complains and

functional graft on tacrolimus, MMF, prednisolone, pantoprazole, trimethoprim/sulfamethoxazole, valganciclovir, doxazosine, amlodipine, carvedilol at twenty-fifth day.

In the third year of transplantation, the patient is in well condition and last hemoglobin, blood urea nitrogen (BUN) and creatinine levels were 13.5 g/dL, 14 mg/dL and 1.4 mg/dL, respectively.

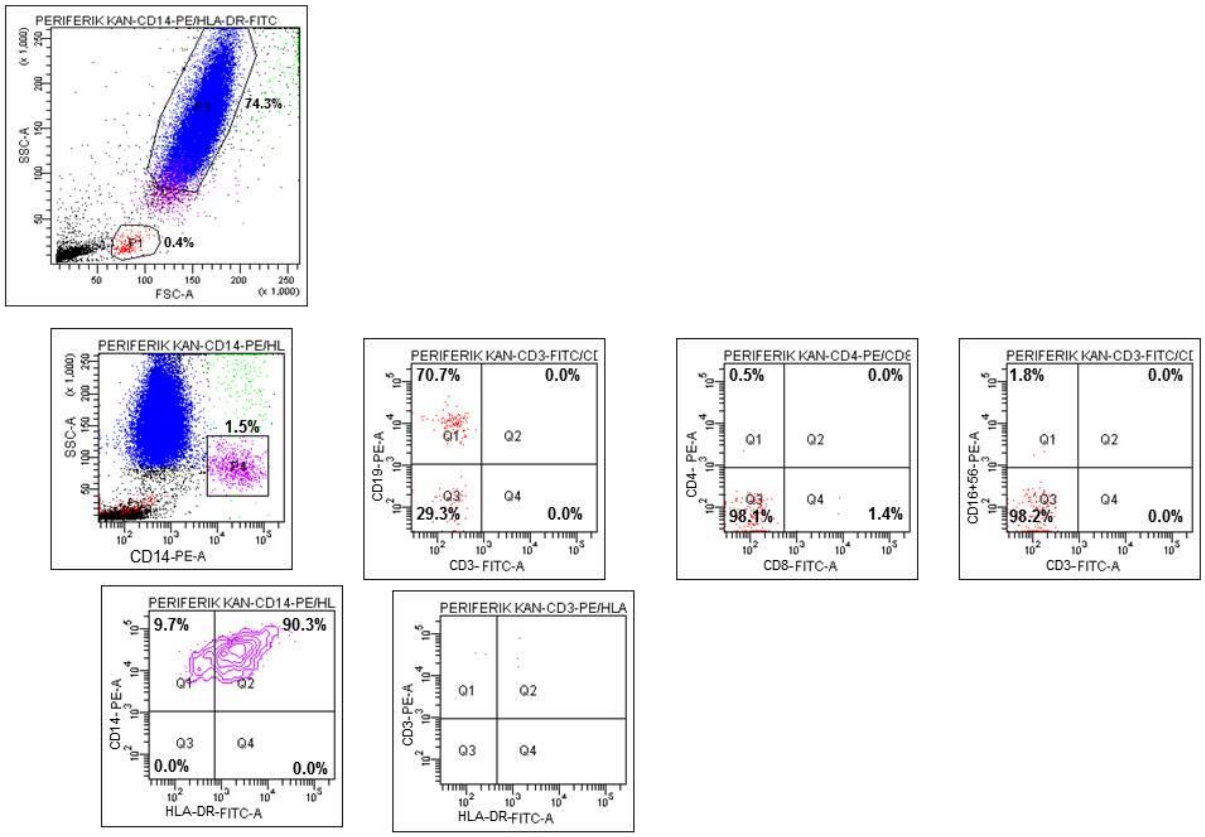

Figure 1. Immunophenotype profile of the patient with trauma associated post renal kidney failure after four days of trauma. P1; represents the gate of lymphocytes, P3; represents the gate of granulocytes and P4; represents the gate of monocytes.

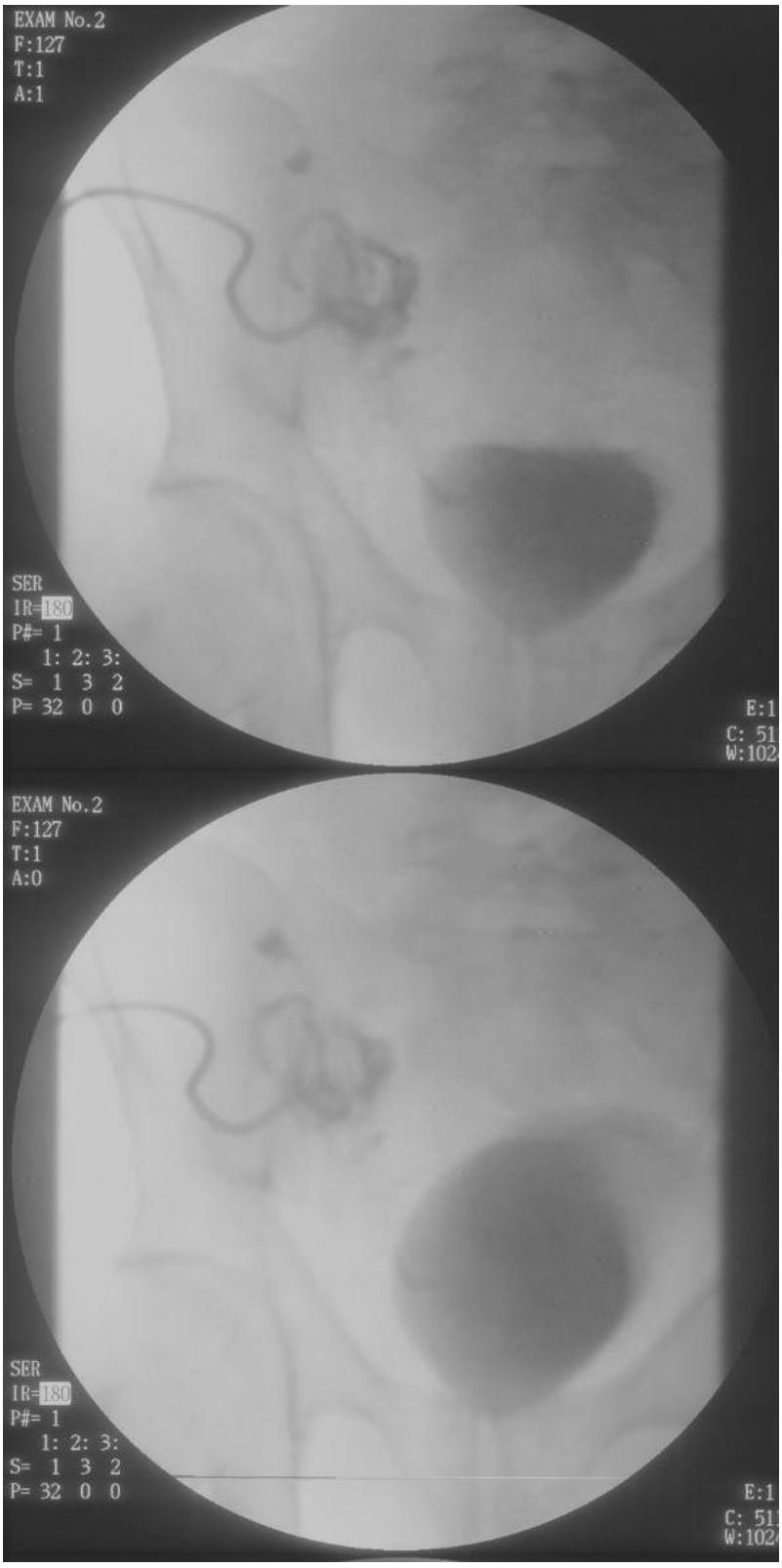

Figure 2. An 8 F nephrostomy catheter (arrowheads) was inserted into the pelvis of the transplanted kidney under US and CT guidance. The CT revealed hyperdense material in the pelvis of the transplanted kidney indicating hemorrhage (arrow).

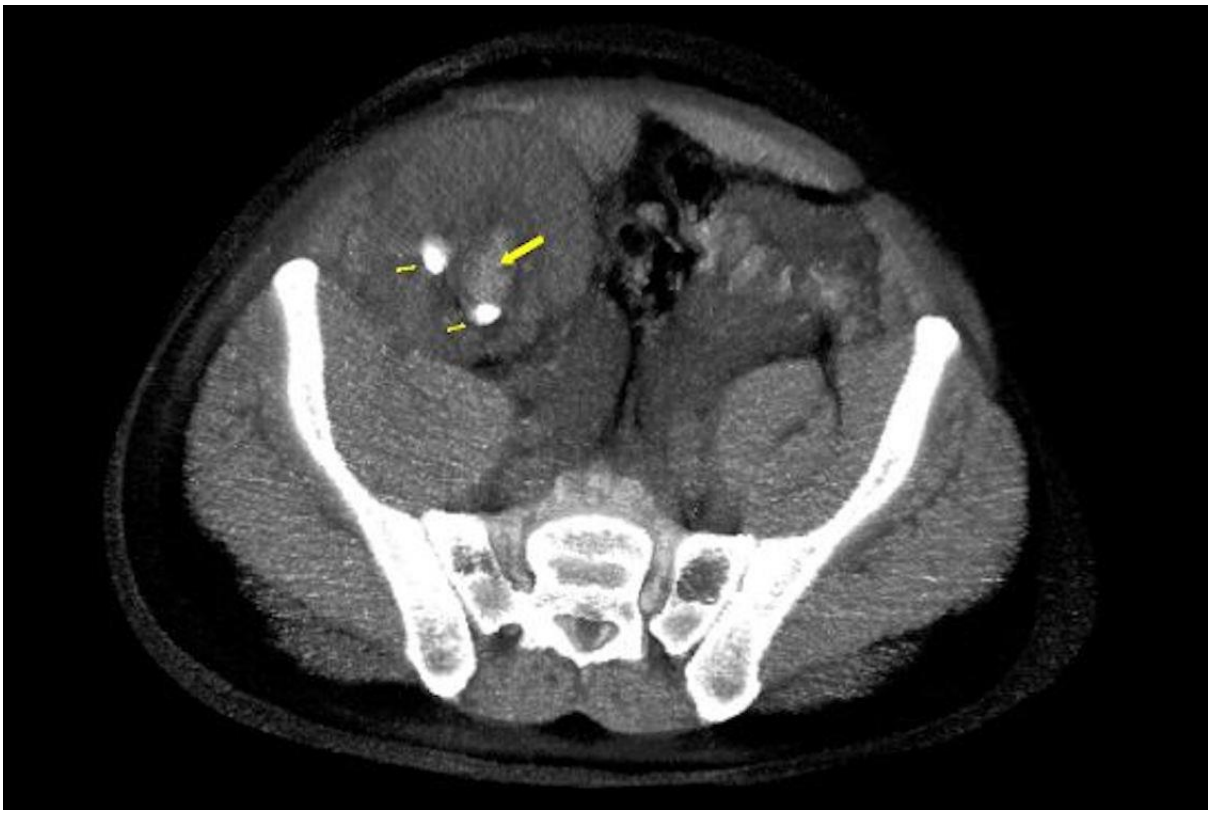

Figure 3. The antegrade pyelogram revealed incomplete filling of the pelvicalyceal system with contrast material. This was consistent with the presence of blood clots in the pelvicalyceal system and the ureter.

Discussion

Acute kidney injury is associated with a high mortality rates range between 25% and 80% depending on the cause and the clinical status of the patient. These data highlight the importance of recognition and appropriate management, usually in collaboration with nephrologists, urologists and other subspecialists. Postrenal kidney failure is caused by obstruction of urine flow. It is divided into extrarenal and intrarenal obstruction. Prompt diagnosis followed by early relief of obstruction is associated with improvement in renal function in most patients [6].

Some transplanted patients experienced posttraumatic rejection episodes, suggesting that same inflammatory mediators associated with acute traumatic inflammation may lead to allograft rejection. This situation may cause to diagnostic confusion between postrenal kidney failure and traumatic allograft rejection [5].

Direct injuries to the renal parenchyma or the urinary bladder may affect the transplanted kidney as it is placed in a retroperitoneal position in the anterior pelvis and unlike native kidney is fixed to that position by a thick fibrosis capsule after transplantation [4]. In our case, patient fell down from the taubouret during bath, and then a massive parenchymal bleeding developed in transplanted renal pelvis. Therefore we believe that showering in the standing position can be preventive for the solid organ transplant recipients.

As informed in previous studies surgical management of an injured transplanted kidney can be limited. A very short vascular pedicle and ureter, dense scarring, and a fibrous capsule may prevent any attempts at the direct repair of parenchymal, collecting system, and vascular pedicle injuries in a transplanted kidney. More treatable ones are nonexpanding hematomas and minor parenchymal injuries that can be managed non-operatively with adequate hydration and observation. More seriously, massive hemorrhage or severely traumatized renal parenchyma can develop and those may require exploration with debridement and drainage or simply a subcapsular nephrectomy [4]. In our case bleeding at renal pelvis caused by a blunt trauma was observed and approached with draining of hematoma by nephrostomy and adequate hydration applications performed.

Since all allogeneic transplants are serious procedures; immunomonitoring of transplant patients is crucial before and after transplantation to prevent graft loss caused by any kind of rejection initiated by a reaction or infection. Immunomonitoring is performed by several methods such as immunophenotyping, intracellular cytokine staining, cytokine levels and expression levels of them, ATP levels of $CD4^+$ T cells and several genomic microarrays [5, 7-9]. However, the correct diagnosis should be done in a short time period, to prevent injury of the graft. In some cases, distinguishing an immune response based acute rejection from inflammation or any kind of trauma could be hard, as the symptoms would direct the clinician toward to pathological investigations, which could be damaging the graft. In the literature, there are 10 distinct cases related to preservation of renal grafts after injury. Playing squash and football, an accident, falling and even coughing while asleep were reported as the major causes of that trauma associated renal graft injuries. Interestingly; all of them have different symptoms with less sign of differential diagnosis. More than that; serum creatinine levels were not elevating in some of those events. Eventually; either pathological investigations or surgical applications were usually preferred in that cases [10-12].

In the presented case, several investigations were performed for trauma, allograft rejection or infection. Both ultrasonography findings of renal allograft and the performed immunological tests guided to exclude the renal acute allograft rejection and to confirm the postrenal kidney failure due to post-traumatic blood clots in the renal pelvis and ureter of the allograft.

Unlike other trauma associated renal graft injury in a renal transplant recipient in the literature, some immunological parameters in a blunt trauma associated post renal kidney failure caused by bleeding are presented first time in that report. The most interesting observation was no detectable $CD3^+$ T cells and regarding that non-activated T cells ($CD3^+$HLA-DR^+) in peripheral blood samples of that patient. Concurrently, trace amount of $CD4^+$ and $CD8^+$ T cells in peripheral blood of trauma case notice a reaction not related with cellular rejection which could be a sign to differ acute rejection and trauma associated renal graft injury. By the help of that data and new information about blunt trauma provided by the patient, we decided to stop ATG administration. Trace amount NK and NK-T T cells sign us non-activated innate immune response in that case. On the other hand, we observed that $CD14^+$ monocyte population close toward to inflammatory response with high amount of $CD14^+$HLA-DR^+ monocytes (90.3%), which actively routes inflammatory response in contrast to $CD14^+$HLA-$DR^{low/negative}$ immune suppressive monocyte population. The expression of major histocompatibility complex (MHC) class II on monocytes is a prerequisite for effective antigen presentation to $CD4^+$ T cells, an important component of the inflammatory immune response. Another point is high $CD14^+$ and $CD14^+$HLA-DR^+ population in trauma case sign us an infection or an elevation on migration of cells after a serious trauma since $CD14^+$HLA-DR^+ cells resembles migratory $CD14^+$ cells in peripheral blood [13].

Pro-inflammatory cytokine IL-1β increases the expression of adhesion molecules such as vascular cell adhesion molecule 1 on endothelial cells. One of the property of IL-1β is promoting the infiltration of inflammatory and immunocompetent cells from the circulation into the extravascular space and then into the tissue. Additionally it is known that IL-1β plays role in blood vessel formation [14]. Accordingly, serum IL-1β and IL-6 levels of the patient were higher than healthy subjects [15]. We believe that elevation of IL-1β together with IL-6 is related with a tissue repairing in that case. Concerning that; elevation of those cytokine

levels allows the migration of monocytes to trauma site by increasing expression of adhesion molecules.

The application of basic immunophenotyping protocols from peripheral blood samples in transplant recipients may help to understand the clinicians for separately rejection from the other situations in a renal transplant recipient with acute renal failure following blunt trauma.

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