Histopathologic Findings of Potential Kidney Donors With Asymptomatic Microscopic Hematuria: Impact on Donation

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ABSTRACT

Introduction. Isolated microscopic hematuria (IMH) is not uncommon in potential kidney donors.

Aim. The aim was to study the kidney biopsy findings of potential kidney donors with IMH and the impact of the histopathologic diagnoses on the decision to accept or decline such donors from kidney donation.

Methods. In this retrospective study, all the potential kidney donors with IMH were identified from the medical records of patients who underwent kidney biopsies between January 2010 and December 2016.

Results. Forty-five such individuals were identified. The mean age of these potential donors was 32.6 years and 76% were male. All of them had normal blood pressure and no significant proteinuria. Seventeen (38%) biopsies showed histopathologic abnormalities; thin basement membrane disease (n = 13; 28%) was the most common cause followed by immunoglobulin (Ig)A nephropathy (n = 4; 9%). Donors with abnormal biopsy findings were excluded from donation. However, 62% of the potential donors had normal kidney biopsy findings and were accepted for kidney donation.

Conclusion. IMH justifies extensive work-up including kidney biopsy to identify donors who may have underlying significant glomerular pathology excluding them from kidney donation. On the other hand, kidney biopsy also helps in accepting the donors if it does not show significant abnormality.

THERE is a great imbalance in the demand and supply of organs for patients with end-stage renal disease (ESRD) and this disparity puts a significant burden on transplantation programs [1]. Acceptance of kidneys from expanded criteria donors and attempts to increase living donation are some of the measure to increase the donor pool. Moreover, living kidney donation constitutes a major source of organs in countries where deceased donor programs are not well established. Recent studies have raised concerns about the long-term outcomes of kidney donors [2,3]. Hence, it is very important to select kidney donors carefully to minimize future health risks. It is also important not to decline living donors from kidney donation if the underlying condition (eg, benign hematuria) poses no significant harm.

Isolated microscopic hematuria (IMH) is a common finding in the general population [4,5], hence many potential kidney donors are also detected to have hematuria on urinalysis. Some centers exclude donors with IMH, whereas others may accept such donors [6]. IMH may be indicative of underlying glomerular pathology, especially if urologic causes of hematuria have been excluded [7]. These potential kidney donors require a full work-up for IMH, which includes

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radiological and urologic investigations as well as kidney biopsy. Kidney biopsy for donors with IMH was reported to be important in identifying underlying glomerular lesions, such as thin basement membrane nephropathy (TBMN) and immunoglobulin (Ig)A nephropathy (IgAN) [7,8].

Previous studies have shown that glomerular abnormalities are common in prospective kidney donors with IMH [7,8]. However, Koushik et al included only 10 patients in their study, 4 patients were detected to have TBMN and 1 patient was diagnosed with IgAN [7]. In another study, 14 potential kidney donors underwent kidney biopsy and all biopsy specimens showed pathological abnormalities [8]. In this study, patients with TBMN, mild mesangial abnormalities, and nonspecific interstitial changes were accepted for kidney donation [8]. Controversy exists about subjecting these potential kidney donors to invasive procedures and accepting them for kidney donation in the presence or absence of pathological abnormalities [9,10].

We perform around 180 kidney transplantations in our hospital each year and around 80% of transplants are from living donors. Potential donors are thoroughly investigated for IMH and if the cause of hematuria remains unclear with noninvasive tests, cystoscopy and kidney biopsy are offered prior to accepting them for kidney donation.

In this study we aimed to review the kidney biopsy findings of potential kidney donors with IMH and its impact on decision making for accepting or declining such donors from kidney donation.

METHODS

We perform around 180 kidney transplantations every year; around 80% of transplants are carried out from living donors. Donors older than the age of 18 years are considered for donation.

In this retrospective study, all the potential kidney donors with isolated hematuria (IMH) were identified from the medical records of patients who underwent kidney biopsies between January 2010 and December 2016. Routine laboratory tests were performed including complete blood count, renal profile, hepatic profile, urine culture, and metabolic screen for kidney stones. Urine dipstick test (Uriflet^{tm}S9ha, Arkray, Minneapolis USA, Inc.) was read by an automated dipstick reader (Arkray Aution Hybrid AU- 4050, USA). The test for hematuria was considered positive if it was read as 1+ or more. Microscopic urine analysis was performed to confirm the presence of hematuria; 5 or more red blood cells per high power field in the urinary sediment were considered positive. Urine tests were repeated on at least two samples separated by at least 1-month duration [11].

Quantitative evaluation of 24-hour urine for proteinuria was performed at two different occasions. Proteinuria was defined as urine protein excretion of $\geq$150 mg/d. Urine albumin creatinine ratio (UACR) was concurrently done and UACR of $>$2 mg/mmol in men or $>$2.8 mg/mmol in women was considered abnormal [12]. Computed tomography (CT) renal angiogram and cystoscopy were done to rule out anatomic lesions in the urinary tract.

Potential donors with albuminuria, proteinuria, and renal stones were excluded from the study.

Ultrasound-guided percutaneous native kidney biopsy was performed and the kidney tissue was divided in three parts. One piece was fixed in 10% formalin, paraffin blocks were made, sections were stained with hematoxylin-eosin (H&E), Masson's trichrome, periodic acid Schiff (PAS), and Congo-red, and were examined using light microscopy. The second piece was snap frozen and examined using immunofluorescence. The third piece of the kidney tissue was fixed in 4% phosphate buffer; semi-thin and ultra-thin sections were prepared. Tissue micrographs were produced and examined under electron microscopy. IgAN was diagnosed on the basis of light microscopy and the immunofluorescence findings. TBMN was diagnosed if there was diffuse uniform thinning of the glomerular capillary basement membrane to $<$200 nm and absence of any other glomerular pathology [13].

Ethical Considerations

This study was approved by the local ethics committee. The study was carried out in accordance with the ethical standards of the Declaration of Helsinki and the Declaration of Istanbul. Due to its retrospective observational design, the need for informed consent was waived.

Statistical Analysis

Data were described as mean $\pm$ standard deviation ($\pm$ SD). Frequencies and percentages were reported where appropriate. Comparison of numerical variables between the study groups was done using unpaired t test for independent samples. P values $<$.05 were considered statistically significant.

RESULTS

A total of 45 donors underwent kidney biopsy for IMH. Of these, 33 (73%) were males and 32 (71%) were genetically related to their recipients. Their mean age at the time of evaluation was 32.6 $\pm$ 8 years (range, 23–53 years). All these potential donors had normal blood pressure and their mean Cystatin C estimated glomerular filtration rate (eGFR) was121 $\pm$ 11.7 mL/min/1.73 m^2 (range, 97–147). The mean serum creatinine level was 77.2 $\pm$ 12.3 μmol/L.

A total of 28 (62%) donors had normal findings on the kidney biopsy and were accepted for kidney donation. However, 17 (38%) donors were found to have histopathologic abnormalities on the kidney biopsy. TBMN was the most common abnormality found in 13 potential donors (29%) and IgAN was diagnosed in 4 patients (9%).

Characteristics of donors with normal and abnormal biopsy findings are shown in Table 1. There were no significant differences between the two groups in regard to mean age, body mass index, blood pressure, serum creatinine, and UACR (Table 1).

DISCUSSION

The present study has included the largest number of kidney donors who underwent kidney biopsy for IMH. We have shown that about 38% of potential kidney donors with isolated IMH had significant pathological lesions on kidney biopsy, which excluded them from donation. However, in 62% of the potential donors radiological/urologic investigations and kidney biopsy failed to reveal any abnormality and these individuals were accepted for kidney donation. It is thus important to perform kidney biopsy