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Case Report

Renal graft biopsy assists diagnosis and treatment of renal allograft dysfunction after kidney transplantation: a report of 106 cases

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Abstract: Acute antibody mediated rejection (AMR) is one of the most important complications after kidney transplantation. Renal graft biopsy is safe and reliable without adverse effects on the patients and transplanted kidneys, which was of great instructive significance in diagnosis and treatment of renal allograft dysfunction after renal transplantation. This paper reported a case series of 106 patients underwent renal allograft biopsies. All biopsies were evaluated according to the Banff 2007 schema. 52 examples were obtained within 1 month after transplantation, and there were another 20 examples in one to two months and other 34 examples in two to three months. Appropriate therapy was applied and clinical outcomes were observed. All patients received renal biopsies and anti-inflammatory and hemostasis treatment without complications. There were 2 cases of hyperacute rejection, and 15 cases of acute AMR. All Paraffin-embedded samples were stained by HE, periodic acid-Schiff (PAS), Masson, and immunohistochemistry (C4d, cd20, cd45RO, SV40). All samples were found C4d immunohistochemical staining positive. Patients with acute AMR were managed by steroid intravenous pulse therapy, Rabbit anti-thymocyte globulin intravenous pulse therapy, anti CD20 monoclonal antibody intravenous therapy and so on. Two cases of hyperacute rejection had renal failure, and received kidney excision; 12 cases in 15 cases of AMR recovered, another 2 cases did not recover with high-level creatine, and other 2 cases of renal allograft received excision.

Keywords: Kidney transplantation, renal insufficiency, renal biopsy, perioperative period

Background

Recently, the success rate of renal transplantation has increased significantly due to the standardized procedure, novel immunosuppressor and improved management of perioperative period. Acute antibody-mediated rejection (AMR), characterized with hormone resistance and refractory, is one of the most common and severe complications jeopardizing the long term survival of the patients after renal transplantation [1, 2]. It is reported that allograft biopsy played an important role in early predicting AMR and guiding treatment, which promoted the long term survival rate of grafts [3].

Case report

A total of 106 patients who underwent renal transplantation between January 2008 and June 2013 in our transplantation institute were included in this study. There were 77 male and 29 female patients with an average age of 38.8 (ranged from 25-60) years old. Among the 106 patients, there were 52 cases undergoing biopsy due to renal insufficiency within 1 month after the transplantation, another 20 cases receiving biopsy within 1-2 months and other 34 cases within 2-3 months.

Routine examinations including clotting time, blood platelet count, liver function test and kidney function test were conducted before renal biopsy. Color Doppler ultrasound (CDU) was employed to guide the renal biopsy. All procedures and potential risks were explained thoroughly to the patients and consent forms were signed before biopsy.

The indications of renal biopsy including: 1) continuous anuria and oliguria; 2) serum creatinine keeps increasing or stabilizes above nor-

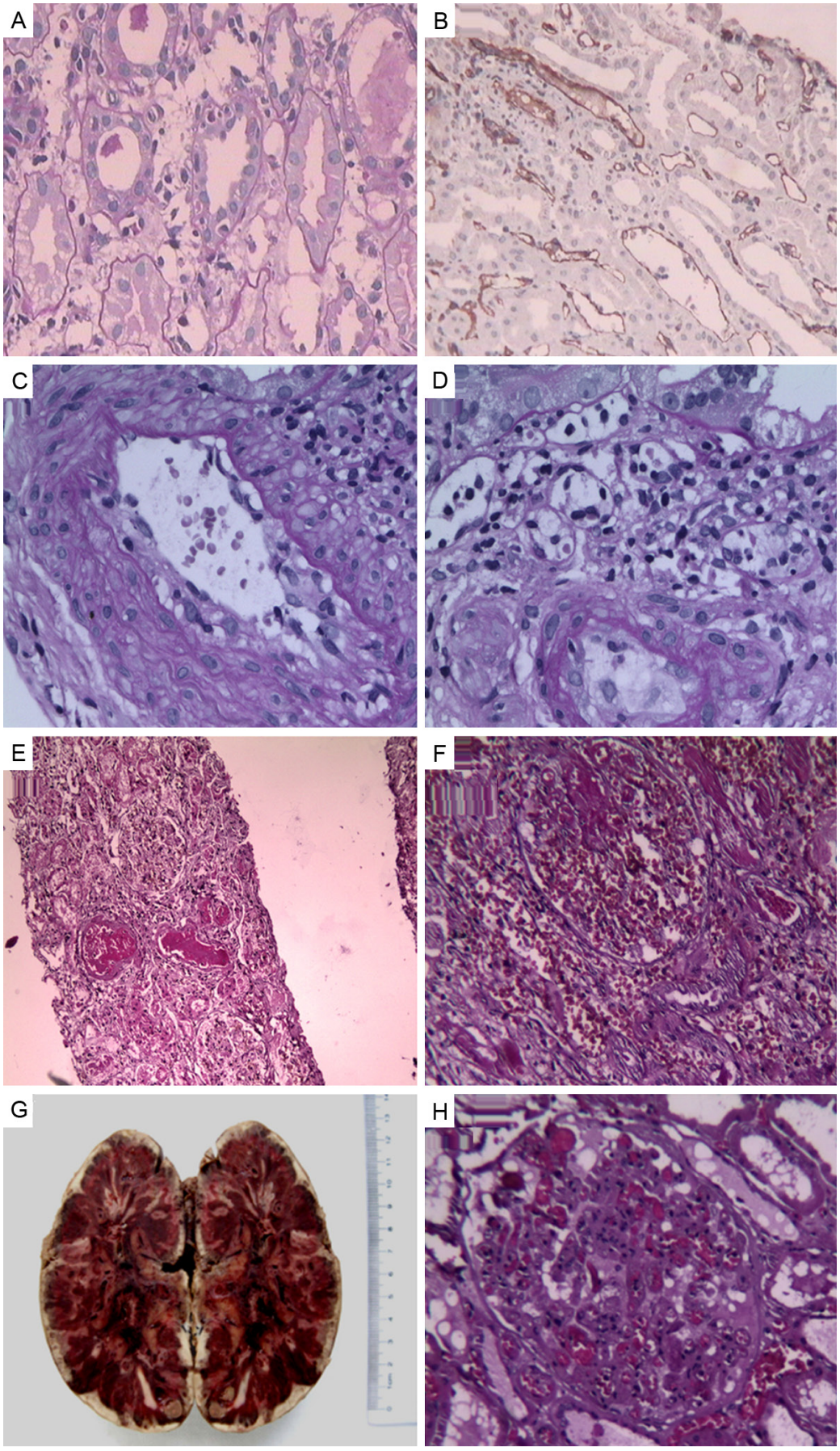
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Figure 1. A, B: Grade I, acute renal tubular necrosis-C4d+, minimal inflammation; A: PAS staining × 200; B: c4d positive, × 200; C, D: Grade II, peritubular capillary inflammatory cells deposition, PAS staining, × 400; E, F: Grade III, transmural arteritis and media smooth muscle layer necrosis, or arterial wall fibrinoid necrosis; E: HE, × 100; F: HE, × 200; G, H: Hyperacute rejection reaction: polymorphonuclear leukocyte sedimentation and microthrombus in glomerular capillary and tubular capillary; G: Resected transplanted kidney; H: HE, × 400.

mal level during regular reexamination; 3) recurrent and unexplained abnormal renal function; 4) increasing blood pressure or persistence of albuminuria and hematuria [3]. The patients were in supine position, so that the transplanted kidney could be easily reached. The skin over the biopsy site was sterilized. After that, local anesthetics were injected into the skin, through the subcutaneous tissue and down to and around the kidney. Under the guidance of CDU, Band biopsy needle was inserted at an angle of 60° into lower renal pole with a depth of 2.2 cm to obtain the tissue sample. The same puncture process was repeated twice regularly. Firm pressure was then applied to the biopsy site until the bleeding has stopped, and a sterile bandage was applied. The kidney tissue samples were sent to the lab for examination, and the patients were under observation of heart rate, blood pressure, urine out, urine color and so on. Hemostatics and antibiotics might be administrated when necessary.

Pathological examinations were conducted by two independent senior pathologists. The obtained biopsy samples were quickly put into the formaldehyde solution. Samples were observed whether they were useless tissue like perirenal fat, and there might be another puncture at a different site if necessary. All patients were excluded with the prerenal, postrenal and infectious etiology. All Paraffin-embedded samples were stained by HE, periodic acid-Schiff (PAS), Masson, and immunohistochemistry (C4d, cd20, cd45RO, SV40). Microscope was used to observe the pathological changes, and samples suspected with rejection reaction would be classified according to the Banff 2007 schema.

Of all the 106 patients, there were 2 cases of hyperacute rejection, and 15 cases of acute AMR. All samples were found C4d immunohistochemical staining positive (**Figure 1**). Among 15 cases of acute AMR, there were 10 cases of grade I. Acute renal tubular necrosis was observed with minimal inflammation (**Figure 1A**, **1B**). By PAS staining, the glomeruli appeared bright red in contrast to the surrounding parenchyma (**Figure 1A**). By immunohistochemical staining, C4d positive cells were observed in grade I cases (**Figure 1B**). In addition, there were 3 cases of grade II. By PAS staining, deposition was observed in peritubular capillary inflammatory cells (**Figure 1C**, **1D**). Moreover, there were 2 cases of grade III. Transmural arteritis and media smooth muscle layer necrosis, and arterial wall fibrinoid necrosis were observed by HE staining (**Figure 1E**, **1F**). Kidney excision was performed in renal failure caused by hyperacute rejection (**Figure 1G**). In hyperacute rejection reaction, polymorphonuclear leukocytes, sedimentation and microthrombus were observed in the glomerular capillary and tubular capillary by HE staining (**Figure 1H**).

Patients with acute AMR would be managed by steroid intravenous pulse therapy, Rabbit antithymocyte globulin intravenous pulse therapy, anti CD20 monoclonal antibody intravenous therapy and so on. Two cases of hyperacute rejection had renal failure, and received kidney excision; 12 cases in 15 cases of AMR recovered, another 2 cases did not recover with high-level creatine, and other 2 cases of renal allograft received excision.

Comment

Perioperative period is the duration of a patient's surgical procedure including ward admission, anesthesia, surgery, and recovery, which generally refers to the three phases of surgery: preoperative, intraoperative, and postoperative [4]. As for different surgeries, perioperative periods may vary. We define the perioperative period of renal transplantation as the duration from the surgery date to 3 months after operation. AMR was defined as the triad involving presence of donor-specific antibody, positive C4d-staining on biopsy, and histopathological evidence of antibody-mediated injury (glomerulitis, peritubular capillaritis or arteritis) [5].

Acute AMR is a common cause of renal failure during perioperative period after transplantation, which, however, is very difficult to diag-

nose in clinic. Renal biopsy is one of the main means to diagnose in current practice. The interaction and communication between the physician and pathologist play an important role in renal biopsy. Several common reasons of the biopsy restrictions includes: 1) renal allograft biopsy is an invasive procedure with the risk of bleeding, hematoma, gross hematuria, and even the renal ruptures; 2) it will take 3-5 days to conduct the pathological analysis, which may delay the best treatment time; 3) many transplantation surgeons analyze the state of diseases by their own experience. Recently, the complications of renal biopsy have been reduced significantly due to the improvement of biopsy procedures and the guidance of ultrasound. Unlike the routine pathological analysis, the pathological analysis of allograft is easier to handle, which has been reduced to 4-5 hours. Sometimes transplantation surgeons failed to make a definite diagnosis, so the pathological diagnosis is the "gold standard" [6-8].

However, renal allograft biopsy is not without limitations. Firstly, biopsy fails to predict early diagnosis, because it is normally conducted after the presentations of clinical manifestations. Secondly, it is not routine to conduct biopsy to all patients after renal transplantation, because it is an invasive procedure with potential complications. Patients may also reject biopsy due to economic issues. Last but not least, biopsy sample is just one part of the allograft, which may cause bias of diagnosis because it cannot present the pathogenesis of the whole kidney [9-11].

The noninvasive diagnosis of renal allograft is one of the main directions of transplantation field recently due to the introduction and development of novel technologies. The purpose of noninvasive diagnosis is not just replacing the renal biopsy in discerning AMR, but also predicting the transplantation risks based on different genetic background and individualizing the immunosuppressor therapies [12-14].

In these large case series, renal allograft biopsy was performed in 106 patients after kidney transplantation. By renal allograft biopsy, 2 cases of hyperacute rejection, and 15 cases of acute AMR were detected. By HE staining, kidney structures with observation of acute renal tubular necrosis with minimal inflammation were classified as grade I of acute AMR (10 cases), of deposition in peritubular capillary inflammatory cells were classified as grade II of acute AMR (3 cases), of transmural arteritis and media smooth muscle layer necrosis, and arterial wall fibrinoid necrosis were classified as grade III of acute AMR (2 cases), of polymorphonuclear leukocytes, sedimentation and microthrombus in the glomerular capillary and tubular capillary were classified as hyperacute rejection (2 cases). By PAS staining, the glomeruli appeared bright red in contrast to the surrounding parenchyma, which highlighted the structure of basement membranes of glomeruli. By immunohistochemical staining, C4d positive cells were detected in both acute AMR and hyperacute rejection samples, which indicated antibody mediated rejection responses after kidney transplantation.

Acute AMR is one of the most significant complications of renal transplantation during perioperative period, which is also one of the main causes of allograft insufficiency. Renal graft biopsy is safe and reliable without adverse effects on the patients and transplanted kidneys, which was of great instructive significance in diagnosis and treatment of renal allograft dysfunction after renal transplantation.

Disclosure of conflict of interest

None.

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