

Importance of a Renal Biopsy

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INTRODUCTION

The definitive diagnostic tool in many renal diseases is a renal biopsy, when performed well. Traditionally, it is done safely percutaneously under local anaesthesia with a biopsy needle and with ultrasound or computed tomography (CT) guidance (1, 2). It can be performed surgically as an open biopsy (3) under general anaesthesia and by the transjugular route (4). Kidney biopsy can also be performed laparoscopically. This involves using an endoscope to explore the abdomen and the biopsy needle is inserted through the laparoscope and guided to the kidney with ultrasound. A renal biopsy should be performed after careful evaluation by the nephrologist. Early initiation of therapy is essential in preserving renal function and preventing further damage to the kidney. The potential complications include gross haematuria, haematoma, infection and arteriovenous fistula. These complications may require surgical intervention. A renal biopsy helps to establish and confirm a suspected diagnosis (5) and may aid in determining the mechanism of disease, whether antibody or complement mediated, and thereby assists in determining disease-specific therapy.

It provides useful prognostic information on the degree of glomerular, vascular and tubulo-interstitial involvements and can also help in determining the effectiveness of recommended therapy, or when treatment is futile. In addition, it aids in assessing genetic diseases along with genetic testing, for example in familial focal segmental glomerulosclerosis (FSGS) and familial nephrotic syndrome. The degree of acute or chronic changes can be ascertained from the histological report (5, 6). Renal biopsy is an important diagnostic tool in the evaluation and management of individuals post kidney transplant and may be performed based on the clinical situation *eg* acute graft rejection or protocol biopsy (7 – 10).

The nephro-pathologist report includes the number of glomeruli in the specimen, the description of kidney specimen by light microscopy, immunofluorescence staining pattern and electron microscopy (11). It is important to recognise the fact that the histopathology report can be affected by the number of glomeruli in a biopsy specimen, particularly in lesions that are focal in nature. The relevant clinical history,

physical examination and laboratory investigation should be considered in determining the nature of the kidney disease. It is therefore important that a thorough history and physical examination be carried out so as to tailor laboratory investigations prior to embarking on the renal biopsy. Therefore, the pertinent clinical presentation, work-up and results should be made available to the nephro-pathologist in order to aid in the conduct of a pathological diagnosis.

INDICATIONS

Proteinuria, haematuria and renal failure are the commonest indications for renal biopsy (12–16). The nephrotic syndrome is a common reason for kidney biopsy in adults and when it is associated with an atypical presentation in children (13). Kidney biopsy is indicated in patients who present with acute renal failure with abnormal urinary sediments, proteinuria, positive antinuclear antibody (ANA), positive anticytoplasmic antibody (ANCA), positive antiglomerular basement antibody (anti-GBM), severe hypertension and prolonged unexplained recovery. Biopsy is indicated in chronic renal failure with proteinuria and dysmorphic haematuria with normal sized kidneys and echopattern. A biopsy is useful when deciding on initiating therapy and measuring response to therapy in known renal diseases *eg* lupus nephritis (LN), HIV associated nephropathy (HIVAN) and focal and segmental glomerulosclerosis (FSGS). A kidney biopsy should be performed in persons with known renal diagnosis with normal kidney sizes and unexplained worsening proteinuria and glomerular filtration rate (GFR).

In many instances, a kidney biopsy is helpful in diagnosing systemic diseases such as primary vasculitis, amyloidosis and as part of the diagnostic criteria in multiple myeloma. Kidney biopsy is also useful in post-transplant cases that present with suspected acute rejection, recurrent disease, proteinuria and worsening renal function. A protocol renal biopsy is advocated after renal transplant by some authorities due to the high incidence of subclinical acute rejection (4 – 6).

BIOPSY PROCEDURE

Biopsies performed at the University Hospital of the West Indies (UHWI), Mona, are done as an inpatient procedure under ultrasound guidance, and in almost all the cases by the nephrologist or a renal resident under supervision of the nephrologist and when indicated by the radiologist under ultrasound or CT guidance. An open kidney biopsy is rarely

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indicated. They are done using a spring-loaded 18– or 20-gauge, 15 cm length or 9 cm (for paediatric), 10 to 20T, automated biopsy needle. Percutaneous kidney biopsy is performed under real-time ultrasound-guidance. Open kidney or transjugular kidney biopsy are options to percutaneous biopsy. Transjugular kidney biopsy provides a histological diagnosis in high-risk patients, making an important contribution to patient management (4).

During the biopsy procedure, review of the biopsy specimen by microscopy in the biopsy room should be carried out to ensure that there is cortical tissue and adequate number of glomeruli. This manoeuvre will reduce cases where a diagnosis cannot be made because of inadequate sample. Outpatients are admitted the same day of biopsy after being evaluated properly as outpatients. Inpatients are evaluated likewise and decision made regarding the timing of renal biopsy. Renal biopsy is followed by 24-hour bed rest. The patient lies supine for 8 to 24 hours. Some nephrologists advocate a 24-hour recovery period. Post biopsy, patients are monitored with serial vital sign recordings according to protocol and observed for macroscopic haematuria, abdominal pain out of proportion, abdominal distention and also importantly elevated blood pressure out of keeping with the patient's clinical status. This should be taken as the first sign of clinically significant sub-nephric haematoma/ haemorrhage and warrants an urgent ultrasound and urology consultation.

CLINICAL EVALUATION

Patients with glomerular disease may be asymptomatic or may present with manifestations ranging from minimal findings to full-blown nephrotic or nephritic syndrome. Others present with symptoms of the systemic disease for example Systemic Lupus Erythematosus (SLE), diabetic microvascular complication or medium or small vessel vasculitis. In the paediatric population, the classic presentation of the nephritic syndrome of "Pepsi" coloured urine following a bout of sore throat or skin infection two weeks previously is well known and thus does not usually warrant a kidney biopsy. Other examples that do not warrant a kidney biopsy is haematuria immediately following an intercurrent infection, as may occur in IgA nephropathy. Patients with rapidly progressive glomerular disease present with rapid onset of renal failure over days or weeks with haematuria (RBC casts) and proteinuria. Patients with chronic glomerulonephritis usually present with hypertension, renal insufficiency and proteinuria.

Laboratory investigations should be geared towards confirming the suspicion of renal impairment, establishing the extent of renal failure, identifying likely causes and other co-morbidities present. A urine analysis with microscopic evaluation should be performed looking for active urinary sediments. A 24-hour urine collection or timed collection or spot urine for protein quantification should also be carried out and serology done to identify an underlying cause. Other

laboratory indications include erythrocyte sedimentation rate, C-reactive protein, serum complement levels and immunological testing in order to determine underlying cause, treatment and prognostic evaluations. Renal imaging is of paramount importance. Ultrasonography of the kidneys is important to evaluate size (17), echopattern and cortico-medullary differentiation, which may indicate chronicity and helps decision to biopsy. Reversible causes for renal failure can also be quickly ruled-out, *eg* obstructive uropathy. Renal scan is valuable in evaluating for renal artery stenosis and assessing split function GFR of the kidneys. Computed tomography and magnetic resonance imaging (MRI) are useful to assess structural function of the kidney and its adjacent structures.

HISTOPATHOLOGY

Light Microscopy

This identifies the number of glomeruli present and the adequacy (5 to 15 glomeruli) of the sample (5). It describes cellularity of the glomerular cells, normal or increased (hypercellular), and can distinguish which cell type is increased (mesangial or infiltrating cell); whether the glomerular basement membrane (GBM) is thickened and whether the capillary loops are patent, collapsed, or filled with material such as hyaline, cells and fibrin; and the presence or absence of scarring (glomerulosclerosis). The tubules and the interstitium must be carefully inspected for the degree of tubulo-interstitial involvement. Tubulo-interstitial fibrosis is the best predictor of the prognosis in renal disease (18).

Glomerular disease are classified on light microscopy as focal or diffuse (< 50% of glomeruli is termed focal and if > 50% is diffuse). If < 50% of an individual glomerulus is involved, the disease is described as segmental; if most (> 50%) of an individual glomerulus is involved, it is called global. Glomerular crescents can also be detected on light microscopy. They are layers of cells (parietal epithelial cells, podocytes, lymphocytes and macrophages) in the Bowman space, and their presence signifies severe disease and poor prognostic outcome. Cellular crescents have better prognosis than fibrous crescents.

Tubulo-interstitial diseases (TID) adversely affect the prognosis of various glomerulonephritides. The presence of TID in the cortical area was correlated significantly with hypertension at presentation, response to treatment and outcome (18).

Immunofluorescence

Immunofluorescent (IF) staining on frozen sections has been the gold standard for immunohistochemical evaluation of renal biopsy specimens. However, immunoperoxidase (IP) is an alternate to IF with the advantage that it can be performed on paraffin sections of formaldehyde-fixed tissue (19). Immunofluorescent immunostaining determines the presence or absence of any underlying immune processes. Staining is directed against specific antibodies (*eg*, IgG, IgA and anti-

GBM) and individual complement components (*eg*, C3, C4 and C5b-9). The pattern of the immune components is also diagnostic. Granular pattern is typical of antigen-antibody complexes (*eg* membranous nephropathy) and a linear pattern occurs in anti-GBM disease (*eg* Goodpastures disease). Antibody or complement location (*eg*, in the mesangium in IgA nephropathy) also provides diagnostic clues. Immunostaining can determine the presence of matrix proteins (silver stain), amyloid fibrils (Congo red) and viral inclusions.

Electron Microscopy

Electron microscopy provides information on the presence and sub-cellular location of immune complexes seen as electron dense deposits. It also provides information on the degree of injury to glomerular cells and the consistency of the basement membrane. It detects fibrils and provides information on the ultra-structure of the kidney, such as podocyte effacement and flattening, which cannot be readily detected by light microscopy. It can help to distinguish definitively between glomerular diseases.

Contraindications and Precautions

Care and precaution should be taken in kidney biopsy to prevent or minimize complications when they occur. A kidney biopsy is not advised in patients with severe hypertension, as they are at increased risk of bleeding. Patients with bleeding disorders or on anticoagulant (*eg* warfarin) or non-steroidal anti-inflammatory drugs (NSAIDs) are usually relatively contraindicated. Aspirin and NSAIDs should be discontinued at least seven days prior to commencement of a kidney biopsy and anticoagulant therapy (*eg* heparin, warfarin) discontinued. Patients with low platelets are at increased risk of bleeding. Morbid obesity is also a risk factor for bleeding. Therefore other methods such as the transjugular approach, with increased yield and reduced complications should be employed. A solitary kidney is a contraindication to percutaneous biopsy but can be performed as an open biopsy when indicated. Active upper urinary tract infection and pyelonephritis should be effectively treated before planning a kidney biopsy. Numerous cysts in the kidney can pose technical difficulty and reduce yield. Open biopsy with resection is advised when an underlying tumour is suspected. Biopsy of a shrunken kidney as a result of disease should be avoided due to the increased chance of bleeding from the presence of fibrous tissue and also because of the likelihood of unhelpful histological pattern.

CONCLUSION

A carefully obtained history may help define a possible cause of glomerular disease: family history of renal disease (FSGS, Alports syndrome), toxins or drugs such as NSAIDs, inter-

feron, gold and penicillamine (minimal change disease), malignancies *eg* lung, breast, gastrointestinal cancers (membranous nephropathy), with Hodgkin disease (minimal change disease) and renal cell carcinoma (amyloid). Therefore, it is imperative and of utmost importance that the clinical presentation be carefully evaluated and as much of this information as possible should be made available to the nephrologist.

Real-time ultrasound-guidance in conjunction with an automated core biopsy system is a safe and accurate method of performing percutaneous renal biopsy.

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