ORIGINAL RESEARCH PAPER

General Medicine

RENAL BIOPSY AND POST BIOPSY COMPLICATIONS-A CASE SERIES AT MULTICENTRES

KEY WORDS:

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BACKGROUND

It is still an essential tool for diagnosis and choice of treatment of several primary or secondary kidney diseases. Moreover, it may help to know the expected time of end stage renal disease. The indications are represented by nephritic and/or nephrotic syndrome and rapidly progressive acute renal failure of unknown origin. Bleeding is the major primary complication that in rare cases may lead to retroperitoneal haemorrhage and need for surgical intervention and/or death. For this reason, careful evaluation of risks and benefits must be taken into account, and all procedures to minimize the risk of complications must be observed. After biopsy, an observation time of 12-24 h is necessary, whilst a prolonged observation may be needed rarely. In some cases it could be safer to use different techniques to reduce the risk of complications, such as laparoscopic or transjugular renal biopsy in patients with coagulopathy or alternative approaches in obese patients.

INTRODUCTION

Percutaneous renal biopsy (PRB) is still considered an irreplaceable tool for diagnosis, prognosis and choice of treatment of several primary or secondary kidney diseases. The indications uniformly recognized by most nephrologists are represented by nephritic and/or nephrotic syndrome and unexplained acute or rapidly progressive renal failure[1].Primary glomerulonephritis are the more common renal disease in renal biopsy registries.Among them IgA nephropathy (IgAN) is the most frequent renal diagnosis. Regarding systemic diseases,SLE is the most frequent indication for PRB, because this last determines the level of activity and/or chronicity of the lesions and the reversibility of renal lesion as a result of therapy. PRB can also be helpful in vasculitis to assess the severity of the damage and the potential reversibility after therapy. In diabetes the use of PRB is motivated by a relatively recent or very late appearance of proteinuria > 1 g and/or a rapid decline in GFR and/or active urinary sediment, in the absence of other signs of microangiopathy (retinopathy and neuropathy).In advanced chronic renal failure, PRB is useful to assess a rescue therapy or to know the causal nephropathy in view of renal transplantation[2].PRB is also an informative procedure in renal transplantation, both in the postoperative, for the differential diagnosis of acute rejection vs other diseases, and in followup of organ transplantation for differential diagnosis between recurrence of primary renal disease, development of glomerulonephritis ex novo, and acute or chronic rejection.

Table 1 List of Indications for renal biopsy

Nephrotic syndrome
Acute kidney injury (when rule out obstruction, and pre-renal causes) Systemic disease with renal dysfunction (in diabetic patients only if it presents with atypical features)
Non-nephrotic proteinuria, and in some circumstances isolated microscopic hematuria
Unexplained chronic kidney disease Familial renal disease (may avoid biopsy in other family members affected)
Renal transplant dysfunction.

NEEDLE TYPES AND SIZE

First used was an aspiration needle, subsequently replaced by the cutting Vim-Silverman needle, which trapped the tissue in the needle and then sheared it off. The evolution of the latter is the TruCut needle, which is a manually operated sheathed needle designed for manual capture of highquality tissue samples with minimal trauma to the patient.Today it is replaced by automatic springloaded biopsy guns and semi-automatic biopsy guns with better and safer performance. The needle size,most used are three: 18 gauge (internal diameter 300 to 400 μm), 16 gauge (internal diameter 600 to 700 μm) and 14 gauge (internal diameter 900 to 1000 μm). The first one is reserved to paediatric patients because the internal diameter of the needle is barely bigger than an adult glomerulus (200250 pmol/L), while the other two are more appropriate for the adult patients [3,4]. On the other hand, the length of this device is almost the same and is around 20 cm.

SAMPLE ADEQUACY

The number of glomeruli is the main determinant of the biopsy adequacy but it varies based on the type of glomerular disease. For example in focal disease, such as focal segmental glomerulosclerosis, the diagnosis can be made by identifying even one glomerulus that presents the typical lesions but the probability to make diagnoses is directly proportional to the number of glomeruli [5]. Therefore, in a kidney in which 20% of glomeruli are sclerotic, if a bioptic sample includes five glomeruli the probability to miss affected glomeruli is about 35%.This percentage falls down to 10% if the bioptic sample includes ten glomeruli and to 1% if it includes twenty glomeruli[6,7].Therefore, the minimum number of glomeruli required to define an adequate bioptic sample is ten, and usually, to get this target at least two different cores are taken which are divided for light microscopy (LM) (placed in formalin or another fixative), immunofluorescence (IF) (placed in transport solution saline solution and quickly freezed), and electron microscopy (EM) (fixed in 2%-3% glutaraldehyde or 1%-4% para formaldehyde)[8]. Actually, the latter is not frequently and widespread performed in the practice of renal biopsy since it is possible to get a diagnosis in most cases with the contribution of the LM and the IF.

COMPLICATIONS

Even if PRB is considered a safe procedure, it is not without complications (Table 2) that, in very rare cases, may also cause death or require extreme procedures such as nephrectomy[9,11]. Furthermore, complications are divided into major complications that need a treatment or an intervention to stop the problem, and minor complications that spontaneously resolve without intervention or further treatment; in both cases, bleeding is the main consequence of PRB and can occur at different levels: (1) in the collecting duct system, causing micro gross haematuria which may result in clots formation in the urine (ureter or bladder) with risk of obstructive renal failure; (2) below the kidney capsule, causing subcapsular hematoma formation that in rare cases may lead to the Page kidney, which consists in renal ischemia caused by prolonged compression of the kidney from haemorrhage with resulting arterial hypertension characterized by high renin levels[12]; and (3) in the perinephric space, causing hematoma formation which may be asymptomatic, in the majority of cases, or result into a

clinically relevant complication, such as lumbar pain, significant drop in haemoglobin concentration, or need for a blood transfusion. However, the risk of complications after renal biopsy is not high.

The study was done at department of medicine and department of nephrology at Patna Medical College and Hospital and private Hospital in Patna. The 100 cases of nephrotic syndrome who underwent biopsy of native kidney between 01 January 2018 to 01 January 2020 were prospectively analyzed for associate post biopsy complications, the overall incidence of bleeding complications were: Transient gross haematuria 3.5%, request for transfusion therapy 0.9%, demand on angiographic control of bleeding 0.6%, request for nephrectomy for control of bleeding 0.01% and death 0.02%. Thus, the risk of using invasive procedures to stop bleeding is very rare. More frequently we can treat this complication with medical treatment such as administration of endovenous fluid and/or blood products[13].

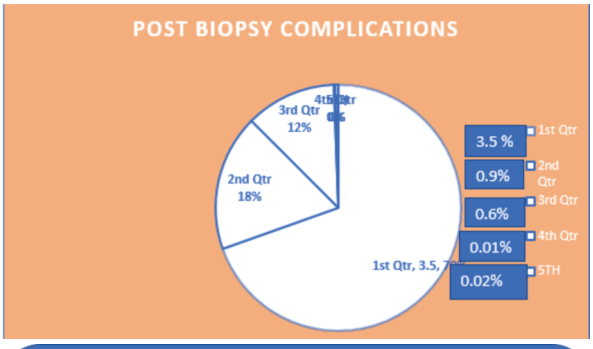

Table 2 Types of complications after renal biopsy

Minor complications	Major complications
Bleeding	Bleeding
Asymptomatic haematoma	Hematoma requiring blood transfusion or invasive procedure to stop bleeding
Microscopic and gross haematuria	Urinary tract obstruction with or without AKI
Anaemia (drop in haemoglobin concentration ≥ 1 g/dL)	Hypotension related to bleeding
Pain (> 12 h)	Nephrectomy
Page kidney	Sepsis
Perinephric infection	Other organs and/or blood vessels perforation
Arteriovenous fistula	Death

Specific symptoms and signs post-biopsy

Lumbar pain: The pain is an extremely common consequence of PRB and usually occurs at the end of anaesthesia. If necessary it is possible to administer a mild analgesic. Otherwise, the onset of greater pain suggests the development of a major complication and further diagnostic tests must be performed.

Microscopic haematuria: It is the most common consequence of this procedure; it is usually asymptomatic[14] and resolves spontaneously over a few days.

Gross haematuria: It occurs in 3% of renal biopsies and typically disappears in few hours or days. Occasionally gross haematuria may cause a significant drop in haemoglobin concentration requiring a blood transfusion or, in rare cases, it may result in clots formation with or without obstructive renal failure. On the contrary, persistent haematuria after three days suggests the onset of major complications such as arteriovenous fistula (AVF)[15].

Acute anaemia: A decrease of haemoglobin concentration ≥ 1 g/dL occurs in more than 50% of uncomplicated renal biopsies[16], whereas a fall ≥ 2 g/dL occurs in 10% of uncomplicated cases and is consequently associated with increased risk of complications[17].

Perinephric hematoma: The presence of asymptomatic hematoma is frequently detected during a renal ultrasound after biopsy and does not constitute per se a complication. Perinephric hematoma is detectable in 90% of patients 24 to 72 h after the procedure, while this percentage drops to 15% immediately after the biopsy. Most of the perinephric hematomas are small, asymptomatic and they resolve spontaneously in few months; only in 2% of cases they may cause a clinically relevant complication such as lumbar pain, a decrease in haemoglobin concentration, or the need for blood transfusion. However, the absence of hematoma at 1 h was highly predictive of an uncomplicated course[18]. Therefore, the routine use of ultrasound at 1 h after PRB may have a role in determining an uncomplicated course[19].

AVF: It is not a frequent complication and is due to trauma of the wall of blood vessels; it is clinically asymptomatic and resolves spontaneously in most cases[20]. In rare cases AVF can cause the development of an aneurysm ,which may manifest clinically as high blood pressure, heart failure, and ki dney failure. Important signs that suggest this complication are the persistence of gross haematuria, the presence of abdominal bruit and palpable trill[21,22] but diagnosis confirmation requires Doppler ultrasound or magnetic resonance imaging, or angiography. The treatment of symptomatic cases is based on superselective transcatheter arterial embolization or, in rare cases, surgery[23].

CONTRAINDICATIONS AND RISK FACTORS

Contraindications to renal biopsy and risk factors must be taken into account to minimize the risk of complications. The presence of intravascular coagulopathy, polycystic kidneys, obstruction of the urinary tract, hydronephrosis, infections of the upper urinary tract are regarded as absolute contraindications. Otherwise, there are some conditions, which require caution, considered as relative contraindications, such as compromised cardiopulmonary function or hemodynamic instability, severe obesity, inability of the patient to cooperate, solitary kidney, advanced age, severe hypertension (> 160/95 mmHg), and renal failure[24]. The last one causes functional alterations of coagulation factors as the von Willebrand factor (vWF) and the Factor Ⅷ, abnormalities in platelet membrane, accumulation of uremic toxins that inhibit platelet aggregation, high levels of prostacyclin and nitric oxide which are factors that reduce platelet aggregation. Another element that often contributes to increase the risk of bleeding in renal failure is the presence of anaemia. Other diseases associated with greater risk of bleeding are those with arteriolar involvement as SLE, vasculitis, scleroderma, amyloidosis and advanced diabetic nephropathy because they interfere with the first mechanism of haemostasis, known as the vascular phase, reducing the arteriolar contraction.

PROCEDURES PRE-BIOPSY

Before performing the PRB it is very important to follow some recommendations to minimize the risk of complications. Renal ultrasound is essential to evaluate the presence of anatomical abnormalities of the kidney (presence of multiple cysts, hydronephrosis, solitary kidney that may represent a risk factor for the development of complications. Laboratory tests may reveal the potential presence of coagulopathy. To totally assess the steps of haemostasis it is useful to use the bleeding time that evaluates the time of platelet aggregation. In case of advanced renal failure and/or prolonged bleeding time, the administration of desmopressin acetate - DDAVP (0.3 g/kg), estrogen and cryoprecipitate has shown a reduction of the bleeding risk[25,26]. Antiplatelet agents and oral anticoagulants have to be withdrawn at least one week before renal biopsy[27], the last ones until normalization of INR, and replaced with low molecular weight heparin (LMWH). Other drugs that may cause alterations in coagulation are the nonsteroidal antiinflammatory drugs (NSAIDs), which should be not taken for at least 5 d before PRB.

ALTERNATIVE APPROACHES FOR RENAL BIOPSY

In some cases, PRB may be contraindicated because of bleeding diatheses or habitus of the patients such as obesity.

In these circumstances we can perform renal biopsy with alternative methods such as under CT guidance[28] or with laparoscopic[29] and transjugular approach[30]. These techniques may have some limits. CT guidance, for example, does not assess any possible movements of the kidney related to breathing, laparoscopic biopsy requires general anaesthesia and transjugular biopsy seems to be associated with a lower diagnostic power due to the need to pass through the medulla first[31]. In obese patients a new approach of PRB under realtime ultrasound guidance has been proposed with the patient in supine anterolateral position (SALP). Moreover, an open renal biopsy may be performed when uncorrectable contraindications are present.This is a safe procedure with 100% of sample adequacy but an important limitation of this technique is the use of general anesthesia.

PERIOD OF OBSERVATION After biopsy, the patient must be at rest for at least 6 to 8 h in the supine position. Blood pressure should be monitored frequently, and urine must be checked to evaluate the presence of gross haematuria. If there are no signs of bleeding within 6 h, the patient may sit up, because most of complications occur within 6 to 8 h. However, since some complications may also occur later, the ideal observation time should be continued for 24 h.

CONCLUSION

PRB is a safe procedure and the risk of development of major complications is very rare. Instead, the minor consequences due to the procedure occour more frequently. These are micro and/or gross haematuria, drop in hemoglobin concentration > 1 g/dL, development of asymptomatic perinephric hematoma. All these minor adverse events can be more safely managed and do not bring particular complications to the patient. It is mandatory to identify risk factors for bleeding such as anaemia, prolonged bleeding time or advanced renal failure, severe arterial hypertension and correct them when possible; where this is not possible, it is recommended postponed the procedure.

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