Review Article

REPORTING AND INTERPRETING MEDICAL RENAL BIOPSIES – A REVIEW ARTICLE

It would be a boring article to read and understand without illustration of figures in pictorial form of histopathology examination features that demonstrate the different types of kidney lesions, you also need to demonstrate figures that show the immunohistochemistry staining features of various kidney lesions and also you need to demonstrate in figure forms differences in electron microscopy examination features of examples of various renal lesions. Every clinician knows how pathology examination of kidney biopsy is done and therefore you need to provide pathology examination figures of various kidney pathologies to demonstrate as well as to provide more meaning and understanding of your article

You should provide a table or tables to summarize for each renal lesion the following:

[A] Histopathology examination features

[B] The immunohistochemistry staining features of each lesion including the positive stains and negative staining of each lesion

[C] Special stain pictures of some kidney lesions

[D] Electron microscopy examination features of various kidney lesions from the archives of your

pathology department but if you cannot get them from your department, you can look through internet data bases and find figures in open access articles that contain figures that are available under the creative commons attribution which permits reproduction of figures provided the original source is properly cited. If you include figures in the article, it would provide improvement to the quality of your article to provide meaningful reading please.

ABSTRACT

Medical renal biopsy is an important tool in patient care in nephrology department. Systematic reporting of a renal biopsy eases the communication between the pathologist and the clinician, thereby improving patient care. H & E (Hematoxylin and eosin) sections alone cannot help to arrive at a diagnosis, Immunofluorescence, special stains and electron microscopy plays an important role too. To arrive at an accurate diagnosis, an expert renal pathologist, who has a thorough knowledge of renal pathology and as well as renal medicine is required to correlate tissue with clinical data. Although a lot of review articles regarding renal biopsies are published, review of literature covering all aspects of renal biopsy are a few especially from India. [Write a little summary about your findings in the review article especially how a combination of histopathology examination features, immunohistochemistry staining features as well as electron microscopy features help in differentiating various renal lesions in the abstract]

Keywords: H & E, Immunofluorescence, Electron microscopy, Histopathology. Microscopy,

INTRODUCTION

For the accurate diagnosis of medical renal biopsies, renal biopsy is often essential. In addition, renal biopsy is frequently used to assess activity and chronicity, which is used to decide upon the appropriate therapy and to determine the prognosis [1]. A proper format is required to report renal biopsies so that all aspects are covered. Special stains supplement the light microscopy, especially Periodic acid–Schiff **(**PAS), Silver methenamine, Masson's trichrome and Congo red. It also helps to stain various components of the renal tissue [2]. Immunofluorescence (IF) is an irreplaceable technique which is used for accurate diagnosis in renal pathology, especially in diseases like IgA nephropathy (IgAN), C1q nephropathy (C1qN) and C3 glomerulopathy (C3G), which cannot be diagnosed without IF [3] Electron microscopy (EM) examination on the other hand must be done on all renal biopsies, but unfortunately, they are available only in large centres [4].

AIMS

The aim of the article was to review the literature related to the interpretation of renal biopsies.

METHODS

Various internet data bases were searched including: PUBMED; Google; Google Scholar; Yahoo, and []]] The search words that were used included: Renal biopsy;

Kidney biopsy; indications for kidney biopsy, histopathology examination of kidney lesions, immunohistochemistry examination features of renal lesions, electron microscopy examination features of renal lesions, flow cytometry examination features of kidney lesions, special staining agents for pathology examination of kidney lesions. Eighteen (18) references were identified to write the article

RESULTS

COMMON INDICATIONS OF MEDICAL RENAL BIOPSY [5]

Common indications for the undertaking of radiology image-guided renal biopsies have been documented to include the following: [5]

- Unexplained acute or rapidly progressive renal failure
- Nephrotic syndrome and significant non-nephrotic proteinuria
- Persistent glomerular haematuria
- Systemic diseases with renal involvement
- Staging of lupus nephritis, classification of IgA nephropathy, classification of diabetic nephropathy

Nephritic syndrome

ADEQUACY OF TISSUE SAMPLING

An adequate renal biopsy is one that contains at least 10 glomeruli on light microscopy and should have atleast one each for immunofluorescence and electron microscopy [6].

LIGHT MICROSCOPY HAEMATOLOGY AND EOSIN SECTIONS) (H & E SECTIONS & SPECIAL STAINS)

H and E sections along with special stains is the back bone to report renal medical biopsies.
H & E sections allow for the counting of the number of glomeruli, general evaluation for ascertaining the percentage of cortex and medulla, cellular characteristics, type of inflammation and to locate the area of interest i.e., whether the disease affects the glomerulus, interstitium, vessels or tubules. Special stains commonly used are PAS, Silver methenamine, Masson's trichrome and Congo red [7, 8]. The utility of the special stains is summarised in Table 1.

Table 1: Utility of the special stains

Special stains	Utility
PAS	Glomerular basement membrane, mesangium, tubular basement membrane, hyaline – pink to red
Silver methenamine	Basement membrane details – stains black
Masson's trichrome	Extracellular glomerular matrix and tubular basement membrane – blue or green
Congo red	Amyloid

If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

IMMUNOFLUORESCENCE

Fluorescein-labelled antibodies are used to examine immunoglobulins (IgG, IgM, and IgA), complement components (C3, C1q, and C4), fibrin, and kappa and lambda light chains. They may be also used for amyloid typing, collagen IV alpha chains in hereditary nephritis, IgG subclasses [8, 9].

ELECTRON MICROSCOPY

Electron microscopy examines glomeruli ultrastructurally and aids to concentrate on deposits, very small deposits, fibrils and changes in cellular and basement membrane structure [4].

INTERPRETATION OF RENAL BIOPSY

Low-power screening examination of the specimen helps in localizing that the defect is in glomerulus, tubules, and interstitium, or blood vessels [9].

a) Distribution of the lesion [10,11]

It is classified as:

- Diffuse: Changes occurring in all the glomeruli.
- Focal: Changes in few glomeruli only.
- Global: Whole glomerulus is involved.
- Segmental: Only some part of glomerulus is involved.

b) Active Vs Chronic lesions [11,12]

The lesions need to be classified as either active or chronic. Table 2 summarises the examples of these lesions.

Table 2: Examples of active and chronic lesions [] If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

Active lesions	**Chronic lesions**
Necrosis	Fibrous crescents
Edema	Tubular atrophy
Cellular casts	Interstitial fibrosis
Active inflammation	Vascular sclerosis

c) Abnormalities in glomerular capsule and glomerular basement membrane [12]

Table 3 summarises the common conditions and associated findings in relation to glomerular capsule while Table 4 elaborates in glomerular basement membrane.

Table 3: Abnormalities in glomerular capsule [] If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

	Common conditions	**Associated findings**
Capsular basement membrane thickening	Diabetes mellitus	Capsular drop
Capsular space obliteration	Glomerulonephritis Crescents or necrosis	

Table 4: Abnormalities in glomerular basement membrane If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

	Common conditions	**Associated findings**

1.Thick GBM		
a. Negative IF		
	Diabetic nephropathy	EM – Lamina densa thick No splitting by silver stain
	Hereditary nephritis	Silver stain irregular EM – Basket weaving
b. Positive IF		
	Membranous nephropathy	Spikes by silver stain Subepithelial deposits - EM
	Membranoproliferative glomerulonephritis	Silver stain – GBM splitting Subendothelial deposits - EM
	Amyloid	Positive light chains depending on type of amyloid
	Fibrillary glomerulonephritis	Variable splitting by silver Fibrils in EM
2. Thick GBM		
	Alport's syndrome	Silver stain irregular EM – Basket weaving
	Benign familial haematuria	Thin GBM – EM

GBM: Glomerular basement membrane, EM: Electron microscopy, IF: Immunofluorescence

d) Cellular proliferation [12, 13]

The three common locations of cellular proliferation are: Endothelial, epithelial, and mesangial cells. Abnormalities in these components with associated diseases in summarized in Table 5.

Table 5: Abnormalities in glomerular components If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

	Common conditions	Associated findings
1.Epithelial	Crescentic GN	
Linear GBM deposition	Anti-GBM disease	Positive anti-IgG linear staining along GBM
Immune complex	IgA nephropathy Post-infectious GN Lupus	Positive immune deposits in mesangium Positive immune deposits along capillary walls Full-house pattern of staining in mesangium and long capillary walls, tubuloreticular inclusions on EM
Pauci-immune	Granulomatosis with polyangiitis Microscopic angiitis	No deposits on IF No deposits on IF
2. Mesangial		

With nodule formation	Light chain deposition disease	Linear staining for light chains along GBM & TBM, granular deposits along GBM & TBM on EM
	Membranoproliferative GN	Double contours with subendothelial deposits, cellular elements and new basement membrane formation
	Diabetic nephropathy	PAS and silver positive nodules with negative IF Thick GBM & TBM
	Amyloidosis	PAS & silver negative nodules with positive IF staining for or light chains in AL amyloidosis
Without nodule formation	Post-infectious GN	Positive granular IgG & C3 along capillary walls; Subepithelial humps and subendothelial deposits in EM
	Ig A nephropathy	IgA deposits in mesangium
	C3 glomerulopathy	C3 in mesangium and along capillary walls on IF, and the absence of IgG
3. Endothelial	Post-infectious GN	Positive granular IgG & C3 along capillary walls; Subepithelial humps and subendothelial deposits in EM
	Membranoproliferative GMN	Positive granular IgG, IgM, C1q, C3 or light chains depending on cause, double contours on EM
	SLE	Full house staining on IF microscopy; mesangial, subepithelial, or subendothelial deposits depending on class of SLE

GN: Glomerulonephritis, TBM:Tubular basement memebrane, SLE: Systemic lupus nephritis, GBM: Glomerular basement membrane.

e) Vascular abnormalities [14,15,16]

Vascular lesions are seen in afferent and efferent arterioles and respond to injuries. Moreover, due to the high blood flow in kidneys, they are more prone to vascular injury. Table 6 shows the vascular lesions in renal biopsy.

Table 6: Common vascular lesions in renal pathology If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

	Common conditions	**Associated findings**
Sclerosis	Hypertension	Ischemic glomeruli with thickening of the glomerular basement membranes and wrinkling of the capillary loops
Thrombosis	HUS/TTP	Thrombi in glomerular capillaries, arterioles
	Malignant hypertension	Onion skinning of the vessel walls with hypertrophy of the media
Fibrinoid necrosis	Malignant hypertension	Onion skinning of the vessel walls with hypertrophy of the media
	Polyarteritis nodosa	Arteritis, with fibrinoid necrosis and inflammation of vessel walls
	HUS/TTP	Thrombi in glomerular capillaries, arterioles
Vasculitis	Vasculitis	Depends on type. For e.g., in granulomatosis with polyangiitis, granulomatous inflammation
Emboli	Atheroembolism	Cholesterol atheroemboli in glomerular capillaries and arteries
Hyalinosis - Eccentric	Hypertension	Ischemic glomeruli with thickening of the glomerular basement membranes and wrinkling of the capillary loops
	Diabetes	Diffuse and nodular glomerulosclerosis

HUS: Hemolytic uremic syndrome, TTP: Thrombotic thrombocytopenic purpura

f) Tubular abnormalities [15,16,17]

Tubular cells may exhibit acute reversible and irreversible damage (necrosis), intracellular accumulations, metabolic storage diseases and vacuoles. It may also show acute tubular necrosis and atrophy. Table 7 depicts the common tubular abnormalities.

Table 7: Common tubular abnormalities [] If this table is your own table, then it is alright but if you reproduced the table from elsewhere then you need to provide reference for the table

Lesions	Common conditions	Associated findings
1.Necrosis	Ischemic and toxic ATN	Flattened tubular epithelial cells, mitotic figures
2. Edema	Ischemic and toxic ATN, thrombosis	Associated with interstitial inflammation; but no inflammation in renal vein thrombosis
3. Inflammation a. Polymorph b. Lymphocyte c. Eosinophil	 Rein vein thrombosis Acute interstitial nephritis, hypersensitivity reaction Churg- Strauss vasculitis	 Increased neutrophils in glomerular capillaries Tubulitis Eosinophil infiltrate Eosinophil infiltrate
4. Granuloma a. Necrotising b. Confluent	 Tuberculosis & fungal Sarcoidosis	 Positive AFB stains in TB Perivascular granulomas
5. Intratubular material a. Pigmented cast	 Myoglobin in rhabdomyolysis	 Positive immunohistochemistry for myoglobin
6. Atrophy a. Focal b. Diffuse c. Disproportionate	 Glomerular ischemia Advanced renal disease Renal artery stenosis & renal vein thrombosis Obstructive uropathy	 Distended Bowman's space, with thickening and wrinkling of glomerular capillaries Focal global glomerulosclerosis Tamm-Horsfall protein in tubules
7. Fibrosis a. Patchy	 Chronic pyelonephritis	 PAS-positive hyaline casts
8. Dilatation	Obstructive uropathy	Tamm-Horsfall protein in tubules

ATN: Acute tubular necrosis, AFB: Acid fast stain, TB: Tuberculosis

g) Interstitial abnormalities [18,19,20]

Interstitium has lesser number of abnormalities. The common ones are edema, inflammation, and fibrosis. Edema is considered acute while fibrosis chronic. Amyloid, immune complex deposits, and immunoglobin light chains may also be seen in interstitium.

SIMPLE FORMAT FOR REPORTING MEDICAL RENAL BIOPSIES

A simple format shown below may help a renal pathologist to report renal biopsies of a ease without causing confusion to the nephrologist. This may also aid the pathologist to focus on important components also.

[If this is not your own chart please provide the reference of the source of the table]

Chart 1: Core of renal biopsy:
Glomerulus - Number of glomeruli Globally sclerosed: Segmental sclerosis: Mesangial/ endothelial/ epithelial proliferation: Basement membrane/ capillary wall thickening: Wire loops: Inflammation:
Tubules – Edema: Inflammation: Atrophy: Casts: Amyloid:
Interstitium – Fibrosis: Edema: Inflammation: Amyloid:
Vessels – Hypertrophy: Hyaline or hyperplastic arteriosclerosis: Amyloid:
Special stains – PAS: Silver: Congo red: Masson Trichrome:
Immunohistochemistry – IgG: IgA:

C3:
Diagnosis:

CONCLUSION

Renal biopsy is a vital tool for the understanding of the pathology of various renal diseases. It helps in evidence-based medicine and proper patient care. Both pathologists and nephrologists should work together for proper clinico-pathological correlation. H & E, special stains, IF, & EM together must be done routinely in all renal biopsies. If properly interpreted, renal biopsies are a great source for appropriate therapeutic strategy as well as to provide key prognostic information.

CONFLICT OF INTEREST – You need to provide conflict of interest statement

ACKNOWLEDGEMENTS – provide an acknowledgement statement thanking any individual or groups that have helped you in the collection of data and writing of the article

REFERENCES **The style of reference writing should be consistent with the use of only one reference writing style**

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