THE ROLE OF RENAL BIOPSY IN GLOMERULAR DISEASES DIAGNOSTIC

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Percutaneous Renal Biopsy has a fundamental role in the clinical practice of Nephrologists to determine an accurate diagnosis, prognosis and consequently the choice of appropriate treatment.
Being renal biopsy an “invasive” procedure, with possible risk of complications, his evaluation should be performed in centers with recognized Nephropathological expertise and supported by all methodologies (LM, IF, EM, Immunohistochemistry), indispensable for a correct diagnosis. Moreover needs a strict clinico-pathological correlation.
Recommandations of International Rheumatologic and Nephrologic Societies

Among different clinical and laboratory parameters, ultimately renal biopsy is considered as the “gold standard” for diagnosis, prognostic evaluation and therapeutic intervention, while clinical features and laboratory parameters frequently shows a modest correlation.
Example of two cases of ANCA-associated vasculitis demonstrating the frequent discrepancies between clinical and morphological features.
CASE 1

A 78 years old caucasian male with history of 20 years hypertension.

In August 2011 fever, astenia and some migrant arthralgia.

Exams

S. Cratinine 1.58 mg/dl

Hg 9.4 gr/dl, Proteinuria 0.3 gr/die, Microscopic Haematuria

ANA, ENA, nDNA, LAC negative.

Cryoglobuline positive (Cryocrit 1%)

Normocomplementemia

C-ANCA (PR3) negative

P-ANCA positive (MPO 6)

Sonography: normal kidneys

Chest x-ray: NORMAL.
In spite of mild renal insufficiency and low titer of MPO-ANCA, histological feature of diffuse massive periglomerular granulomatous reaction necessitating strong therapy.
Impressive periglomerular granulomatous reaction. Glomerular remnant is evident.
CASE 2
A 78 years old caucasian female with history of crusted rhinitis.

Normal renal function without urinary abnormalities.

December 2011: slight fever, astenia, arthralgias and tongue ulcerative lesion.

January 2012: she developed marked dispnea with oliguria and was admitted to nephrology department.
Exames

S. Cratinine 6.2 mg/dl
Hg 7.72 gr/dl
Proteinuria 0.6 gr/die  Microscopic Haematuria
ANA, ENA, nDNA, LAC, Cryoglobuline, Anti-GBM antibody : negative
Normocomplementemia
C-ANCA (PR3) negative
P-ANCA positive (MPO>100)
Sonography: normal kidneys
Chest x-ray: Suggestive of haemorrhagic alveolitis
In spite of severe renal insufficiency and high titer of MPO_ANCA, histological feature of focal segmental necrotizing extracapillary glomerulonephritis.
Pauci immune pattern with scanty deposits of C3
## Impact of Renal Biopsy in Clinical Management

<table>
<thead>
<tr>
<th></th>
<th>Authors / n° of cases</th>
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<tbody>
<tr>
<td></td>
<td>PAONE / 100</td>
<td>TURNER / 80</td>
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<tr>
<td><strong>Non Diagnostic RB</strong></td>
<td>13%</td>
<td>3%</td>
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<tr>
<td><strong>Changed Diagnosis</strong></td>
<td>--</td>
<td>44%</td>
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<tr>
<td><strong>Changed Prognosis</strong></td>
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<td>57%</td>
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<tr>
<td><strong>Changed Therapy</strong></td>
<td>19%</td>
<td>31%</td>
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Clinical Renal Syndromes are relatively few

Asymptomatic proteinuria
Asymptomatic hematuria
Nephrotic syndrome
Nephritic syndrome
Rapidly progressive renal failure
Acute renal failure
Chronic renal failure
Also glomerular cells are relatively few:

Mesangial

Endothelial

Visceral epithelial (Podocytes)

Parietal epithelial
Conversely the number of totally different types of nephritis is extremely vast and quite every year there is a description of new forms.
Disease that typically cause the nephrotic syndrome

- Focal segmental glomerulosclerosis (all variants)
- Idiopathic membranous glomerulopathy
- Minimal change glomerulopathy
- Diabetic glomerulosclerosis
- Type I membranoproliferative glomerulonephritis
- Idiopathic mesangioproliferative glomerulonephritis
- Amyloidosis
- C1q nephropathy
- Fibrillar glomerulonephritis
- Monoclonal immunoglobulin deposition disease
- Type II membranoproliferative glomerulonephritis
- Pre-eclampsia/eclampsia
- Immunotactoid glomerulopathy
- C3 nephropathy
- Collagenofibrotic glomerulopathy
Disease that typically cause hematuria and nephritis

Lupus nephritis
IgA nephropathy
Idiopathic immune complex proliferative glomerulonephritis
Pauci-immune/antineutrophil cytoplasm antibody glomerulonephritis
Postinfectious acute diffuse proliferative glomerulonephritis
Thin basement membrane lesion
Antiglomerular basement membrane antibody glomerulonephritis
Alport’s
Disease other than glomerulonephritis that typically cause acute renal failure

- Thrombotic microangiopathy (all types)
- Acute tubulointerstitial nephritis
- Acute interstitial nephritis IgG4 related
- Acute tubular necrosis
- Atheroembolization
- Light chain cast nephropathy
- Cortical necrosis
Disease other than those already listed that typically manifest as chronic renal failure

- Arterionephrosclerosis
- Chronic sclerosing glomerulonephritis
- End stage renal disease not otherwise specified
- Chronic tubulointerstitial nephritis
- Miscellaneous other diseases
- Adeguate tissue with nonspecific abnormalities
- No pathologic lesion identified
For all these reasons a correct diagnostic evaluation of renal biopsy needs nephropathological expertise supported by all methodologies. To confirm this we show some example of the main histological lesions.

All morphological slides show similar lesions in four different diseases.
MESANGIAL PROLIFERATION

Definition: At least 4-5 cells per mesangial area
Immunofluorescence

• A: Mesangial deposits of IgA
• B: Segmental deposits of IgM
• C: Mesangial deposits of C1q
• D: Granular deposits of C3
Mesangial deposits of IgA

Segmental deposits of IgM

Mesangial deposits of C1q

Granular deposits of C3
Electron microscopy

- A: Mesangial electrondense deposits
- B: Foot process effacement
- C: Finger prints
- D: Subendothelial and subepithelial deposits
Mesangial deposits

Foot processes effacement

Finger prints

Subendothelial + subepithelial deposits
Final diagnosis
Mesangioproliferative GN

- A: IgA nephropathy
- B: IgM nephropathy
- C: Lupus nephritis (class II mesangial)
- D: C3 nephropathy
BASEMENT MEMBRANE ALTERATIONS

A: Diffuse regular thickening of glomerular basement membranes

B: Diffuse "spikes" at silver stain

C: Huge subendothelial deposits

D: Double contour appearance at silver stain
Thickenig of GBM

A

subendothelial deposits

C

Spikes

B

Double contours

D
Immunofluorescence

A: Diffuse granular parietal subepithelial deposits of IgG

B: Subendothelial deposits of C3

Electron Microscopy

C: Continuous subepithelial deposits

D: Double contour with subendothelial deposits
Granular parietal subepithelial deposits

Subendothelial deposits

Subepithelial deposits

Subendothelial deposits (double contour)
Final Diagnosis

- A-B: Membranous glomerulonephritis
- C-D: Membranoproliferative glomerulonephritis