The Prevalence of Different Classes of Lupus Nephritis in Jordan University Hospital

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Abstract

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease involving almost all organs of the body. There is a high incidence of renal involvement during the course of the disease with varied renal pathologic lesions. A renal biopsy contributes towards diagnosis, prognostic information, and appropriate management.

Aim: To study the prevalence of different classes of SLE using the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification in our facility.

Methods: This study was carried out at the Jordan University Hospital (JUH) in June and July 2011. We acquired an approval for this study from the IRB (Institutional Review Board) of the Jordan University Hospital. We retrieved 36 renal biopsies from our files beginning from 2002-2010 that have the diagnosis of SLE and they were reviewed and reclassified by two pathologists.

Results: Of the 36 renal biopsies, only one was classified as class I, 5 were class II, one was class III, 23 were class IV, 6 were class V, and none of the biopsies were classified as class VI.

Conclusion: Class IV was the most prevalent class in the JUH cases with almost equal numbers of class IVS and IVG subclasses, while there was only a single case of class III (IIIS) which is very low compared to other studies.

Keywords: Lupus erythematosus, International Society of Nephrology, renal biopsies.

Introduction

The prevalence of SLE varies with race, sex, and age with the highest incidence being in African American females. Increased incidence of SLE within families suggests a genetic predisposition. SLE occurs predominantly in females of child-bearing age with a male to female ratio of 1:10.1 Renal involvement is observed in most SLE patients at some point during the natural history of the disease.

Nearly 5% of SLE patients develop renal disease in the first year of diagnosis.¹ Approximately 20% of SLE patients with renal disease include children and older adults.² Although relatively rare in children, at least two thirds of childhood cases will develop renal disease which is much higher than the rate in adults.³ Concerning the classification of lupus nephritis, a new revised classification was proposed in order
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to accommodate the clinicopathologic and pathogenetic insights. This revised classification introduced several important modifications concerning quantitative and/or qualitative differences between classes III, IV, and V lesions. This new classification is based exclusively on glomerular pathology and as such represents a classification of lupus glomerulonephritis. Its use has increased the percentage of lupus nephritis biopsies meeting criteria for class IV. As it has gained wide spread acceptance, the ISN/RPS classification is already providing a standardized approach to renal biopsy interpretation needed to compare data outcome across centers. Although a UK-wide study demonstrated improved inter-observer reproducibility, the reproducibility of the assessment of disease activity and chronicity was suboptimal according to their results and there were more diagnoses of class IV lupus nephritis, with fewer diagnoses of class III and V.

Table (1): The (ISN/RPS) classification of lupus nephritis 2003.

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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</table>
| Class I | Minimal Mesangial Lupus Nephritis  
Normal glomeruli by LM, but mesangial immune deposits by IF |
| Class II | Mesangial Proliferative Lupus Nephritis  
Purely mesangial hypercellularity of any degree and/or mesangial matrix expansion by LM, with mesangial immune deposits. A rare isolated subepithelial of a subendothelial deposit may be visible by IF or EM, but not by LM. |
| Class III | Focal Lupus Nephritis  
Active of inactive focal, segmental or global endo- or extra-capillary glomerulonephritis involving <50% of glomeruli, typically with focal subendothelial immune deposits, with or without mesangial alterations.  
III (A) Active lesions focal proliferative lupus nephritis  
III (A/C) Active and chronic lesions (focal proliferative sclerosing lupus nephritis)  
III (C) Chronic inactive lesions with scars (focal lupus nephritis)  
*indicate the proportion of glomeruli with active and with sclerotic lesions  
*indicate the proportion of glomeruli with fibrinoid necrosis and with cellular crescents  
*indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, arteriosclerosis or other vascular disease |
| Class IV | Diffuse Lupus Nephritis  
Active or inactive diffuse, segmental, or global endo- and/or extra-capillary glomerulonephritis involving ≥50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class is divided into diffuse segmental (IV-S) when ≥50% if the involved glomeruli have segmental lesions, and diffuse global (IV-G) when ≥50% of the involved glomeruli have global lesions. Segmental is defined as a glomerular lesion that involves less than half of the glomerular tuft. This class includes cases with diffuse wire-loop deposits, but with little or no global proliferation.  
IV-S (A) or IV-G (A) Active lesions (diffuse segmental or global proliferative lupus nephritis)  
IV-S (A/C) or IV-G (A/C) Active and chronic lesions (diffuse segmental or global proliferative and sclerosing lupus nephritis)  
IV-S (C) or IV-G (C) Chronic inactive lesions with scars (diffuse segmental or global sclerosing lupus nephritis)  
*indicate the proportion of glomeruli with active and with sclerotic lesions  
*indicate the proportion of glomeruli with fibrinoid necrosis and with cellular crescents  
*indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, arteriosclerosis or other vascular disease |
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<table>
<thead>
<tr>
<th>Class</th>
<th>Membranous Lupus Nephritis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class V</td>
<td>Global or segmental subepithelial immune deposits or their morphologic sequelae by LM and by IF or EM, with or without mesangial alterations</td>
<td>16.7%</td>
</tr>
<tr>
<td>Class VI</td>
<td>Advanced Sclerosing Lupus Nephritis</td>
<td>0%</td>
</tr>
</tbody>
</table>

*May occur in combination with III or IV, in which case both will be diagnosed
*May show advanced sclerosis

**Methods**

This is a retrospective study done at the Jordan University Hospital where we retrieved cases of lupus nephritis from our files from 2002 – 2010. There were 36 specimens stained with hematoxylin and eosin, PAS, Masson trichrome, and Congo red, and cut at 4 micrometer sections. We also retrieved the immunofluorescence results for these biopsies. No electron microscopic studies were available for these biopsies.

The biopsies were reevaluated and reclassified by two pathologists in the department according to ISN/RPS 2003 classification independently.

**Results**

The 36 specimens belonged to patients with an age range of 14-40 years, where 4 were males and 32 were females.

All the biopsies were consistent with the diagnosis of lupus nephritis with 100% concordance of classification between the two pathologists as follows:

**Table (2): Prevalence of lupus nephritis cases in JUH (2002 – 2010).**

<table>
<thead>
<tr>
<th>Class</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Class II</td>
<td>5</td>
<td>13.9%</td>
</tr>
<tr>
<td>Class IIISA</td>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>Class IVG</td>
<td>11</td>
<td>30.5%</td>
</tr>
<tr>
<td>Class IVS</td>
<td>12</td>
<td>33.3%</td>
</tr>
<tr>
<td>Class V</td>
<td>6</td>
<td>16.7%</td>
</tr>
<tr>
<td>Class VI</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

*See figures [1-6]*

Class IVG was further subdivided into IVGA, 5 cases; IVGA/C, 3 cases; IVGC, 3 cases; IVSA, 6 cases; IVSAC, 6 cases; and IVSG, 0 cases.

The immunofluorescence was consistent with lupus nephritis in all the cases and showed a “full house” pattern in all of them.

*LM= light microscopy; IF= immunofluorescence microscopy; EM= electron microscopy*

Adapted from ATLAS OF NONTUMOR PATHOLOGY, Non-Neoplastic Kidney Diseases, D’Agati V, Jennette J, Silva F, p. 325

**Figure (1):** Class I Lupus Nephritis (40x)

**Figure (2):** Class II Lupus Nephritis (40x)

**Figure (3):** Class IIISA Lupus Nephritis (40x)
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Class I lupus nephritis comprises a minimal number of renal biopsies and may or may not present with clinical symptoms. In one study, lupus nephritis was detected in 373 patients, 179 (48%) were class IV, 63 (16.9%) were class II, 73 (19.57%) were class III, and 74 (19.9%) were class V using the modified WHO classification.11 By adding the number of cases, and the percentages of classes, we find out that the number of cases is more than 373, and the percentages are more than 100%; this could result from the fact that some specimens have combined classes.

In another study of 25 patients having childhood lupus nephritis, most patients were class III (36%) or IV (40%) disease, whereas at follow-up biopsy, they mostly were class II disease (60%).12 Yet in a retrospective analysis of 99 biopsies of lupus nephritis using ISN/RPS classification, the prevalence of each category was as follows: class I, 3%; class II, 13%; class III, 9%; class IVS, 20%; class IVG, 46%; class V, 8%; and class 6, 1%.12

Comparing the prevalence in JUH to the previous studies, it seems that we have a lower percentage of class III and a higher percentage of class IVS. Although Markowitz and D’Agati pointed to the fact that the new ISN/RPS classification of lupus nephritis have led to a significant increase in the number of cases of class IV, with a reciprocal decline in lupus nephritis class III and class V, still the number of class III nephritis in our group is too small. This may reflect racial, socio-economical or seasonal distribution which needs to be verified.

**Conclusion**

Our patient sample with lupus nephritis reclassified according to ISN/RPS classification have a lower percentage of class III and a higher percentage of class IV for reasons to be determined.

**Competing interest statement by all authors:**

No competing interests to declare by any of the authors.

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**Discussion**

A kidney biopsy in an SLE patient with any degree of a clinical renal disease plays an important role in the diagnosis and management.7, 8 It is useful in establishing an initial pathologic diagnosis early during the course of SLE, including the various glomerular lesions and the parameters indicating severity, activity, chronicity, and other concomitant lesions. Such renal biopsies may serve as a baseline for a subsequent course of renal disease and correlation with clinical findings. Sometimes, other SLE related or unrelated renal lesions requiring a different treatment approach9 or “silent lupus nephritis” of varying severity may become evident.10 Such information will enable the clinician to select a specific treatment protocol for an individual patient.
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References


انتشار الأصناف المختلفة لالتهاب الكلية الذاتي

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الملخص
الذبابة الجبهي ومرض جهازي ذاكي المناقة يصيب تقياً جميع أعضاء الجسم. وهناك نسبة حدوث عالية لإصابة الكلية خلال مجرى المرض مع آفات كليوية مرتبطة مختلطة. عملاً بأن الخزعة الكلوية تضيف للتواصل إلى التشخيص، وتضيف معلومات تكاملية، والعلاج المناسب.

الهدف: دراسة نسبة حدوث الأصناف المختلفة لالتهاب الكلية في الذبابة الجبهي في الخزعة الكلوية في مستشفى الجامعة الأردنية.

المنهج: جمع الفريق 36 عينة خزعات كليوية من ملفاتنا في مستشفى الجامعة الأردنية، ثم درسها في شهر حزيران وتموز 2011، وكانت هذه الخزعة كلاماً تتشخيصية الآلاحي الكلي الذاتي، ثم أعدنا دراستها وتصنيفها من قبل اختصاصي علم أمراض.

النتائج: من ال36 عينة، كانت هناك عينة واحدة من صنف I، وخمس عينات من صنف II، وعينة واحدة من صنف III، وعينات من صنف IV، وعينات من صنف V، ولم يكن هناك أي من العينات من صنف VI.

الاستنتاج: صنف VI كان الأكثر حدوثاً في مستشفينا وقليلاً بحسب متساوية، من المرتبة G و S VI. بينما كانت هناك حالة G VI واحد من صنف III. وهذا يعتبر قليلاً جداً بالمقارنة مع الدراسات المنشورة عالمياً.

الكلمات الدالة: الذبابة الجبهي، الجمعية الدولية لأمراض الكلية، الخزعة الكلوية.