

Original Article

Immune Complex Deposition in Certain Forms of Childhood Nephritis

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Abstract

Objectives: To verify the deposition of immune complexes in various types of childhood nephritis.

Methods: This study was carried out in Middlesex Hospital, University College, London and AL-Hussein University Hospital, Cairo, during the period from Dec., 1996 to Nov., 1999. It included 52 patients with nephritis, selected according to certain inclusion criteria to be evaluated histopathologically for determining the intensity of immunoglobulin and complement deposition in the glomeruli as they have the most important role in glomerular injury and progression of the disease process in nephritis. After thorough clinical and laboratory evaluation of all cases, they were divided into three groups: lupus nephritis (20 cases), APSGN (18 cases) and IgA nephropathy (14 cases). Renal biopsies were done for all cases and examined by light, electron and immunofluorescence microscopy.

Results: Our results showed that cases of lupus nephritis were subdivided into: stage II (3 cases), stage III (4 cases), stage IV (11 cases) and stage V (2 cases). There were various amounts of immune complex and complement deposition in all stages (IgG, IgA, IgM, C3, C4 & Cq1). Stage IV lupus nephritis showed the highest intensity of immune complex deposition especially IgG, IgM and C3. These deposits were more marked and more diffuse than in other stages. In APSGN, 16 out of 18 cases (89%) showed mesangial deposits of all immune complexes except C1q. All cases of APSGN showed marked significant deposition of C3 (100%) and C4 (75%). The least was IgA and IgM (3 & 2 cases respectively). All IgA nephropathy patients showed immune deposits in the mesangium and along the capillary wall. IgA was predominantly deposited in all cases (100%) and the second predominant immune complex was C3 (78.6%). There was a strong correlation between intensity of immune complex deposits detected by IF microscopy and the ultrastructural changes found on electron microscopy examination. Also, the degree of immune deposition is related to the severity of nephritis and to the pattern of glomerular damage.

Conclusions: We can conclude that immune complex deposits have both diagnostic and prognostic values for patients with nephritis.

INTRODUCTION

Glomerulonephritis (G.N.) is one of the leading causes of both acute and chronic renal failure in childhood⁽¹⁾.

Various types of G.N. are met with in children and the immunologic injury of the kidney is the most important pathology that results in G.N. The immune complexes accumulate in the glomeruli and activate the

complement system leading to immune injury⁽²⁾.

Glomerular and interstitial macrophage accumulation is the feature of almost all forms of human G.N. and the intensity of macrophage infiltrates correlates with loss of renal function and histological damage. Local macrophage proliferation has an important mechanism of renal injury and it

also has useful diagnostic and prognostic indications for human G.N.⁽³⁾.

Renal biopsy is considered as an irreplaceable tool in assessing diagnosis, prognosis and guiding the treatment of many forms of nephritis. With introduction of ultrasound guided biopsy, renal biopsy became easier and safer⁽⁴⁾.

The aim of this study is to verify deposition of immune complex in various forms of childhood nephritis as they play the major role in the pathogenesis and progression of the disease.

SUBJECTS AND METHODS

This work was carried out in the nephrology department of Middlesex Hospital, University College, London during the period from Dec. 1996 to Nov. 1998 and in the pediatric nephrology unit, Al-Hussein University Hospital, Egypt, during the period from Dec. 1998 to Nov. 1999.

Our study included 52 cases selected from many patients who presented with signs and symptoms of nephritis. Their age ranged from 3 to 18 years. They were 21 males and 31 females.

After clinical and laboratory evaluation of all cases, they were divided into 3 groups: systemic lupus nephritis (20 cases), IgA nephropathy (14 cases) and acute post-streptococcal glomerulonephritis {APSGN} (18 cases).

– Cases of IgA nephropathy were finally diagnosed by biopsy.

Cases were selected according to the following inclusion criteria:

– Atypical presentation of nephritis as in APSGN.

- Persistent hypertension beyond 3 wks.
- Persistent haematuria or proteinuria beyond 6 wks.
- Oliguria and azotemia persisting more than 2 wks.
- Second episode of gross haematuria.
- Anuria.
- Presence of nephrotic syndrome.
- Family history of nephritis and prior history of renal disease.
- Significant systemic symptomatology.

All cases were subjected to the following:

I- Detailed history and clinical examination.

II- Routine investigations including:

a- CBC, ESR, Renal function tests, serum C3 ... etc.

b- Serologic tests for APSGN

c- Detailed urine analysis

d- ANA and dsDNA antibodies for cases with lupus nephritis. Anti Lo & anti Ra were also done.

III- Renal biopsies were done for all cases who fulfilled the inclusion criteria guided by ultrasound.

Biopsies were examined by light microscopy, electron microscopy and immunofluorescent microscopy.

* Light microscopy: Macrophage and monocyte infiltration and thickening of capillary walls (done for all cases).

* Electron microscopy: Ultrastructural damage in the glomeruli (done for selected cases (33 only) who showed specific findings on light and IF microscopy examination).

* Immunofluorescence microscopy: Immune complex deposits (done for all cases)

* All cases of lupus nephritis and IgA

nephropathy and 16 cases of APSGN showed immune complex deposition in the glomeruli.

* Lupus nephritis cases were subdivided into: 3 cases stage II, 4 cases stage III, 11 cases stage IV and 2 cases stage V.

RESULTS

These are shown in Tables (1-4).

Table (1): Light Microscopy results of all studied cases (N^o = 52)

Microscopic Findings	SLE II No. = 3		SLE III No. = 4		SLE IV No. = 11		SLE V No. = 2		APSGN No. = 18		IgA N No. = 14	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Inflammatory Cell Infiltration	3	100	4	100	11	100	2	100	18	100	14	100
Mesangial Cell Proliferation	3	100	4	100					18	100	4	28
Focal Proliferation					5	45					2	14
Diffuse Proliferation					3	27						
Segmental Proliferation					4	36					4	28
Global Proliferation					2	18						
Wire Loop Lesion					5	45						
Capillary Proliferation			3	75			2	100		100	6	43
Endothelial Cell Proliferation									18	100		
Segmental Sclerosis					1	9	2	100				
Segmental Proliferation												
Increased Matrix	2	67									2	14

— All cases show cellular infiltration. Other pathologic changes vary from one group to another and from one stage to another but these changes are more marked in stage IV SLE. These changes are related to the severity of the disease.

Table (2): Immunoperoxidase and immunofluorescence microscopy results in SLE cases (N^o = 20)

Immune deposits	SLE II No. = 3		SLE III No. = 4		SLE IV No. = 11		SLE V No. = 2	
	No.	%	No.	%	No.	%	No.	%
IgG	3	100	1	25	11	100	2	100
IgA	2	67	4	100	9	82	1	50
IgM	3	100	2	50	11	100	2	100
C3	3	100	4	100	9	82	2	100
C4	2	67	1	33	3	27	1	50
Cq1	3	100	2	50	10	91	2	100

CHI-SQUARE = 112.591.

D.F. = 15

PROB. = 4.486E-07

p < 0.001 (H.S.)

- All cases showed immune deposits.
- There is a significant difference between all stages in deposition of certain immune complexes.
- The amount of deposits is strongly correlated with the severity of the disease.

Table (3): Immunofluorescence microscopy results in APSGN cases (N^o = 16*) and IgA nephropathy cases (N^o = 14)

Immune Deposits	APSGN		IgA Nephropathy	
	No.	%	No.	%
IgG	8	50	0	0
IgA	3	19	14	100
IgM	2	12.5	7	50
C3	16	100	11	78.6
C4	12	75	0	0
Cq1			9	64.2
	Chi ² (16.58) p value (0.00233)		Chi ² (10) p value (0.07523)	

- Two out of 18 cases of APSGN showed no immune deposits, while all cases of IgA nephropathy showed deposition of immune complexes.
- C3 and IgA were deposited in all cases of APSGN and IgA Nephropathy respectively.

Table (4): Electron microscopy results of studied cases (N^o = 33)

Findings	SLE II No. = 3		SLE III No. = 2		SLE IV No. = 10		SLE V No. = 2		APSGN No. = 10		IgA N No. = 6	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Mesangial Dense Deposit	2	67	2	100	9	90	2	100	-	-	5	83
Subendothelial Dense Deposit	2	67	1	50	4	40	1	50	10	100	2	33
Subepithelial Dense Deposit	1	50	1	50	6	60	1	50	10	100	2	33
Intramembranous Dense Deposit	1	50	1	50	3	30	1	50				
Glomerular Basement Membrane Hump									10	100		

CHI-SQUARE = 282.496.

D.F. = 15

PROB. = 4.486E-07

p < 0.0001 (H.S.)

* The degree of structural changes correlates with the severity of the disease and distribution of immune deposits.

* Ultrastructural changes are more marked in different stages of SLE than both APSGN & IgA. Nephropathy cases and the difference is statistically significant.

DISCUSSION

This study was carried out on 52 patients presenting with different forms of nephritis. Renal biopsies were done for all cases and examined by light microscopy, immunofluorescence microscopy and electron microscopy. Originally, patients

were divided into: SLE "20 cases", APSGN "18 cases" and IGA nephropathy "14 cases".

Our results showed that interstitial inflammatory cells "macrophages, monocytes, plasma cells and polymorph nuclear leukocytes" were found in all cases. These findings are in agreement with those

reported by Niamsheng et al. (1998)⁽⁵⁾. Also, Akashi, et al. (1995)⁽⁵⁾ found that macrophage monocyte cell levels were significantly higher in the interstitium in lupus nephritis and play an important role in the progression of the disease.

Combined light and immunofluorescence (IF) microscopy examination of SLE cases showed that 3 out of 20 patients (15%) were stage III "pure mesangiopathy". IF examination revealed mesangial IgG, IgA, IgM, C₃, C₄ and C_q dense deposits. These data are consistent with those of Claudio, et al. (1998)⁽⁶⁾ who noted that stage III SLE nephritis cases average 10%-20%, and are characterized by the presence of various amounts of immune complexes and complement deposition in the mesangial area.

Stage III SLE nephritis was detected in 4 out of 20 cases (20%) IF examination showed mesangial deposits of all immune complexes and complement. Claudio, et al. (1998)⁽⁶⁾ reported that class III SLE nephritis cases average 10%-25% of their patients and are characterized by mesangial deposition of IgM, IgG, IgA, C₃, C₄ & C1q.

The present study showed that 11 out of 20 patients with lupus nephritis were class IV and IF examination identified diffuse mesangial, epithelial and subepithelial dense deposits of IgG, IgA, C₃ & C₄. These data agree with those of Thomas and Janet (1994)⁽⁷⁾ who found that class IV lupus nephritis are characterized by abundant deposits of all immunoglobulins and complement.

Stage V lupus nephritis was found in 2 cases only (10%) and IF examination

showed mesangial, subendothelial and subepithelial dense deposits of different immune complexes. These findings approximate those reported by Thomas & Janet (1994)⁽⁷⁾ and Claudio, et al. (1998)⁽⁶⁾.

It is evident from this work that the amount of immune deposits is related to the stage grading and the severity of glomerular affection. Stage IV in our cases showed marked and diffuse deposition of all types of immunoglobulins and complement. Claudio et al. (1998)⁽⁶⁾ stated that the amount and location of deposits are related to the severity and pattern of glomerular changes.

IF examination of APSGN cases showed immune deposition in 16 out of 18 cases (89%).

Significant deposition of C₃ (in 100% of patients) and C₄ (in 75%) were found in our cases. The least deposits were those of IgA & IgM, (3 & 2 cases respectively). These data are supported by those reported by Cynthia (1997)⁽¹¹⁾ who found that granular subepithelial deposits of C₃ in cases with APSGN were more abundant than other types of immune complexes.

All cases of IgA nephropathy (14) showed immunoglobulin and complement deposition in the mesangium and along the capillary wall. IgA was the predominant immunoglobulin deposited in the mesangium in all cases. C₃ was the second predominant one (78.6%).

Feehally (1997)⁽⁸⁾ has given evidence that diffuse mesangial IgA deposition is the defining hallmark for IgA nephropathy. IgM, IgG and C₃ occur less commonly.

The present study showed a strong correlation between immunoglobulin and

complement deposition detected by IF microscopy and the ultrastructural changes on electron microscopy examination.

It has been concluded from this work that renal biopsy should be done when indicated for all patients with nephritis for

evaluation, staging and follow-up. Immune deposits detected by IF microscopy examination are important indicators for assessment and progression of renal pathology in nephritis.

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