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Contribution of Electron Microscopy to the Final Diagnosis of Renal Biopsies in Egyptian Patients

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Abstract There are few publications studying the impact and cost benefit relationship of electron microscopy in the diagnosis of glomerulopathies in routine service. The aim of this study is to assess the contribution of EM to the final diagnosis of renal glomerular diseases in Egyptian patients. Retrospective evaluation of 120 renal biopsy specimens received for primary diagnosis at EM center of Ain Shams university Specialized hospital, Cairo Egypt during 2007in the knowledge of light microscopic, immunofluorescence and electron microscopic findings. It was found that EM was essential for diagnosis in 25% of renal biopsies, corresponding to 100% of hereditary glomerulopathies and 23.5% of other glomerulopathies, It was useful to the dignosis in 41.67% of the cases, confirming the preliminary diagnosis. In 33.33% of cases EM was considered unhelpful in diagnosis. It's concluded that the importance of EM has not decreased during the last years. New glomerular diseases and variants can be diagnosed only by EM as fibrillary glomerulonephritis and immunotactoid glomerulopathy. Routine evaluation of allograft biopsies should include EM to achieve better recognition of capillary lesions of chronic rejection. EM provides useful diagnostic information in about 66% of native renal biopsies. Kidney biopsy protocols should include EM in all biopsy cases. If electron microscopy cannot be performed routinely on all such biopsies, tissue should be reserved for EM studies.

Keywords Renal biopsy · Glomerulonephritis · Electron microscopy

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Introduction

Nephropathology is the only anatomic pathology subspeciality that uses transmission EM for evaluation of specimens. EM allows detailed evaluation of the cellular and extracellular components of each glomerular compartment and assessment of the thickness, contour, and integrity of the glomerular basement membrane (GBM) and mesangial matrix [1].

Recent reports have analysed the routine use of EM critically. Its use in other areas of diagnosis such as tumours has declined considerably; in addition, in view of the unavoidable financial pressure for the reduction of costs due to investigations and diagnostic routines, the selection of cases for EM has been quite rigorous [2].

The objective of the present study was to assess the role of EM in the diagnosis of glomerular diseases in 120 renal biopsies analysed by the same pathologist with the systematic use of light microscopy, immunofluorscence and EM.

Methods

All the renal biopsies received during 2007 at the EM center of Ain Shams University specialized hospital in Cairo-Egypt, were retrieved and reviewed. The age of the patients ranged between 45 days and 65 years (mean 32.5 years). A total of 120 cases were received. The light microscopy, immunofluorscence and EM findings were reviewed for definition of the final diagnosis. Each case was first analyzed using light microscopy and IF findings together with the clinical and laboratory data for the morphological interpretation of the glomerulopathy. These findings were then reevaluated together with the ultrastructural study in order to determine the impact of EM on the

diagnosis of glomerular diseases. At least one glomerulus was examined by electron microscope , not including globally sclerotic glomeruli. The contribution of EM to the final diagnosis was graded as essential- diagnosis could not be reached without it; supportive—it increased the level of confidence in the final diagnosis and non helpful.

Results

Primary glomerulonephritis was observed in 56.67% of the cases, systemic diseases with glomerulonephritis in 35%, hereditary nephropathies in 4.17%, diverse glomerular diseases in 4.17%. There was sharp predominance of IgA nephropathy (16.67%) followed by membranoproliferative glomerulonephritis (10.83%) in the primary glomerulonephritis group and of lupus nephritis (26.67%) in the glomerulonephritis associated with systemic diseases. Of the 120 cases, EM had an essential role in 30 cases (25%), had a helpful or supportive role in 50 cases (41%), and was unhelpful in 40 cases (33.33%).

EM was essential for diagnosis when it revealed important morphological features that had not been clearly observed via light microscopy or IF. (Table 1).

Discussion

The role of EM in renal biopsy diagnosis and has been the subject of several publications. This study was undertaken to assess the contribution of EM to the final diagnosis of renal glomerular diseases in Egyptian patients. The importance of such assessment resides in the fact that most histopathology laboratories in Egypt do not have immunofluorescence capability, and only a minority can use EM which is usually performed in the laboratories of major university hospitals. For Egypt with few resourses, the diagnosis of glomerular diseases needs to be made possible

Table 1 Contribution of electron microscopy to diagnostic categories

	Essential	Helpful	Non helpful	No. of cases
I. Primary glomerulopathies				
Minimal change disease	2	2	1	5
Focal segmental glomerulosclerosis	–	8	–	8
Membranous glomerulonephritis	3	6	–	9
IgA nephropathy	5	15	–	20
Proliferative glomerulonephritis	2	3	2	7
Membranoproliferative glomerulonephritis type I	3	5	5	13
Membranoproliferative glomerulonephritis type II	1	1		2
Crescentic glomerulonephritis	–	2	2	4
Total	16	42	10	68
II. Secondary glomerulopathies				
Lupus nephritis	–	2	30	32
Benign nephrosclerosis	1	3	–	4
Diabetic glomerulopathy	1	1	–	2
Amyloidosis	2	2	–	4
Total	4	8	30	42
III. Hereditary nephropathies				
Alport syndrome	2	–	–	2
Thin basement membrane disease	2	–	–	2
Congenital nephrotic syndrome	1	–	–	1
Total	5			5
IV. Glomerulopathies , miscellaneous				
Eclampsia nephropathy	–	1	–	1
Cryoglobinaemic glomerulonephritis	1	–	–	1
Immunotactoid glomerulopathy	1	–	–	1
Chronic rejection	2	–	–	2
Total	4	1	–	5
			–	Total 120

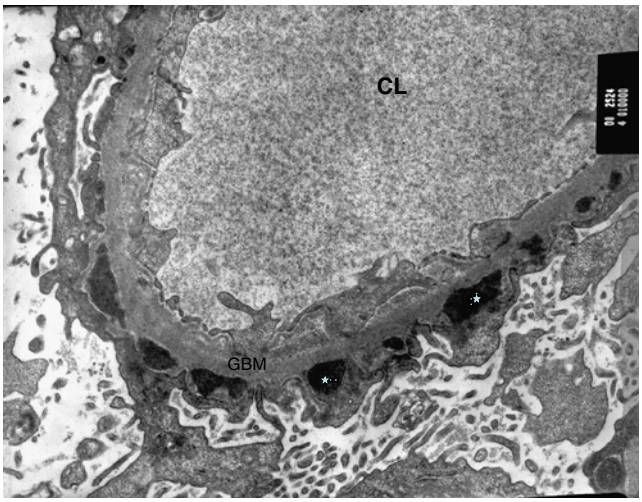

Fig. 1 Membranous glomerulonephritis showing multiple subepithelial electron dense deposits (*). CL (capillary lumen). GBM (glomerular basement membrane)

by first using less expensive methods before employing EM. Several studies provided justification for its use [3–9]. In this study the routine use of EM in conjunction with light microscopy and IF was found to have an essential role in 30 cases (25%), a helpful role in 50 cases(41.67%), In about 33% of cases EM was considered non helpful. These figures are compatible with those cited [3–9]. Pearson et al. in 1994, [10] concluded that EM has an integral role in the diagnosis of renal disease, and tissue should be taken for EM in all cases if possible. In some selected cases, when light microscopy and IF results are already known, the ultrastructural findings could be predicted. Hass in 1997 [11] evaluated the use of EM in the diagnosis of 233 native renal biopsies. He concluded that EM provides diagnostic information in nearly half of native renal biopsies. Wang et al., in 1998 [12] found that EM provided useful diagnostic informations in about one third of renal biopsies. Sementilli et al. [13] studied 200 consecutive renal biopsies via light microscopy, IF and EM, they concluded that EM was essential for the diagnosis in10% of cases.It was contributory in 5.5% of the cases and it was essential for diagnosis of hereditary nephropathies. Moreover Collan et al. [14] found that in biopsies performed for primary kidney disease, EM was essential for diagnosis in 18.3%, clearly contributed in 53.5%, and has no influence on the final diagnosis in 28.2% of cases. EM was considered most useful in the current study in the diagnosis of minimal change disease (2 cases), IgA nephropathy (5 cases) , early membranous nephropathy (3 cases) Fig. 1. Rivera et al. [15] found that EM was essential for the final diagnosis of 73% of renal biopsies of 48 children with nephrotic syndrome, and was supportive in afurther 27%, Therefore they concluded that EM needs to continue to be performed for all these patients. In the three cases that showed focal glomerular changes similar to mesangiocapillary glomerulonephritis, EM established the diagnosis by demonstration of subendothelial electron dense deposits. There are reports of focal or segmental glomerulonephritis [16]. One case diagnosed as type II membranoproliferative glomerulonephritis was diagnosed initially by light microscopy as diffuse proliferative glomerulonephritis, however EM altered the diagnosis by detection of the characteristic deposits.EM led to discovery of this condition (dense deposit disease) which is uniquely different from all other forms of renal diseases. Confirmation of the diagnosis of dense deposit disease require electron microscopy, althought the diagnosis can be suspected with high confidence if the typical light microscopic and immunofluorescence findings are observed, [17]. The diagnosis of three cases of proliferative glomerulonephritis was established by finding the subepithelial deposits (humps). Herrara [18] concluded that IF evaluation alone is incapable of unequivocally discriminating between epi/intramembranous and subendothelial deposits in the majority of situations. Among the systemic diseases, lupus nephritis was the most frequent in which light microscopy and IF are sufficient for adequate definition of the various types of lupus lesions and for identifying active or chronic lesion [19], However Herarra [18] reported that there are several ultrastructural findings that in the proper clinicopathologic context are most suggestive of a diagnosis of lupus include fingerprints in immune-complex deposits, tubuloreticular inclusions, and immunecomplexes along tubular basement membrane, especially with a full-house immunofluorescence profile. The early thickening of the GBM in a case of diabetic nephropathy and a case of benign nephrosclerosis was demonstrated only via EM as reported by Sementilli [13].

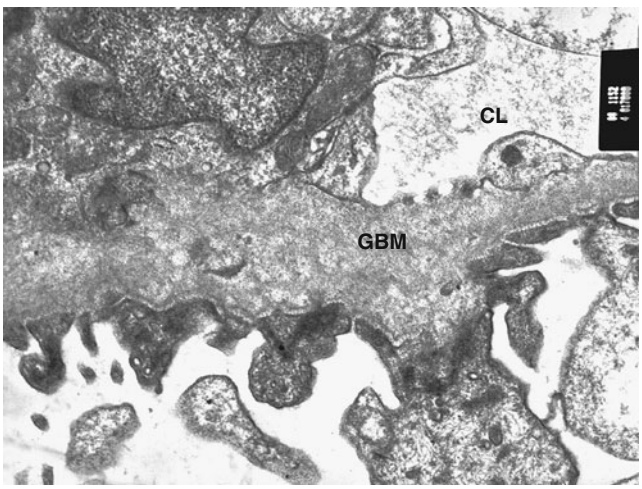

Fig. 2 Alport syndrome showing lamellation of the lamina densa creating the basket weave appearance

In hereditary nephropathies group, EM was essential for diagnosis of all cases. In Alport syndrome glomerular basement membrane exhibits variable thickening with lamellation of the lamina densa creating the basket weave (Fig. 2). In thin basement membrane disease, EM allowed measurement of the thickness of the GBM which is less than 200 nm. In congenital nephrotic syndrome EM demonstrated visceral epithelial cell damage characterized by extensive foot process fusion, microvillous transformation and pseudocyst formation. In hereditary nephropathies EM makes the definite diagnosis. LM can be normal at first and IF is always negative but EM allows documentation of alterations at the glomerular basement membrane level as changes in thickness, contour and integrity [13].

The microtubular configuration in the dense deposit raises the possibility of cryoglobinaemic glomerulonephritis. The finding of parallel fibrils of coss-sectional diameter more than 30 nm was essential for the diagnosis of immunotactoid glomerulopathy. Jennette et al. [1] reported that electron microscopy is particularly useful in diagnosing glomerular deposits that have distinct ultrastructural textures in pathologic glomerular deposits, such as amyloidosis, fibrillary glomerulonephritis, immunotactoid glomerulopathy, cryoglobinaemia, monoclonal immunoglobulin deposition disease, collagenofibrotic glomerulopathy, and fibronectin glomerulopathy.

In the two renal transplant specimens EM was essential for diagnosis of chronic rejection. This agree with Herrara et al. [20]. They reported that there is general agreement among renal pathologists that electron microscopy is of importance in the evaluation of renal specimens from patients with proteinuria to distinguish between transplant glomerulopathy and recurrent or de novo glomerulonephritis in order to correctly manage these patients and to predict survival of the graft.Evanyi et al. [21] concluded that EM search for transplant capillaropathy and transplant glomerulopathy doubled the frequency of diagnosis of chronic rejection. Incorporation of EM into the evaluation of late dysfunction biopsies is strongly recommended because L M per se proved to be insenstive in the diagnosis of chronic rejection.

In conclusion this study suggests that the importance of EM has not decreased during the last few years. Its routine use to evaluate routine renal biopsies is not wasteful even in the current medical economic climate. The EM diagnosis has an impact on the prognosis and mode of therapy of glomerular diseases No treatment have been devised to slow the progressive degeneration of the glomerular basement membrane in Alport syndrome, but patients with Alport syndrome are good candidates for renal transplant therapy as they are young and usually otherwise healthy. Thin glomerular basement membrane is usually not associated with proteinuria or reduction of glomerular filtration rate. Minimal change disease has good response to corticosteroids. EM was considered unuseful when the sample processed for ultrastructural examination contain only globally sclerotic glomeruli or does not contain glomeruli at all. Because only about 33% of the EM reports did not have any influence on the diagnostic process , it is recommended that kidney biopsy protocols should include EM in all biopsy cases or at least tissue should be reserved for EM studies of all cases.

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