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Glomerulonephritis in the elderly

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Abstract. The records of 7086 patients reported to the MRC Glomerulonephritis Registry between 1978 and 1990 were examined; 1368 patients were aged >60 years at the time of biobsy. In 1978 12% of patients aged >60 years underwent biopsy, whereas in 1990 30% of patients were aged >60 years. The most common reasons for biopsy were nephrotic syndrome (31%), acute renal failure (26%) and chronic renal failure (25%). In patients presenting with nephrotic syndrome, the most common histological appearance was membranous nephropathy (36.6%), minimal changes (11%) and amyloidosis (10.7%). Secondary nephrotic syndrome was associated with amyloidosis (32 patients), diabetes mellitus (11 patients) and carcinoma (10 patients). Glomerulonephritis in the elderly is not uncommon and the apparent increasing incidence is most likely due to an increased referral of patients for investigation rather than a true increase in the incidence of this condition.

Key words: elderly patients; glomerulonephritis; nephrotic syndrome

Introduction

There is an increasing number of elderly patients being accepted to renal replacement programmes [1] and as a consequence increasing numbers of elderly patients are being referred for nephrological assessment. The first report of renal biopsy findings in the elderly was by Moorthy and Zimmerman [2] who reported a retrospective analysis of experience in a single centre of 115 patients aged >60 years presenting with renal disease. Since then there have been a number of further reports [3–6]. These reports indicate that glomerular disease in the elderly is not uncommon. The study of Davison and Johnston [5] reported experience from the UK Medical Research Council (MRC) Glomerulonephritis Registry between the years 1978 and 1990 and this confirmed the increasing number of elderly patients undergoing biopsy: of those patients reported in 1978, 12% were >60 years, while in 1990, 30% of patients undergoing biopsy were aged 60 years or greater.

In elderly patients the studies reported so far indicate that the nephrotic syndrome is the most common cause for referral for biopsy, with renal function impairment being a close second. It seems that elderly patients are unlikely to undergo renal biopsy after presenting with asymptomatic proteinuria and/or haematuria. We have examined the records of the MRC Glomerulonephritis Registry to identify the details of patients aged 60 or greater undergoing renal biopsy with particular reference to nephrotic syndrome and renal functional impairment.

Patients and methods

The MRC Glomerulonephritis Registry [7] accumulated clinical and pathological data from 20 centres throughout the United Kingdom on 7086 patients undergoing renal biopsy between 1978 and 1990. Clinical, laboratory and histological data was provided by referring clinicians on standard forms and entered on the operating system of the Leeds University mainframe computer (Amdahl 5860) in the form of 480 character records. The data were transformed and analysed using the SPSS statistical package.

The data files of patients aged >60 years were analysed to identify the indications for renal biopsy and to examine further the clinical characteristics of patients presenting with nephrotic syndrome or renal functional impairment.

Patients were considered to have a nephrotic syndrome if the referring clinician had indicated that this was the principal mode of presentation and, in addition, the 24 h urinary protein excretion was recorded as being >3. 5 g/24 h.

Renal function impairment was not specifically defined in the MRC Glomerulonephritis Registry but the diagnosis was considered if the referring clinician indicated that the clinical indications for biopsy were chronic renal failure or acute renal failure, and this was confirmed by reference to the serum creatinine recorded at the time of biopsy.

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Table 1. Indications for renal biopsy

Presentation	>60 years	21–40 years
Nephrotic syndrome	31%	24%
Acute renal impairment	26%	12%
Chronic renal impairment	25%	12%
Asymptomatic urinary abnormality	8%	35%
Hypertension	1%	2%
Unrecorded	9%	15%
Total	1368	1934

Table 2. Nephrotic syndrome: patient group

Total number	317
Male/female	198:119 (1.7.1)
Mean age	68.2 years
Median creatinine	158 μmol/l
Median proteinuria	8.0 g/24 h
Haematuria	100/297 (34%)
Hypertension[a]	124/314 (39%)

[a]Diastolic pressure >95 mmHg or treatment with antihypertensive medication.

Results

Of the 7086 patients reported to the MRC Registry between 1978 and 1990, 1368 were aged >60 years at the time of biopsy. The indications for renal biopsy in this group are shown in Table 1. For companson the indications for renal biopsy in the patients aged 21–40 years undergoing biopsy for the same time interval are also shown.

Nephrotic syndrome

Of the 1368 patients reported to the Registry, 424 (31%) had the nephrotic syndrome as reported mode of presentation. Of this group, 317 patients satisfied the additional selection criteria of a 24 h protein excretion rate of >3.5g. Details of this patient group are shown in Table 2. The male/female ratio was 1.7:1. The median proteinuria was 8 g/24 h and 124 patients (39%) were hypertensive (a diastolic pressure >95 mmHg or treatment with an antihypertensive medication at the time of biopsy).

Table 3 details the histological findings in this group of 317 patients. As can be seen, the most common causes were membranous nephropathy, minimal change nephropathy and amyloidosis, accounting for 58% of the group. There was, however, as expected, a wide range of histological findings.

A secondary cause for nephrotic syndrome was identified in 103 (32%) patients (Table 4). Of the secondary causes, amyloidosis was the most frequent, accounting for 34 patients. Malignancy was known to be present at the time of biopsy in 15 patients (carcinoma 12, lymphoma 3) and in this group the most frequent histological appearance was membranous nephropathy (Table 5).

Table 3. Nephrotic syndrome: histological appearance

Histological appearance	No.	%
Membranous nephropathy	116	36.6
Minimal change	35	11.0
Amyloidosis	34	10.7
Mesangiocapillary GN	19	6.0
Mesangial proliferative GN	18	5.7
Focal/segmental GN	17	5.4
Focal segmental glomerulosclerosis	16	5.0
Diabetic nephropathy	11	3.5
Diffuse endocapillary proliferative GN	7	2.2
Interstitial nephritis	6	1.9
Benign nephrosclerosis	5	1.6
IgM nephropathy	4	1.3
Crescentic nephritis	3	<1.0
Anti-GBM disease	3	<1.0
Acute tubular necrosis	3	<1.0
IgA nephropathy	2	<1.0
Arteritis	1	<1.0
Unclassified	17	5.4
Total	317	100

Table 4. Secondary nephrotic syndrome

Secondary cause	No.
Amyloidosis	32
Diabetes mellitus	11
Carcinoma	10
Vasculitis[a]	7
Exposure to gold/penicillamine	7
Benign nephrosclerosis	5
Interstitial nephritis	5
Persistent systemic infection (PSI)	4
Hepatitis B—positive serology	3
Lymphoma	3
Exposure to toxic hydrocarbons	3
Systemic lupus erythematosus	3
Acute tubular necrosis	3
Henoch–Schonlein purpura (HSP)	2
Carcinoma + PSI	1
Carcinoma + diabetes	1
Diabetes + HSP	1
Amyloid + gold exposure	1
Amyloid + diabetes	1
Total	103

[a]Including polyarteritis nodosa and Wegener's granulomatosis.

Renal function impairment

At the time of biopsy 348 patients were reported as having chronic renal impairment and 353 an acute renal impairment. The median creatinine in these groups was 532 and 703 μmol/l respectively, confirming significant functional impairment (Table 6).

In the patients with chronic renal impairment, the most common histological findings were benign nephrosclerosis, focal segmental, glomerulonephritis,

Table 5. Malignancy-associated nephrotic syndrome

Histological appearance	Carcinoma	Lymphoma
Membranous nephropathy	6	2
Minimal change	2	1
Proliferative GN	2	–
Focal segmental glomerulosclerosis	1	–
Diabetic nephropathy	1	–

Table 6. Clinical details of patients presenting with renal functional impairment

	Acute renal impairment	Chronic renal impairment
Number	353	348
Male/female	1.4:1	1.6:1
Mean age (range)	68 (60–88)	67 (60–85)
Median creatinine	703	532
Median proteinuria	0.7	1.1
Hypertensive	30%	49%
Haematuria present	56%	38%

crescentic glomerulonephritis and interstitial nephritis. Idiopathic glomerulonephritis was considered to be present in 21% and secondary glomerular disease in 63% (16% being unclassified). In the patients presenting with acute renal insufficiency the most common histological appearances were crescentic glomerulonephntis (61 patients), interstitial nephritis (43), focal segmental glomerulonephritis (40) and acute tubular necrosis (34). Of the 353 patients with acute renal impairment, 121 were considered to have secondary glomerulonephritis (systemic vasculitis 55, malignancy 37, and diabetic nephropathy 14). Systemic vasculitis consisted of microscopic polyarteritis (33 patients), Wegener's granulomatosis (13) and polyarteritis nodosa (11). Patients with malignancy were paraproteinaemia (17 patients), carcinoma (17) and lymphoma (3).

Discussion

All recently published reports indicate that, contrary to previous opinion, glomerulonephritis is not uncommon in elderly patients. There is no reason to believe that the incidence of glomerular disease in the elderly is increasing and all the evidence would suggest that the increasing number of elderly patients undergoing biopsy are a reflection of increasing referral rates.

Nephrotic syndrome is a common mode of presentation of glomerular disease in the elderly, and deserves to be investigated in a manner similar to that undertaken in younger patients [8]. Many different histological appearances can be identified but that most frequently seen is membranous nephropathy similar to that reported in younger adult patients with nephrotic syndrome [9]. Although minimal change nephrotic syndrome is usually described as a condition of childhood and adolescence it is not uncommon in adults [10,11], and in our series was the second most frequent glomerular abnormality. In our study mesangiocapillary glomerulonephritis was relatively common (19 patients), whereas previous reports have suggested that this is rare [12]. Some other histological appearances were not surprising by their paucity. For instance, IgA nephropathy was present in only two of the 371 patients presenting with nephrotic syndrome. This is perhaps not so surprising as nephrotic syndrome, although recognized, is a relatively uncommon presentation of IgA nephropathy.

Table 7. Renal functional impairment: most common histological findings (as percentage of total in each group)

	Chronic	Acute
Benign nephrosclerosis	14	6
Focal/segmental GN	13	11
Crescentic GN	10	17
Interstitial nephritis	9	12
Acute tubular necrosis	1	10
Paraproteinaemia	6	5
Amyloid	5	1

A secondary cause of nephrotic syndrome was present in 103 of the 307 patients (32%), a figure that accords well with other reported series [11,13]. The most common cause of secondary nephrotic syndrome was renal amyloidosis. Similarly a malignancy-associated nephrotic syndrome was common, and was generally associated with membranous nephropathy. It should be remembered, however, that malignancy may manifest itself after the development of nephrotic syndrome and, as the present series is based on features present at the time of biopsy, suggests the prevalence rate may be a significantly greater.

Renal impairment in elderly patients undergoing renal biopsy was associated with four clinical situations: systemic disease, hypertension, interstitial nephritis and malignancy. The most frequently seen systemic disease in both patient groups was systemic vasculitis. The finding that systemic vasculitis is a leading canse of acute renal impairment in elderly patients is in keeping with the findings of previously reported series. Moorthy and Zimmerman [2] reported that of 32 patients with acute renal impairment, 24 had either crescentic nephritis, Wegener's granulomatosis or 'vasculitis'. Similar findings were also reported elsewhere [3,14,15].

In elderly patients with chronic renal impairment the most common biopsy finding was hypertensive nephrosclerosis. This is not surprising as hypertension becomes increasingly common with increasing age. Cox [16] reported a prevalence of 30% in those aged >60 years. A diagnosis of hypertensive nephrosclerosis, however, is not without difficulty as sclerosis may be seen in patients with ischaemic nephropathy secondary to renal vascular disease [17], and in addition, glomerulosclerosis is a condition common to end-stage renal

disease of widely different aetiology, and may be a consequence of ageing [18].

Interstitial nephritis was frequently seen in patients with either acute or chronic renal impairment. This may well be due to polypharmacy, particularly with diuretics and non-steroidal anti-inflammatory drugs, as elderly patients with multiple pathologies are frequently prescribed a treatment regimen involving multiple agents. To this must be added the fact that drug metabolism and renal excretion is altered in the elderly, increasing the risk of drug toxicity [19].

Not surprisingly malignancy-associated glomerular disease is relatively common. Paraproteinaemia (in particular myeloma) was most common in the patients presenting with acute renal impairment, whilst carcinoma was the most common association in patients with chronic renal impairment.

In conclusion, renal biopsy findings in elderly patients present few surprises. Conditions that are more common in the elderly—hypertension, paraproteinaemia and amyloidosis—as expected, are more frequently encountered than in younger patients. Interstitial nephritis occurs commonly and is most likely due to a combination of ageing and multiple drug therapy. These expected findings are increasingly being reported due to the increasing referral of elderly patients for investigation of urinary and/or renal functional abnormalities. Renal biopsy is thus an important investigation in the assessment of the elderly with renal functional or urinary abnormalities in view of the frequent finding of reversible pathology.

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