Childhood Nephrotic Syndrome in Ilorin

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Summary

Adedoyin OT, Gbelee HOD, Adeniyi. Childhood Nephrotic Syndrome in Ilorin. Nigerian Journal of Paediatrics 2001; 28:68. A cohort of 17 children (12M:5F), aged 3-16 years, with nephrotic syndrome seen at the University of Ilorin Teaching Hospital, Ilorin, between January 1995 and December 1998 were studied. Renal biopsies were performed in eight patients. Five (63 per cent) of the biopsies showed focal mesangial proliferative glomerulonephritis while one each showed minimal change, membranoproliferative, and mesangial proliferative glomerulonephritis on light microscopy. Only three (17.6 per cent) of the 17 patients were steroid responsive, while six (35 per cent) were steroid resistant. The predominant histological finding in the steroid resistant cases was focal mesangial proliferative lesion. Case fatality rate was 12 per cent from two deaths. The histopathological findings in the two patients who died of end-stage renal disease, consisted of minimal change lesion and membranoproliferative glomerulonephritis, respectively.

Introduction

CHILDHOOD nephrotic syndrome whose aetiology is varied, presents features which make diagnosis relatively easy. Advances in molecular biology and HLA phenotyping have afforded better insight into the pathogenesis of the various histological types of renal disease manifesting as nephrotic syndrome. In temperate countries, the minimal change nephropathy, which is usually steroid responsive and occurs in younger age groups, is the commonest histological picture associated with nephrotic syndrome (NS). Conversely, in the Tropics where the syndrome occurs in the older age group and is largely unresponsive to steroids and other agents, a range of histological types have been described, and some of these have been identified with Plasmodium falciparum. The trend then is towards progressively worsening nephropathy and end stage renal disease within 5-10 years of diagnosis. In East and West Africa where considerable studies have been carried out, NS is associated in most cases, with structural glomerular damage, non-selective proteinuria and deposition of immune complexes of IgG, IgM and C3 classes. Plasmodium malariae and Plasmodium falciparum specific immune complexes deposits have also been identified in a significant number of cases. Reviews of the histological characteristics of NS in Nigeria showed significant differences between the patterns seen in the north and south of the country. Nigeria’s expansive land mass spans across dense tropical rain forest in the south through savannah grassland in the middle belt to arid, dry semi desert in the far north. A predominance of membranoproliferative glomerulonephritis (MPGN) followed by quartan malaria nephropathy (QMN) has been reported in the northern states. Furthermore, cases of focal mesangial proliferative glomerulonephritis are now being reported where QMN was previously reported. Nonetheless, idiopathic NS continues to be found in most centres where it remains true to form as steroid sensitive and occurring in the younger age. This emergent information has prompted a study of the problem as seen at the University of Ilorin Teaching Hospital situated strategically in the middle belt of the country at the edge of the rain forest and expansive savannah grassland. This communication presents the clinical, biochemical and histological features of cases seen at our paediatric nephrology clinic over a three and a half year period in order to cover both rainy and dry seasons of the year.

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Patients and Methods

The patients consisted of 17 children who satisfied the clinical and biochemical criteria for the diagnosis of nephrotic syndrome and were seen between January 1995 and December 1998. These criteria consisted of the presence of significant oedema, heavy proteinuria >2.0 g/24 hours of urine and serum albumin less than 2.5 g/dl. Investigations undertaken on these patients included (a) urinalysis using the Multistix which evaluated the level of proteinuria, haematuria, pH and specific gravity of the urine, (b) plasma electrolytes, urea and creatinine levels (c) urine microscopy, culture and sensitivity (d) complete blood counts, (e) blood culture and (f) renal biopsy. During the period of study, there were industrial actions by health workers in the country, for about three months each, in 1995 and 1998, respectively, and this disrupted investigations and follow up of cases. Thus, for technical and financial reasons, renal biopsy was possible in only eight cases.

All the 17 patients were managed conservatively, with thiazide diuretics and spironolactone for the oedema. They were also commenced on oral steroid therapy in form of prednisolone at 2mg/kg up to a maximum of 60mg daily in three divided doses. The duration of the steroid therapy in each patient varied, depending on the response. Those who were steroid responsive received the drug for between 3 and 6 months on alternate days after an initial one month daily dosage therapy to induce remission. For those who were steroid resistant, therapy was maintained for 2 to 4 weeks.

Results

The 17 patients (12 males and five females) were aged, 3-16 years (mean, 8.8 years). There were 12 (70.5 per cent) patients in the 3-10 years age group, and five (29.5 per cent) in the 11-16 years age group. The range of urinary pH was 6.0-8.0 with a mean of 6.9, while that of urinary gravity was 1010-1025 with a mean of 1017 (Table I). Urinary white blood cells were >5 per high power field in three (17.6 per cent) patients (Table II), and coliform organisms were cultured in the urine in one of the three. This particular patient who did not undergo a renal biopsy, defaulted from follow up; consequently, the steroid response status was not known. Table I also shows the range and mean values of sodium, potassium, urea and creatinine; these were normal in most cases. The mean packed cell volume was 36 (range 27.45; Table I), while Plasmodium malariae was identified in the blood film in one patient who did not undergo renal biopsy and was subsequently lost to follow up (Table II). Plasmodium falciparum was obtained from the blood film in three patients (Table II). One of the three had renal biopsy that revealed focal mesangial proliferative glomerulonephritis; this patient defaulted early, and the steroid response status was not known, while the third case was steroid resistant. Five (63 per cent) of the eight renal biopsies performed showed focal mesangial proliferative glomerulonephritis.

Only three (17.6 per cent) of the 17 patients were steroid responsive. Six (35 per cent) were steroid resistant including a 10-year old child whose biopsy was reported as showing minimal change on histology, and who later died. Renal biopsies were obtained in five of the six steroid resistant patients. Three of them had focal mesangial proliferative glomerulonephritis, one minimal change lesion; and the third had membranoproliferative glomerulonephritis (Table II).

The remaining eight (47 per cent) defaulted and were lost to follow-up but all of them had a minimum of four weeks of steroid therapy without clearance or even reduction of proteinuria as at the time of default. They were presumed to have steroid resistant NS as they still had massive proteinuria. Case fatality rate was 12 per cent from two deaths. The histopathological classification of the renal biopsy in the two patients that died included the one reported as being of minimal change and the other, membranoproliferative glomerulonephritis. The cause of death in both was

| Table I |
|------------------|------------------|------------------|------------------|
| **Urine pH**     | **Urine Sp. Gravity** | **Serum Sodium (mmol/l)** | **Serum Potassium (mmol/l)** | **Serum Urea (mmol/l)** | **Serum Creatinine (mmol/l)** | **PCV (%)** |
| **Meq**          | 6.9              | 1017             | 135.5            | 3.8              | 6.1                | 93.4     | 36 |
| **Range**        | 6.0-8.0          | 1010-1025        | 126-145          | 3.3-5.4          | 2.9-13.0           | 23-420   | 27-45 |
Table II

Steroid Responsiveness and other Characteristics in 17 Patients with Nephrotic Syndrome

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Renal Histology</th>
<th>Steroid Response Status</th>
<th>P. malariae</th>
<th>P. falciparum</th>
<th>Pyuria (&gt;5 wbc/lpf)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Focal mesangial proliferative (FMP)</td>
<td>Resistant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>FMP</td>
<td>Resistant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>FMP</td>
<td>Resistant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>FMP</td>
<td>Defaulted</td>
<td>-</td>
<td>Positive</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>FMP</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Membrano-proliferative</td>
<td>Resistant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>Mesangio-proliferative</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Minimal change</td>
<td>Resistant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Died</td>
</tr>
<tr>
<td>9</td>
<td>No renal biopsy</td>
<td>Responsive</td>
<td>-</td>
<td>Positive</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>No biopsy</td>
<td>Responsive</td>
<td>-</td>
<td>-</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>No biopsy</td>
<td>Responsive</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>No biopsy</td>
<td>Resistant</td>
<td>-</td>
<td>Positive</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>No biopsy</td>
<td>Defaulted</td>
<td>-</td>
<td>Positive</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>No biopsy</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>No biopsy</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>No biopsy</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>No biopsy</td>
<td>Defaulted</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Note: "Defaulted" implies that the patient stopped attending for follow-up after initial regular attendances for a period of time.

wbc/lpf = white blood cells per high power field

end stage disease from chronic renal failure.

Discussion

Although this study involved a small number of patients, it nevertheless, represents an attempt at defining the common histological patterns of the various renal lesions presenting as NS in the middle-belt of Nigeria. It is worth noting that previous efforts along this line except for a few studies only went as far as classifying NS according to response to therapy. This study outlines histological classification of 17 patients on light microscopy. Our inability to examine the renal biopsy specimens obtained under electron microscopy and also carry out immunofluorescent studies limits the interpretation of our data.

Comparing our findings with those reported by others, the male preponderance observed in the present series is similar to that reported by others, although a study from Port Harcourt had shown no sex difference. Furthermore, most of the patients in this series (70.5 per cent) were aged 10 years or less, a finding that is similar to the 78.7 per cent reported from Enugu. The rate of eight (47 per cent) renal biopsies out of a possible 17 in this series, was relatively high, considering that in some Nigerian studies, very few or no renal biopsies were carried out.

Four histological groups (focal mesangial proliferative, mesangial proliferative, minimal change and membranoproliferative) were identified in this small series with a preponderance of focal mesangial proliferative lesion, which accounted for 63 per cent of the histological types in the eight patients biopsied. This contrasts with a preponderance of quartan malaria nephropathy (QMN) in the Ibadan series and membranoproliferative glomerulonephritis (MPGN) in the Zaria series, although a sizeable 34 per cent of the Zaria series had QMN. However, in consonance with findings in Ibadan and Zaria, minimal change lesion was not prominent in our series in which only one out of the eight renal biopsies carried out had minimal change nephropathy. It is worthy of note that electron microscopy and immunofluorescence tech-
niques were used in the analysis of the specimens in the Ibadan and Zaria series, which was not the case in this study; this may therefore, have accounted for the rarity of QMN in our series, a rarity which has however, also been documented in Ghana \(^{19}\) and South Africa.\(^{20}\)

The only patient with minimal change lesion in this series was a 10-year old boy whose initial histology indicated minimal change lesion but who never responded to steroids but rather, started deteriorating about six months after diagnosis, with persistent hypertension, chronic renal failure and ultimately end stage renal failure and died. This clinical progression naturally raised doubts about the histology report but a repeat biopsy could not be carried out because of the complication of chronic renal failure that had already set in. It is suspected that the child may have subsequently developed a worse histological type in keeping with similar findings by McGovern\(^{21}\) in which nine patients who were initially classified as minimal change lesion subsequently developed focal glomerulosclerosis and six of them died.

The trend of the histology of NS in Nigeria indicates that there may well be distinctive predominant histological types in the various regions. While MPGN appears to predominate in Zaria\(^{8}\) (northern Nigeria), QMN predominates in Ibadan\(^{19}\) (western Nigeria) and, as the present series shows, focal mesangial proliferative lesion may be the predominant histological type in Ilorin (middle belt of Nigeria). The number in our series is however, too small to draw a valid conclusion. With regard to response to therapy, only 17.6 per cent in our series could be said to have achieved remission following steroid therapy. This rate was low when compared to 23 per cent and 56 per cent remission rates obtained in Port Harcourt\(^{15}\) and Ghana\(^{30}\) respectively, using steroids only, but it is similar to that reported from Zaria\(^{8}\) and Ibadan.\(^{19}\) These rates are in contradiction to much higher remission rates of 77 per cent in Jordan\(^{27}\) and 80 per cent reported from the western world.\(^{25}\) These contrasting figures are understandable since there is a preponderance of the usually steroid-sensitive Minimal Change Nephrotic Syndrome in these areas.

A case fatality rate of 12.2 per cent over a three and a half-year follow up period in this study, is comparable to the 12.2 per cent reported in a five-year follow up period by Hendrickse in Ibadan,\(^{24}\) and the 13 per cent in a two and a half-year follow up period in Enugu,\(^{11}\) but higher than 5.5 per cent over a 12.5-year follow up in Enugu.\(^{14}\) The cause of death in our two patients was end stage renal disease following chronic renal failure and this was similar to the cause in some of the patients in the Emugu,\(^{14}\) Zaria,\(^{8}\) and Ibadan\(^{24}\) series and indeed, elsewhere.

Our observations over the years have indicated that there are high follow-up default rates associated with chronic diseases in children who need prolonged and sometimes, expensive care in Nigeria. Poverty, ignorance and frustration seem to account for such defaults resulting in incomplete, inadequate or partial treatment as seen in this series. This leads to rapid deterioration and death in many cases. It has also been observed that sometimes, parents seek or try alternative therapy from traditional healers and only turn to the hospital when the condition becomes terminal. In recent times, this scenario has been aggravated by intermittent strike actions by health workers leading sometimes, to loss of confidence in the hospital system by patients and their relations. During the years of this study, there were two prolonged industrial actions in 1995 and 1998 respectively, and these resulted in the virtual closure of many hospitals in the country, ours included, for about six months. One way out is the active involvement of social workers in the management of chronic illnesses like nephrotic syndrome. They could help to collect reliable and traceable addresses of these patients and their families; such information would aid home visits should they become necessary. Meanwhile, there is a need for an ongoing, more detailed and prospective study to elucidate more clearly, differences if any, in childhood nephropathies seen in the vast ecological expanse of Nigeria especially in the middle belt zone, sandwiched as it is, between the rain forest of the south and the dry zones of the north.

References


