ACUTE DIFFUSE GLOMERULONEPHRITIS WITH THE NEPHROTIC SYNDROME

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Most cases of the nephrotic syndrome — marked oedema, heavy proteinuria, hypoalbuminaemia and hypercholesterolaemia — are associated with subacute or chronic renal diseases such as membranous or proliferative glomerulonephritis, diabetic glomerulosclerosis, systemic lupus erythematosus, amyloidosis or renal venous hypertension. That the nephrotic syndrome may be associated with the acute renal condition, acute diffuse glomerulonephritis, is not generally recognized. We are therefore reporting 4 patients with this association, in which the diagnosis of acute nephritis was proved on renal biopsy.

CASE REPORTS

The 4 subjects were urbanized Johannesburg Bantu and were studied at Baragwanath Hospital. The initial laboratory investigations quoted in the case reports were carried out within 1 or 2 days of admission to hospital. Renal biopsy was performed by the percutaneous method.[1] In all cases treatment in hospital consisted of a standard regime of bed-rest, low-salt diet, chlorothiazide diuretics and penicillin.

Case 1

F.S., a 20-year-old male, was admitted to hospital complaining of throbbing headache, vomiting, blurring of vision, and swelling of the feet for 1 week. On examination there was considerable peri-orbital, ankle and sacral oedema, and the blood pressure was 186/114 mm.Hg. The left ear-drum was injected. Proteinuria varied between 1 and 4 G. per litre (Esbach) and microscopy of the urine showed 20 - 25 red blood cells, 5 - 10 pus cells, and numerous hyaline casts per high-power field. The haemoglobin level was 20 G. per 100 ml., and the erythrocyte sedimentation rate (ESR) 36 mm. in 1 hour (Wintrobe). The blood-urea, serum-cholesterol, and serum-albumin levels were 31 mg., 405 mg., and 1·3 G. per 100 ml., respectively, and the antistreptolysin O titre was 500 units per ml.

Renal biopsy, performed 1 month after the onset of symptoms, showed swelling of all the glomeruli and moderate proliferation of the epithelial and endothelial cells. The basement membrane of the glomerular capillaries was focally thickened.

On treatment with the standard regime, the patient lost 20 lb. in weight in 4 weeks and was discharged with a blood pressure of 130/80 mm.Hg, minimal oedema and proteinuria of 1 G. per litre. On follow-up examination 9 months later, he was clinically and biochemically normal. Repeat renal biopsy showed no pathological changes.

Summary. This patient had acute diffuse glomerulonephritis and the nephrotic syndrome; 9 months later he had recovered clinically, biochemically and pathologically.

Case 2

T.M., a male aged 30 years, was admitted with a history of swelling of the whole body, non-productive cough, and effort dyspnoea for 2 days. On examination the temperature was 99°F. and the blood pressure was 200/110 mm.Hg. He was in congestive cardiac failure and oedema was generalized and marked. Proteinuria varied between 1 and 15 G. per litre, and microscopy of the urine showed hyaline and granular casts, and about 20 red cells per high-power field. The haemoglobin level was 13 G. per 100 ml., the white-cell count 12,300 per c.mm. (of which 67% were polymorphonuclear cells), and the ESR 25 mm. in 1 hour (Wintrobe). The blood-urea, serum-cholesterol and serum-albumin levels were 87 mg., 320 mg., and 1·5 G. per 100 ml., respectively.

In addition to the standard regime of therapy, the patient was digitalized and lost 18 lb. in weight in 2 weeks. Renal biopsy, performed 3 weeks after the onset of symptoms, showed swelling and ischaemia of all the glomeruli, marked proliferation of the endothelial and epithelial cells, and numerous polymorphonuclear leukocytes within the glomerular tufts. Many hyaline casts were present in the tubules.

On discharge from hospital 5 weeks after admission, the patient was clinically normal apart from a proteinuria of 1 G. per litre. When seen 6 months later he was still clinically well and examination of the urine and the blood biochemistry was normal. Repeat renal biopsy showed that the swelling, ischaemia and leukocytic infiltration of the glomeruli had disappeared, but the endothelial and epithelial proliferation, although less, was still present.

Summary. This patient had acute diffuse glomerulonephritis presenting with congestive cardiac failure and the nephrotic syndrome; 6 months later he was clinically and biochemically normal, but pathologically, proliferative glomerular changes were still present.

Case 3

R.M., a 19-year-old female, complained of cough productive of white sputum, hoarseness, effort dyspnoea, headache, and swelling of the face and legs for 1 week. On examination the temperature was 99·2°F. and the blood pressure 170/120 mm.Hg. Ankle oedema was marked and numerous rhonchi were heard throughout both lung fields. Proteinuria ranged between 1 and 12 G. per litre, and microscopy of the urine showed 10 - 15 red cells and occasional hyaline casts per high-power field. The haemoglobin level was 12·4 G. per 100 ml. The blood-urea, serum-cholesterol, and serum-albumin levels were 60 mg., 245 mg., and 1·5 G. per 100 ml., respectively.

The patient responded rapidly to the standard regime of treatment and, on discharge 2 weeks after admission, was clinically normal apart from minimal oedema and proteinuria of 1 G. per litre. Six weeks later, however, she was readmitted with all her original symptoms. On examination she was apyrexial, the blood pressure was 110/70 mm.Hg, and numerous rhonchi were again present in the chest. Oedema was gross and generalized, proteinuria varied between 0·5 and 9 G. per litre, and urinary microscopy showed numerous erythrocytes and pus cells. Culture of the urine yielded a growth of *B.coli*. The blood-urea, serum-cholesterol, and serum-albumin levels were now 30 mg., 285 mg., and 1·5 G. per 100 ml., respectively.

Renal biopsy, performed about 2 weeks after this second admission to hospital, showed that all the glomerular tufts were swollen and bloodless, the endothelial and epithelial cells were markedly increased in number, and the basement membrane of the glomerular capillaries was diffusely thickened.

Response to the standard regime was again rapid and, on discharge 4 weeks after admission, the patient was clinically normal. Eleven months later she was still well clinically. Biochemically she was also normal, but an attempt at repeat renal biopsy was unsuccessful.

Summary. This patient had acute diffuse glomerulonephritis with one relapse, in which both the original attack and the

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relapse were associated with the nephrotic syndrome. She was clinically and biochemically normal 11 months after the relapse.

Case 4

J.M., a male aged 43 years, complained of swelling of the whole body for 9 days and frontal headache for 1 day. Three weeks previously he had contracted a 'cold'. On examination the temperature was 99°F. and the blood pressure 165/90 mm.Hg. Oedema was marked and generalized. Proteinuria varied from 2 to 6 G. per litre, and there were numerous erythrocytes and hyaline and granular casts on microscopy of the urine. The haemoglobin level was 16·7 G. per 100 ml. and the ESR was 31 mm. in 1 hour (Wintrobe). The blood-urea, serum-cholesterol, and serum-albumin levels were 25 mg., 415 mg., and 0·67 G. per 100 ml., respectively.

On renal biopsy, performed 2 weeks after the onset of oedema, all the glomerular tufts were swollen, the epithelial and endothelial cells were moderately increased in number, and the basement membrane of the glomerular capillaries was diffusely thickened. The tufts were mildly infiltrated with polymorphonuclear leukocytes and the tubules contained numerous hyaline casts.

On the standard regime of therapy, the patient lost 20 lb. in weight in 2 weeks. On discharge 3 weeks later he was free of oedema and normotensive, but still had a proteinuria of 2 - 3 G. per litre, and had 10 - 20 red cells per high-power field on microscopy of the urine. When seen one year later he was asymptomatic, but the blood pressure had risen to 200/120 mm.Hg. The urine contained 0·5 G. per litre of protein and 10 - 15 red cells per high-power field on microscopy. The blood-urea, serum-cholesterol and serum-albumin levels were normal. An attempt at repeat renal biopsy failed.

Summary. This patient had acute diffuse glomerulonephritis and the nephrotic syndrome, in which disappearance of the syndrome was followed by persistent haematuria and proteinuria and the development of hypertension, indicating progression to chronic glomerulonephritis.

DISCUSSION

The clinical, laboratory and pathological findings in these 4 cases leave no doubt that they were examples of acute diffuse glomerulonephritis complicated by the presence of the nephrotic syndrome. They thereby differed from the average case of acute nephritis, in which oedema and proteinuria are not severe, and hypoalbuminaemia and hypercholesterolaemia are slight or absent.[2]

The association of acute nephritis and the nephrotic syndrome is not generally recognized; we have been able to find only 3 reports in the British and American literature.[3-5] Wilson and Heymann[3] studied 111 White children with acute nephritis and found 5 in which this association occurred. Leather[4] reported 5 patients, 4 children and 1 adult, among Uganda Africans, in whom the diagnosis of acute nephritis was proved on renal biopsy. Parrish *et al.*[5] described a single patient.

The nephrotic syndrome in acute nephritis differs from the common forms of the syndrome caused by subacute or chronic renal disease in at least 2 respects. Firstly, it has a far more favourable prognosis. In all 4 cases reported here, the nephrotic syndrome disappeared over a period of several weeks or months. In 3 patients this was associated with complete clinical resolution of the acute nephritis. In 1 of these the follow-up renal biopsy was normal, in another all the changes except the endothelial and epithelial proliferation had disappeared, while in the third the attempt at repeat renal biopsy failed. In the fourth patient the disappearance of the nephrotic syndrome was followed by the development of signs suggesting progression to chronic glomerulonephritis. All 5 patients of Wilson and Heymann[3] recovered completely over an average period of 5 months. Of Leather's[4] 5 patients, 1, a child, made a full clinical recovery after 18 months. Another, an adult, improved considerably over a 3-week period in hospital. The outcome of the remaining 3 patients could not be assessed from the data in Leather's paper. The patient of Parrish *et al.*[5] recovered completely, apart from residual thickening of the basement membrane of the glomerular capillaries on follow-up renal biopsy. By contrast with this generally favourable picture, the prognosis of the nephrotic syndrome in subacute or chronic renal disease, in adults particularly, is usually poor.

Secondly, the genesis of the hypoalbuminaemia appears to be different in the acute and chronic forms of the nephrotic syndrome. In the chronic forms it would be generally agreed that, although factors such as increased catabolism of albumin may play a part,[6] the primary and principal cause of the hypoalbuminaemia is prolonged and heavy loss of albumin in the urine.[2] In acute nephritis with the nephrotic syndrome, urinary losses of albumin may be a factor in perpetuating an already established hypoalbuminaemia, but they do not satisfactorily explain the development of a severe degree of hypoalbuminaemia within a matter of a few days. Thus, all 4 of our patients *presented* with pronounced hypoalbuminaemia, yet the interval between the onset of symptoms and the time of presentation was only 2 - 9 days. The hydraemia of acute nephritis may account for part of this hypoalbuminaemia, but for the rest, other factors such as increased degradation or decreased synthesis of albumin must be postulated. It is of interest that the dissociation between the degree of hypoalbuminaemia and albuminuria has also been observed in the nephrotic syndrome produced experimentally in rats by the injection of nephrotoxic serum; hypoalbuminaemia often appeared at a time when the urinary excretion of albumin was negligible.[7]

SUMMARY

Four patients with acute diffuse glomerulonephritis associated with the nephrotic syndrome are described. Three patients made full clinical and biochemical recoveries. In the fourth, the nephrotic syndrome disappeared, but signs suggesting progression to chronic glomerulonephritis developed. The hypoalbuminaemia of the nephrotic syndrome in acute nephritis cannot be adequately explained by loss of albumin in the urine.

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