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THE NEPHROTIC SYNDROME IN PREGNANCY

RENAL BIOPSY STUDIES

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The association of the nephrotic syndrome and pregnancy is not uncommon in the urbanized Johannesburg African, and previous communications[1,2] have dealt with the clinical aspects of this condition. The purpose of the present paper is to report on the renal pathology underlying the syndrome.

MATERIAL AND METHODS

Seven patients were included in this study, from all of whom renal biopsy material was obtained. These patients constitute 25% of all the pregnant nephrotic patients we have seen to date. All the patients studied satisfied the conventional criteria for the nephrotic syndrome, presenting with marked oedema, proteinuria, hypo-albuminaemia and hypercholesterolaemia, in the absence of hypertension or azotaemia (Table I). All were first seen and diagnosed during pregnancy. Two patients stated that the onset of the oedema was in the first month of pregnancy and 2 said it was in the second month. In 2 cases oedema was first noted 2 years before conception and in 1, 4 months before. Six patients were delivered of full-term, normal infants. The seventh was delivered of twins in the 37th week of pregnancy. One of these twins died of asphyxia following an internal version and breech extraction for a transverse lie. None of the cases was complicated by hypertension (defined as a blood pressure greater than 120/80 mm.Hg) or impairment of renal function during the period of observation. After delivery the full syndrome was still present in all cases. The oedema, however, usually regressed shortly after delivery. In all cases treatment of the oedema consisted principally of bed rest, a high-protein, low-salt diet and chlorothiazide. Steroid therapy was not given.

Percutaneous renal biopsy[3] was performed either during the first half of pregnancy or in the postpartum period. In 2 cases biopsy was done twice, at the 16th week of pregnancy and again after delivery.

Biopsy material was fixed in formol sublimate and sections were cut at 5μ thickness. Slides were stained with haematoxylin and eosin, the periodic-acid Schiff technique, and elastic-Masson when necessary. Unfortunately there was insufficient material in the biopsy specimens for frozen sections to be examined for fat.

PATHOLOGICAL FINDINGS

Table II summarizes the main pathological findings in the 7 subjects.

All cases showed essentially similar features, the appearances being those of the Ellis type II or membranous glomerulonephritis. The most striking change was seen in the glomerular basement membrane which showed varying degrees of thickening (Figs. 1 and 2). This appearance was seen focally in some glomeruli, diffusely in others, and affected all or most glomeruli. The capillaries in general presented a rather rigid appearance with reduction in their lumens in some instances. Case 3 showed early necrosis of some glomerular tufts (Fig. 3). There was slightly increased cellularity in the tufts of case 5. Tubular casts were a variable feature, being present in 2 cases. There was slight atrophy of the proximal convoluted tubules in case 3. The latter biopsy was also striking for the large number of foamy macrophages in the interstitial

TABLE I. DATA CONCERNING 7 PATIENTS UNDERGOING RENAL BIOPSY

Case	*Age (yrs.)*	*Parity*	*Serum albumin (g.%)*	*Plasma cholesterol (mg.%)*	*Blood urea (mg.%)*	*Proteinuria (g./l. Esbach)*	*Outcome of pregnancy*	*Time of biopsy*
1	18	0	0·8 - 0·9	360 - 418	14 - 32	1·5 - 18	Full-term normal delivery	(*a*) 16th week of pregnancy (*b*) 3 months post-partum
2	25	2	1 - 1·5	305 - 350	11 - 18	0·5 - 5	Full-term normal delivery	2 weeks postpartum
3	22	0	1·2 - 2·2	196 - 245	13 - 21	1·5 - 9	Full-term normal delivery	3 weeks postpartum
4	24	2	0·4	670	17	0·5 - 9	Full-term normal delivery	18th week of pregnancy
5	29	5	1·8 - 1·9	310 - 321	10 - 28	0·25 - 2	Twins at 37th week, 1 of whom died of asphyxia	3 weeks postpartum
6	21	2	1·0	540	15	1 - 6	Full-term normal delivery	(*a*) 16th week of pregnancy (*b*) 1 week postpartum
7	23	1	0·7 - 1·1	265 - 305	11 - 16	1·5 - 7	Full-term normal delivery	1 week postpartum

TABLE II. RENAL BIOPSY FINDINGS IN 7 CASES OF THE NEPHROTIC SYNDROME IN PREGNANCY

Case	*No. of glomeruli*	*Basement-membrane thickening*	*Capillaries of tuft*	*Tubules*	*Interstitial tissue*	*Vessels*
1 (*a*)	5	Diffuse, affecting every glomerulus	Normal and patent	Granular casts, occasional hyaline droplets in proximal convoluted tubules	Normal	Normal
(*b*)	13	Diffuse, affecting every glomerulus	Slightly reduced lumens	Granular casts, occasional hyaline droplets in proximal convoluted tubules	Normal	Normal
2	5	Affecting all parts of every glomerulus	Some with reduced lumens	Normal. No casts	Normal	Normal
3	7	Affecting all parts of every glomerulus. Early hyalinization of some glomeruli	Some with reduced lumens	Slight atrophy of proximal convoluted tubules. Occasional hyaline casts	Contains numerous foamy macrophages	Slight thickening
4	30	Affecting all parts of every glomerulus	Some with reduced lumens	Granular degenerative changes of proximal convoluted tubules. Occasional hyaline casts	Single focus of lymphocytic infiltration	Normal
5	25	Affecting all glomeruli, diffuse in some, focal in others	Some with reduced lumens	Normal, occasional casts	Normal	Normal
6 (*a*)	28	Affecting all parts of every glomerulus	Some with reduced lumens	No casts. Occasional hyaline droplets	Normal	Normal
(*b*)		Affecting all parts of every glomerulus	Some with reduced lumens	No casts. Occasional hyaline droplets	Normal	Normal
7	3	Affecting all glomeruli diffusely	Some with reduced lumens	Normal	Normal	Normal

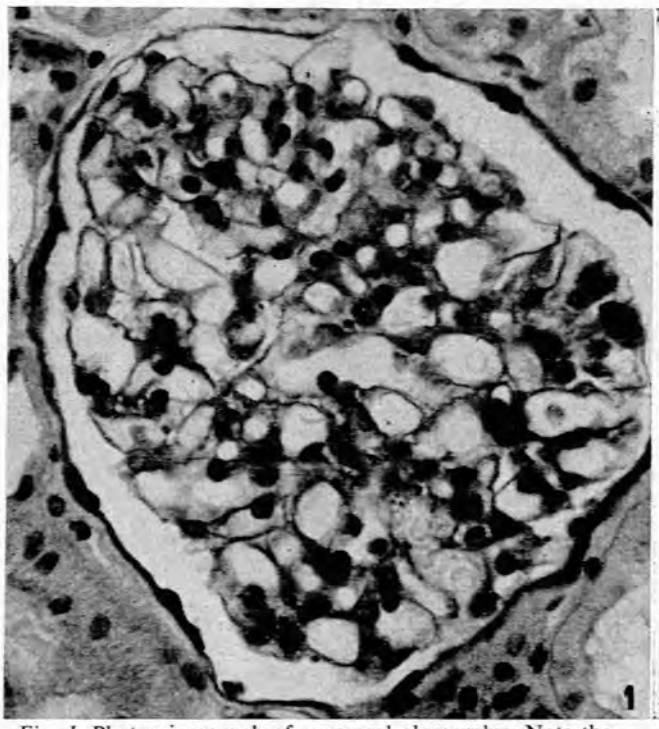

Fig. 1. Photomicrograph of a normal glomerulus. Note the delicate basement membrane. (periodic-acid-Schiff × 600).

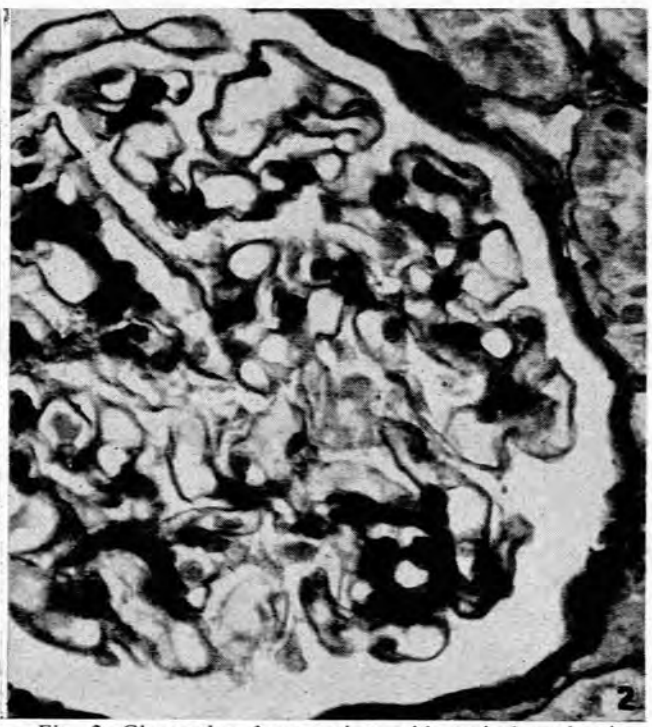

Fig. 2. Glomerulus from patient with typical nephrotic syndrome. There is marked, diffuse basement-membrane thickening (periodic-acid-Schiff × 600).

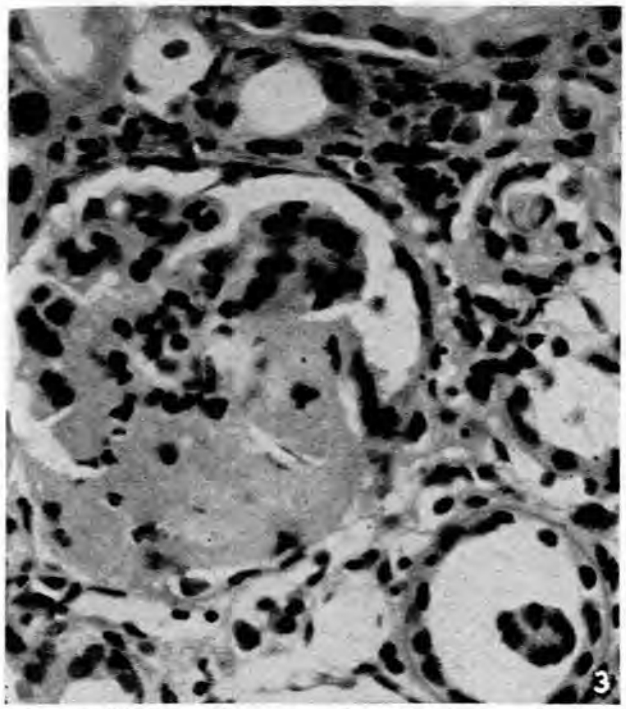

Fig. 3. Kidney with more advanced changes showing partial fibrosis of a glomerulus and atrophy of tubules. (haematoxylin and eosin×600).

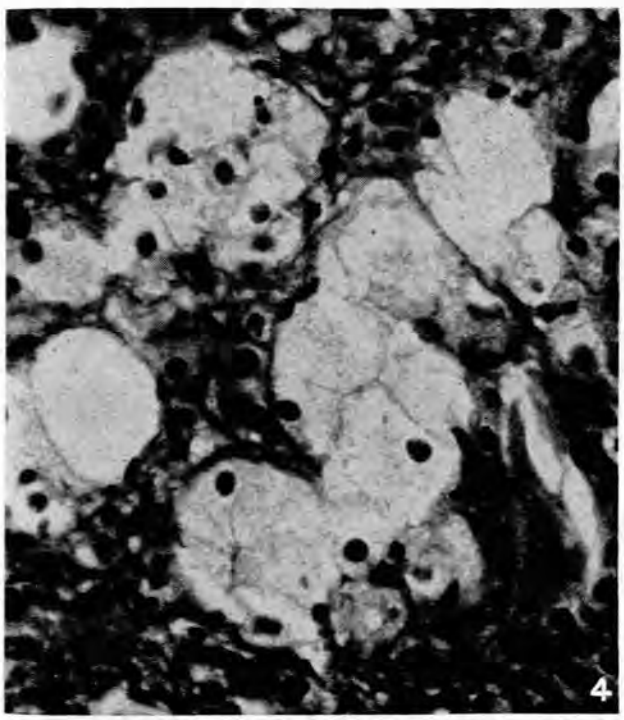

Fig. 4. Foamy macrophages in the interstitial tissue (haematoxylin and eosin×600).

tissue (Fig. 4). In all the other subjects the interstitial tissue was normal. In no case was there any significant abnormality in the arterioles or arteries.

DISCUSSION

Renal-biopsy studies have shown that the nephrotic syndrome may be associated with a variety of renal lesions — membranous glomerulonephritis, proliferative glomerulonephritis, a combination of these, diabetic glomerulosclerosis, systemic lupus erythematosus, amyloidosis, renal-vein thrombosis, nephrosclerosis,[4,5] and nephrocalcinosis.[6] It is therefore of interest that these 7 African patients with the nephrotic syndrome associated with pregnancy all showed the changes of membranous glomerulonephritis (Ellis type II nephritis). The number of cases is admittedly small, but our findings in non-pregnant African nephrotic patients are essentially similar (unpublished observations). Of note also, is the absence of any progression in the renal lesion in the 2 patients in whom biopsy was done at the 16th week of pregnancy and again after delivery.

Previously we have demonstrated that the association of the nephrotic syndrome and pregnancy in the African usually has a favourable outcome,[2] as shown by the cases in this series. By contrast, some British and American authorities have stated that the maternal and foetal prognosis is poor.[7-10] The reasons for this divergence of opinion are obscure. In part it may be due to the inclusion of cases of the syndrome complicated by hypertension or azotaemia, factors, it would be generally agreed, which affect the outcome of pregnancy adversely.

A further reason may be that prognosis in the pregnant nephrotic patient is related to the nature of the underlying renal lesion. Our own observations indicate that, when Ellis type II or membranous glomerulonephritis is associated with pregnancy, the maternal and foetal prognosis is good. The same may not be true of other lesions responsible for the nephrotic syndrome. Renal biopsy studies in a British or American series of pregnant nephrotic patients have not yet appeared, but some idea of the possible findings may be gained from observations in non-pregnant cases. In these it has been shown that a substantial number are due to lesions other than membranous glomerulonephritis.[4,5] Thus about half of the 98 cases of the nephrotic syndrome reported by Kark *et al.*[4] were due to such lesions as diabetic glomerulosclerosis (15 cases), systemic lupus erythematosus (18 cases), proliferative glomerulitis (6 cases), or mixed proliferative and membranous glomerulonephritis (12 cases). Many of these are characterized by a more florid and active form of glomerular disease than pure membranous glomerulonephritis and pursue a more rapidly progressive clinical course. It is possible that such lesions are aggravated by pregnancy but, even if this is not so, their natural rate of progression may be so rapid that, in the course of pregnancy, considerable deterioration in renal structure and function may occur.

SUMMARY

In 7 African cases of the nephrotic syndrome in pregnancy renal biopsy was performed either during or after pregnancy.

All cases showed the changes of membranous glomerulonephritis. In 2 cases in which biopsy was done at the 16th week of pregnancy and again after delivery, no progression in the renal lesions was observed.

The bearing of these findings on maternal and foetal prognosis is discussed.

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