CONGENITAL NEPHROTIC SYNDROME IN A CHINESE INFANT

By A. Nadarajah
(Department of Pathology, University of Singapore)
and
Freda M. Paul
(Department of Paediatrics, University of Singapore)

The nephrotic syndrome is characterised by generalised oedema, hypoproteinaemia, hyperlipaemia and gross albuminuria. It is not difficult to recognise the syndrome. In most cases in childhood the aetiology is not known.

In the newborn the nephrotic syndrome is rare; the first case recorded was by Gautier and Miville in 1942. Their report concerned one infant in whom the fatal illness appeared at the age of 17 days. Since then, about 100 cases of the congenital nephrotic syndrome have been published, about one-half of which have been reported from Finland (Kouvalinen, 1963). The reasons for this apparently high incidence in Finland are not known. In Singapore, Wong (1960) reported a series of 97 cases of the nephrotic syndrome in children but there was not a single case of neonatal nephrosis. Below, we report the first case of the congenital nephrotic syndrome in Singapore.

CASE REPORT

K.T.S. was a 20 day old male Chinese infant admitted to hospital on 15/1/64. The presenting symptom was generalised swelling of the body for two weeks. The baby was delivered normally at a nursing home on 26/12/63 and weighed 6 lbs. 14 ozs. at birth. The swelling, which was first noticed when the child was 7 days old, had begun in the hands and feet and had progressively spread to affect the abdomen, scalp and face. The mother also observed that the child vomited his milk feeds. The bowel habits were normal and nothing unusual was noted about the micturition habits.

The mother gave no history of toxaemia, infections or ingestion of any drugs during this pregnancy.

The parents are both healthy and they are not related to each other in any way. The mother has had six pregnancies, two ending in abortions at seven and thirteen weeks of gestation respectively. Another male child died at the age of 10 days from biliary atresia and bronchopneumonia. The urines of the parents and living siblings have been examined and found to be normal.

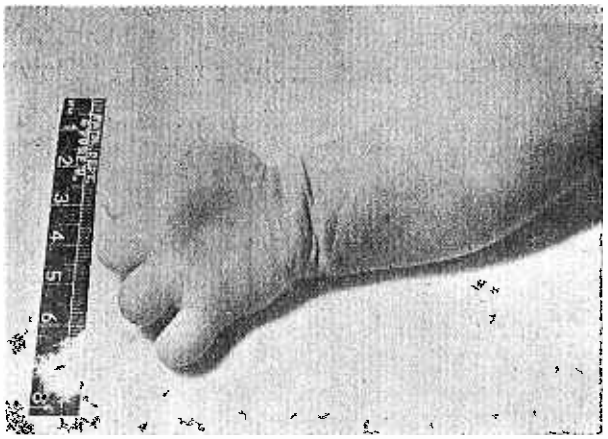

Fig. 1. Show the pitting oedema of the hands.

On examination, the child was found to be grossly oedematous, with pitting oedema of the face and hands (Fig. 1). The weight of the child was 9 lbs. 2 ozs., an increase of 2 lbs. 14 ozs. since birth. The child did not look dehydrated. No abnormality was detected in the heart and lungs. The blood pressure was 140/90 mm.Hg. There was minimal ascites on admission. The liver and spleen were not palpable. The right kidney was palpable on admission. As the ascites increased the right kidney was more difficult to palpate. The bladder was not palpable and the scrotum was not oedematous.

INVESTIGATIONS

All the laboratory investigations pointed to a nephrotic syndrome complicated by hematuria and uraemia.

The urine on admission showed macroscopic haematuria. The urinary protein ranged from

2,000 mgm.% to 3,000 mgm.%. There were 200 to 300 red blood cells, 30 to 40 pus cells and 1 to 2 epithelial cells per high power field. Granular casts were also present. The specific gravity was 1.005. No sugar could be detected.

The haemoglobin was 14.2 gms.% The white cell count was 14,000 per cu. mm. with polymorphs 98%, lymphocytes 20%, monocytes 4% and eosinophills 8%. The erythrocyte sedimentation rate (Westergren) was 9 mm. and 7mm. per hour respectively on two different occasions.

The blood urea, done on two occasions, was 81 mgm.% and 95 mgm.% respectively. The blood cholesterol was 200 mgm.%. Serum alkaline phosphatase was 14 King Armstrong Units. The serum electrolytes were as follows:-

Serum sodium	100 mEq/litre.
Serum potassium	6.2 mEq/litre.
Serum chloride	72 mEq/litre.
Serum calcium	7.8 mEq/litre.
Serum phosphorus	10.7 mEq/litre.

The Sulkowitch test for urinary calcium was done and this was within normal limits.

The Kahn test was negative.

Our clinical impression of the case was that of the nephrotic syndrome complicated by uraemia, hypertension and haematuria. The child was put on oral tetracycline and feeds of glucose. However, he was unable to retain his feeds probably because of uraemia. The urinary output was very poor; only 10 cc. of urine per day and this was loaded with albumin. On 20/1/64, the child's haemoglobin dropped to 6.8 gms.%, the child appeared more oedematous, and died.

AUTOPSY FINDINGS

The body was that of a pale male Chinese infant showing gross generalised oedema. There were 10 cc. of straw coloured fluid in each pleural cavity and about 20 cc. in the peritoneal cavity.

The kidneys were large and prominent, protruding well into the abdominal cavity (Fig. 2). The right kidney weighed 33 Grams and the left kidney weighed 34 Grams (expected weight about 15 grams each). Both kidneys were pale, showed foetal lobulation and numerous petechiae beneath the capsule and in the substance. With a hand lens numerous pin point cystic areas were visible in the cortex. The renal pelves, ureters, bladder and urethra appeared normal. The renal arteries and veins were normal.

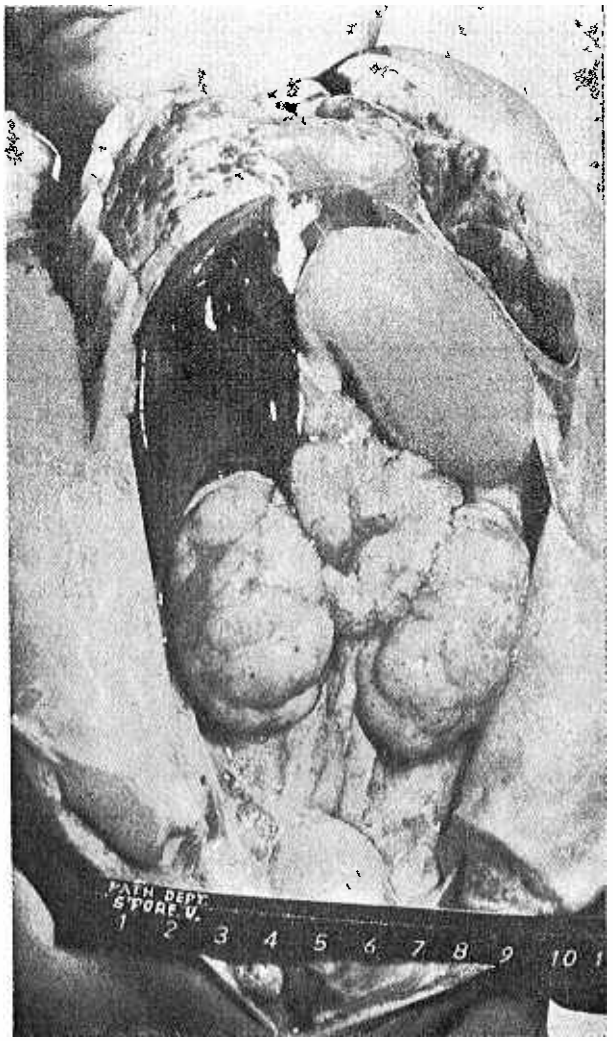

Fig. 2. Picture at autopsy to show the large prominent kidneys with petechiae on the surface.

Other significant findings were pulmonary oedema and dark patchy depressed areas in both lungs. There was an unusually large ductus arterious 1.4 cm. long with a luminal diameter of 0.8 cms.

Microscopically, the kidneys showed marked changes in the glomeruli and tubules. All the glomeruli showed varying degrees of thickening of the basement membrane of the tufts (Fig. 3). In some of the glomerular tufts the digitations were adherent to each other and to the wall of Bowman's capsule. Occasional

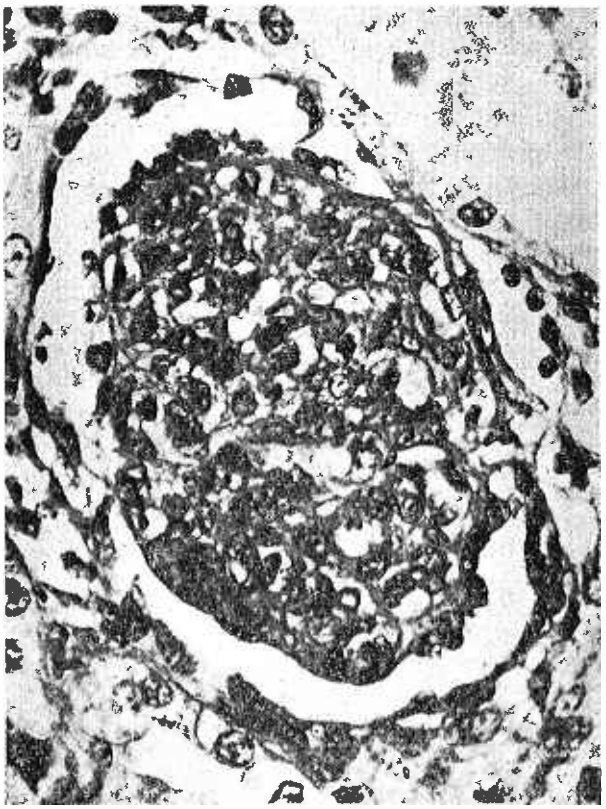

Fig. 3. Glomerulus showing thickened basement membrane and adherence of the glomerular tufts to the wall of Bowman's capsule. PAS x 500.

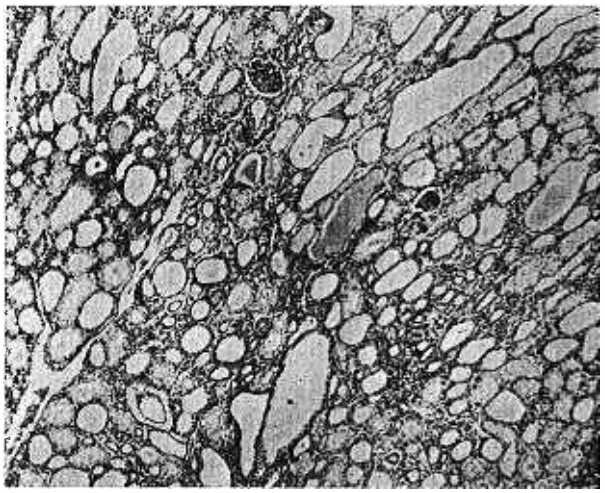

Fig. 5. Cortical tubules showing cystic dilatation. Some of the tubules contain hyaline and blood casts. HE x 45.

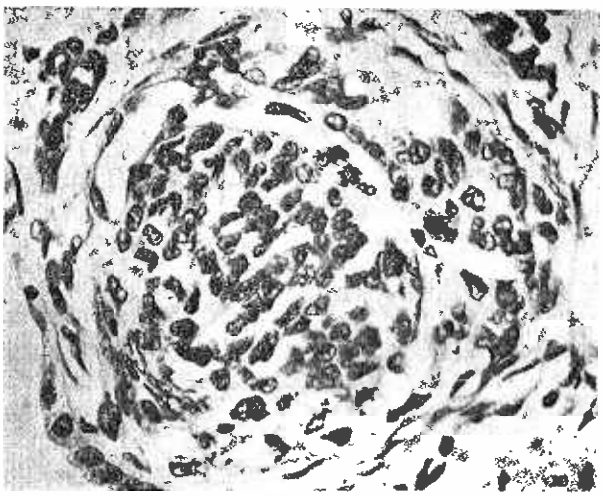

Fig. 4. Glomerulus showing capsular epithelial proliferation and crescent formation. HE x 500.

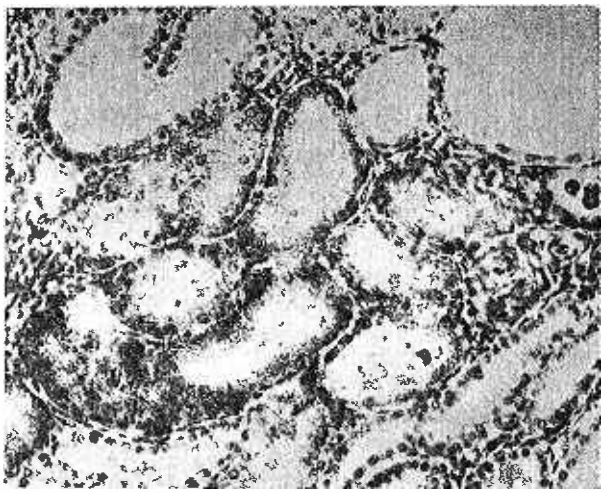

Fig. 6. Tubular epithelial cells showing lipid vacuolation. Sudan III x 150.

glomeruli showed proliferation of the capsular epithelium with the formation of epithelial crescents (Fig. 4). The glomerular capillaries were strikingly ischaemic.

Many of the cortical tubules were cystically dilated and contained hyaline and blood casts (Fig. 5). Some of the cortical tubules showed varying degrees of degeneration of their lining epithelium. There was also fairly marked lipid vacuolation of some of the tubular epithelial cells (Fig. 6). There was a mild lymphocytic infiltration of the interstitium.

The lungs showed changes consistent with uraemic pneumonitis. There was a fibrinohaemorrhagic exudate in the alveoli, with hyalinisation of the exudate in some areas. The alveolar septa were not thickened and there were hardly any polymorphonuclear cells in the exudate. Microscopic examination of the other organs did not reveal any significant abnormality.

DISCUSSION

The nephrotic syndrome is uncommon during the first few months of life and indeed during the first year. It is well known that there is familial incidence in this condition. Fanconi, Kousmine and Frischknecht (1951) reviewed the problem of congenital and familial nephrosis and described a family of five siblings, three of whom developed the nephrotic syndrome at the 4th, 10th and 24th day of life. All these babies died.

In our patient there was no family history of the nephrotic syndrome nor any maternal history of toxaemia or drugs, and the urines of the two living siblings were normal. The clinical and autopsy findings in another male child who had died previously were not related to the nephrotic syndrome.

Although the clinical features and laboratory findings pointed to a nephrotic syndrome, there were a few unusual findings. The micro E.S.R. was low. To date there has been no mention of E.S.R. values in reported cases of the congenital nephrotic syndrome. The haematuria and azotaemia resemble very closely the haematuric phase of the nephrotic syndrome that one sees in older children. The urinary amino-acid estimation was not done in this case; an increase in the urinary amino-acid concentration has been reported in other cases. Woolf and Giles (1956) described two types of abnormal urinary amino-acid pattern in the nephrotic syndrome. The first of these is characterised by increased excretion of ethanolamine, B amino butyric acid and other amino-acid compounds, suggestive of a disturbance of intermediate amino-acid metabolism. The second type related to azotaemia, hypertension, and renal failure was attributed to renal tubular insufficiency.

It is well known that in the nephrotic syndrome in children low albumin and high lipoprotein values and a more or less decreased gamma-globulin are characteristic. The expected rise in globulin is seen in the pherogram of this patient (Fig. 7).

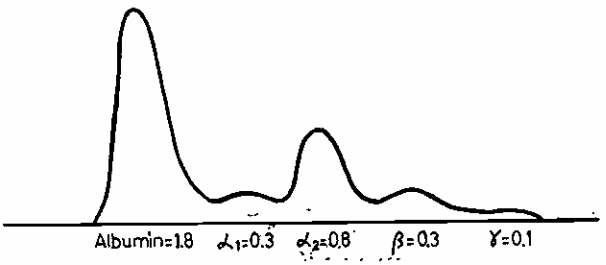

Fig. 7. Pherogram of the patient showing a decreased albumin concentration and an increased 2 globulin.

Varying pathological changes have been described in the congenital nephrotic syndrome. Cystic dilatation of the cortical tubules is a striking lesion and has been noted in almost all the reported cases. (Hallman & Hjelt, 1959). Lipid vacuolation of the tubular epithelial cells and tubular degenerative changes are also fairly constant.

By micro-dissection, Giles et al (1957) found that the first part of the proximal convoluted tubules was replaced by a long and narrow neck, the remainder of the proximal tubules being ballooned in many areas. The other parts of the tubules were considerably wider than normal. Impressed by these changes these workers suggested that the disease is probably a primary tubular disorder. This, however, does not provide an explanation for the massive proteinuria.

Paatela (1963) did renal micro-dissection on 30 infants with the congenital nephrotic syndrome. She found irregular wide cyst-like dilatations alternating with narrow atrophic

segments of the tubules. In 20 of the patients the proximal convoluted tubules had a narrow atrophic neck segment. In eighteen of the cases slight dilatations lined with normal epithelium were found in the distal convoluted tubules.

Striking as these morphological changes may be, they probably represent, as Allen (1962) suggests, cystic dilatation of the tubules following tubular blockage by dense protein casts.

The glomerular changes described in the congenital nephrotic syndrome have not been as constant as the tubular changes.

Eiben et al (1954) in a report of one case found that the majority of the glomerular tufts were dilated and contained numerous red blood cells. The basement membrane of the glomerular capillaries was not thickened but the majority of the glomeruli showed some cellular proliferation.

Parker and Piel (1960) in a report of 5 cases of the congenital nephrotic syndrome stated that the principal glomerular change was persistence of a larger number than normal of the immature type of glomerulus covered by a layer of cuboidal cells. Persistence of these immature glomeruli, they considered, resulted in atrophy of their corresponding tubules and hypertrophy of the remaining tubules.

Hallman and Hjelt (1959) in a review of 18 cases noted that the glomeruli of infants dying soon after birth did not reveal changes characteristic of nephrosis. The older the infant the greater were the changes in the glomeruli. These changes consisted of thickening of the basement membrane of the glomerular capillaries, proliferation of endothelial cells and in the most advanced cases thickening of Bowman's capsule, adhesions between the capsule and the glomerular tufts and crescent formation.

It is interesting to note, that the case reported by us shows many of the glomerular changes described by Hallman and Hjelt (1959) as being present only in older children who have survived their illness for a considerable time. Further, this child had hypertension and uraemia when only 20 days old. Moreover, the child died at the age of 22 days, not from secondary infection, as is usual in the congenital nephrotic syndrome, but from renal failure.

Farquhar et al (1957) did electron microscopic studies on cases of the congenital nephrotic syndrome and showed fusion of the foot processes and vacuolation of the ephithelial cells of the glomerular capillaries. It is noteworthy that Folli et al (1958) and Vernier et al (1961) have shown that this same change is characteristic of a variety of forms of the nephrotic syndrome in older children and adults.

The aetiology of the congenital nephrotic syndrome remains obscure. Kouvalinen (1963) from observations based on immunological studies, postulates that possibly kidney antibody is transmitted from the mother to the foetus. However, in the light of animal experiments, a specific immune tolerance should develop for protein that has entered the foetal body during intrauterine life. In these cases, however, he suggests that possibly because of a genetic or other defect, these foetuses do not develop such a tolerance.

SUMMARY

1. A case of congenital nephrotic syndrome complicated by uraemia and hypertension in a 20 day old Chinese infant is described.

2. The clinical, laboratory and autopsy findings are discussed and the literature briefly reviewed.

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