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Infantile nephrotic syndrome

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Summary

Four infants, two boys and two girls, with congenital nephrotic syndrome are reported in a single family. The disease process began during the first year of life. The disorder did not respond to corticosteroid therapy. One infant received cyclophosphamide therapy as well without avail. All four children died from intercurrent infection. The family tree is suggestive of an autosomal recessive inheritance.

Introduction

In the reported series of the nephrotic syndrome in childhood, only 1-5% of the cases occur in the first year of life (Barnett, Forman and Lauson, 1952; Arneil, 1961; Cornfield and Schwartz, 1966; McDonald, Wiggelinkhuizen and Kashula, 1971). A familial incidence has been recorded among these infants (Vernier, Brunson and Good, 1957; Parker and Piel, 1960; Hansen and Coye, 1961; Cornfield

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and Schwartz, 1966). The term 'congenital nephrosis' was used to describe the condition starting in the first few weeks of life.

Norio, Hjolt and Hallman (1964) and Norio (1966) in extensive studies of congenital nephrosis came to the conclusion that the disorder is a hereditary one, transmitted in an autosomal recessive way and is much more common in Finland than in other countries.

The Finnish workers described the main features of the syndrome as premature birth, large placenta, distended abdomen, proteinuria and dysproteinemia of the nephrotic type, high susceptibility to infection together with resistance to all therapies and consequently with a fatal outcome.

Hoyer *et al.* (1967) reported from U.S.A. three siblings with congenital nephrosis belonging to a family of Finnish extraction.

We here report our experience with an Iraqi family of nine children, four of whom died from

congenital nephrosis. Our aim is to show that this hereditary condition can exist in a different geographic location and in patients of a different ethnic background. Our patients also presented some minor differences in their clinical features from those reported previously.

Case 1

M.H. was 9 months old when admitted to the Children's Hospital, Mosul, in April 1964 for 'body swelling' which had started a month before. He was the product of a normal pregnancy and delivery and was of 'normal birth weight'. He had only minor infections in the first month of life.

On admission his weight was 9300 g. Blood pressure was 110/85 mmHg. His face looked puffy, his abdomen was distended and his scrotum swollen. No other abnormality was detected on physical examination.

Urinalysis revealed heavy proteinuria and blood examination hypoalbuminaemia (Tables 1 and 2). The diagnosis of nephrotic syndrome was made. The child received 2 months of treatment with antibiotics without any change in his oedema or proteinuria. This was followed by a month's course of prednisolone in a dose of 2 mg/kg body weight/day. Towards the end of this course of treatment the condition became progressively worse, so prednisolone was discontinued. He died a week later in a febrile illness in spite of further antibiotic treatment.

TABLE 1. Urinary findings

Patient	Protein	RBC/HPF	WBC/HPF	Casts
M.H.	+++	3	2	-
E.H.	+++	10	8	+
A.H.	++++	4	3	+
G.H.	++++	3	3	-

Case 2

E.H. is the sister of the first patient. She was the product of normal pregnancy and delivery. Her birth weight was 3 kg. She was first seen at the age of 10 months in June 1966. Initially she had swelling of her feet and later of all her body. On admission to hospital she showed generalized oedema and ascites. Her blood pressure was 100/70 mmHg. No eye or

ear abnormality was detected. She had massive proteinuria and hypoproteinaemia. The electrophoretic pattern was consistent with the nephrotic syndrome (Tables 1 and 2).

Prednisolone treatment was initiated in a dose of 30 mg/day. Initially some degree of improvement was noticed, as evident by reduction in body weight, oedema, ascites and proteinuria. However, 5 weeks from start of therapy the child developed bronchopneumonia. This was followed by increase in fluid retention. Penicillin was given and prednisolone was tapered off gradually. She died 2 months after admission. No autopsy was allowed.

Case 3

A.H. was the third patient of this family, and was brought for examination at the age of 1 week. She appeared to be a healthy baby weighing 3100 g. Urinalysis revealed no abnormality nor did two subsequent examinations at monthly intervals. The baby continued to thrive until March 1970 when she was 11 months old. She then started to show swelling of the face and lower extremities. Her weight was then 8.250 kg, and blood pressure was 100/70 mmHg. Urine examination revealed massive proteinuria and the serum protein electrophoresis showed changes consistent with a nephrotic pattern. Prednisolone treatment was begun, but after 20 days the child developed a fever and was given penicillin and gentamicin. In spite of this the child succumbed a week later. No autopsy was done.

Case 4

G.H. was the fourth affected baby in this family. At 3 days of age he weighed 3500 g. His physical examination and urinalysis revealed no abnormality.

Three subsequent monthly urine examinations were also normal. At 8 months of age in October 1972 his eyes became puffy. His blood pressure was 95/65 mmHg and his weight was 10 kg. Both eyes and ears looked normal.

Laboratory investigations revealed a marked proteinuria and nephrotic pattern on serum protein electrophoresis. Cyclophosphamide, 25 mg/day, was given for 9 days by which time no detectable clinical or laboratory change was observed. The dose was put up to 50 mg/day for 1 week with a further rise to

TABLE 2. Blood values

Patient	Hb g/100 ml	WBC/mm ³	Urea mg/100ml	Cholesterol mg/100 ml	Albumin g/100 ml	α 1 globulin g/100 ml	α 2 globulin g/100 ml	β globulin g/100 ml	γ globulin g/100 ml	Total globulin g/100 ml
M.H.	10	7000	35	320	1.75	—	—	—	—	2.05
E.H.	8.7	16000	42	290	1.04	0.084	1.39	0.51	0.31	2.29
A.H.	9	5200	30	—	2.5	0.33	2.1	0.33	1.3	4.06
G.H.	10.5	8000	20	260	0.41	0.18	1.65	0.32	0.32	2.47

FIG. 1. Patient's pedigree: ○, female; □, male.

75 mg/day when a reduction in proteinuria was observed. A day later the child developed cough and fever and the abdominal distension and proteinuria increased. Ampicillin was given and cyclophosphamide was put up to 100 mg/day. Prednisolone 2 mg/day was added 4 days later. The patient continued to show clinical deterioration with the increase of the oedema and ascites. He was infused with 50 ml of low salt albumin, and died 4 weeks later.

The parents of the four patients were first cousins; the children's maternal grandmother and paternal grandmother were sisters. Both father and mother were physically normal. They had normal urine, normal blood cholesterol and negative VDRL tests. They had five other healthy children, four girls and two boys, with no physical or laboratory evidence of a renal disorder. The father had three brothers and one sister, and the mother had five brothers and a sister; all were in good health with no renal disease, eye or ear abnormality.

Discussion

The four children in one family suffered from a nephrotic syndrome as evident by heavy proteinuria, massive oedema and consistent changes in serum proteins. In all the onset of the illness occurred within the first year of life. They were all uninfluenced by corticosteroids, and one by cyclophosphamide therapy in the usual doses. They all showed a high susceptibility to infection and poor response to antibacterial therapy. They all progressed to a fatal outcome after a short period of survival.

These are the features of congenital nephrotic syndrome similar to those reported by Norio *et al.* (1964). The study of the family tree suggests an autosomal recessive mode of inheritance (Fig. 1). This is consistent with the views of Nario *et al.* (1966).

Some features of congenital nephrosis described by other workers namely: premature birth, failure to thrive and onset under 3 months of age were not observed in our patients (Norio *et al.*, 1964; McDonald *et al.*, 1971).

No histological study of the kidneys, pre or post mortem, were possible in our cases. Previous studies by other workers have shown in a number of cases, especially those of Finnish extraction, specific changes consisting of dilatation of the proximal tubules, segmental atresia of the tubules and increase in the size of glomeruli with distension of Bowman's space. On electron microscopy the epithelial foot processes were characteristically fused but the basement membrane was not thickened (Hansen and Coye, 1961; Norio *et al.*, 1964; Hoyer *et al.*, 1967).

The pathogenesis of the syndrome is not yet clear. Early onset in some cases, as early as the first few days of life, is a point against the theories of infection or hypersensitivity as a cause. Hoyer *et al.* (1967) in their extensive study came to the conclusion that immune mechanism or maternal antibodies as suggested by Lange (1963) and Kobayashi (1966) are unlikely causes of renal damage in these children. They expressed the view that the autosomal mode of inheritance suggests a metabolic defect acting on the kidneys rendering the glomerular basement membrane abnormally permeable, leading to the development of the syndrome.

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Lead poisoning with low blood lead levels

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Summary

Two cases are reported in which symptomatic lead poisoning coincided with normal haemoglobin concentrations and blood lead levels below 80 $\mu\text{g}/100\text{ ml}$. Urinary coproporphyrins and amino laevulinic acid concentrations were elevated. These latter tests are useful for confirmation of clinical diagnoses and for the screening of industrial lead workers.

Introduction

A lead hazard exists in many industries and even where protective measures are enforced, workers have shown indices of exposure only just below danger levels (Gibson, Mackenzie and Goldberg, 1968). Several tests are available for detecting those in danger of becoming intoxicated. Measurements of blood lead and haemoglobin concentration are widely used for such screening. Two cases are described to draw attention to the limitations of these particular tests whether used in a prophylactic capacity in industry or to confirm clinical lead poisoning.

Methods

Blood and urinary lead concentrations were measured by E. King of National Occupational Hygiene Services using the classical monocolour di-

thizone technique (King and Thompson, 1961). Within the relevant range of blood lead concentrations, 50-100 $\mu\text{g}/100\text{ ml}$ whole blood, results are accurate to within $\pm 5\text{ }\mu\text{g}$.

Case 1

A 20-year-old man mixed lead sulphate and lead stearate powders in the manufacture of plastics. An extractor fan was ineffective. Dust readily penetrated his gauze mask. Within 3 weeks of starting the job he developed central abdominal, colicky pain; this was quickly followed by vomiting. The condition was not recognized and after a week at home he resumed work. Within 3 hr he was prostrated by abdominal colic. He was admitted to hospital the next day; at that time the haemoglobin was 14.2 g/100 ml and the blood lead 75 $\mu\text{g}/100\text{ ml}$. The pains diminished over a period of 4 days. Four weeks later at outpatients, the blood lead was 73 $\mu\text{g}/100\text{ ml}$. Against advice, he again resumed work. Within 3 weeks he was re-admitted to hospital, the symptoms had recurred. Vomiting started at the onset of the abdominal colic; it was intractable and was evoked by any oral food or fluid for 3 days after the colic had ceased. He also complained of postural dizziness, parasthesiae in the hands and face and that 'the use had gone out of his legs'. Examination revealed an ill-defined blue line on the upper gum which had disappeared within 5 days but there was no neurological abnormality.

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