CONGENITAL NEPHROTIC SYNDROME OF THE FINNISH TYPE

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Conflict of Interest: *None*

SUMMARY
Congenital Nephrotic Syndrome of the Finish type (CNF) is a rare and severe disease. A neonate with CNF is described. The diagnosis carries a dramatically poorer prognosis than nephrotic syndrome diagnosed after one year. The clinical course is one of persistent oedema and recurrent infections leading to death. The gene for the Finish type has been mapped to the long arm of chromosome 19. Case reports show it to be responsive to captopril and indomethacin. It is uniformly resistant to steroids and immunosuppressive drugs.

Key words: Congenital nephrotic syndrome of the Finnish type (CNF), captopril, indomethacin

INTRODUCTION
Nephrotic syndrome is a clinical diagnosis defined by the presence of heavy albuminuria, hypoalbuminemia and oedema.[1] It is classified as congenital if it presents at birth or appears during the first months of life.[2] CNF is most frequent in Finland but has been reported in various ethnic groups worldwide.[3,4] A diagnosis in this case was made on the basis of the clinical features, autopsy report and histological evaluation. To the best of our knowledge, this is the first report from Ghana.

CASE REPORT
A female was born at 38 weeks of gestation by spontaneous vaginal delivery weighing 2.6kg to non-consanguineous parents. The pregnancy was uneventful. Apgar scores were satisfactory at birth and child was breastfeeding well. She presented at 3 weeks of age with an 11 day history of periorbital oedema that appeared to improve by the end of each day. Her urine characteristics and output were said to be normal. There was an antecedent history of a pustular rash on the face that had resolved spontaneously. Mother denied any history of renal disease in the family. This was her first child.

Clinical examination revealed a normal looking neonate with a purulent eye discharge affecting both eyes and generalized pitting oedema. She was not in respiratory distress. Her anterior fontanelle was large (6cm across). The cranial sutures were widened up to the occiput. Her head circumference was 35cm (50^{th} centile) and body length 48cm (25^{th} centile). She had significant ascites but no masses were felt on abdominal palpation. Blood pressure was not recorded due to the unavailability of an appropriate cuff size. A provisional diagnosis of a hypoproteinaemic state from sepsis or renal disease was made and urgent investigations requested.

Initial results revealed a normal complete blood count and ESR but abnormal blood chemistry and urinalysis. Serum sodium - 110mmol/L, potassium - 4.7mmol/L, urea - 6.9mmol/L, Total Protein - 17g/L, albumin 6g/L. Urinalysis gave a pH of 6.0 and microscopy showed amber colour, blood was positive (++), ketones – negative, glucose was positive (++) and protein was positive (++++). The specific gravity of the urine was 1.015, urobilinogen (normal) and biluribin was negative. Urine microscopy showed 5 pus cells, 15 red blood cells, 3 epithelial cells per high power field and granular casts(+)

She was given two units of Fresh Frozen Plasma as a protein source due to the lack of albumin infusions in the hospital. An abdominal ultrasound showed a normal echo pattern and size of both kidneys. Liver and spleen size were normal.

Subsequent blood chemistry evaluations revealed deteriorating albumin, and sodium levels, as well as rising potassium. Creatinine levels crept up from an initial 183 µmol/L to 201 µmol/L on day 5 to 314 µmol/L on day 10 of admission. A single cholesterol estimation was recorded as 5.72 mmol/L on day 10 of admission. Retroviral screen was negative.

She breastfed well throughout her admission but her oedema appeared to worsen. On the tenth day of admission she developed loose stools, accompanied by a temperature of 38 degrees Celsius. She was started on intravenous cefuroxime. A possible diagnosis of congenital nephrotic syndrome was entertained on the ba-

sis of the consistent laboratory results of heavy proteinuria and hypoalbuminemia. She died that day.

Autopsy findings
Female infant showing marked generalized pitting oedema. The other major systems were normal except for the respiratory system which showed rubbery oedematous lungs. The genito-urinary system revealed slightly oedematous kidneys. Cut surface of the kidneys were very pale with hemorrhagic rimming of the cortico-medullary junction. The cortex was of normal thickness. Medulla and pelvi-calyceal system were normal. Ureters and bladder were grossly normal. The conclusion was that the findings were consistent with a nephrotic syndrome.

Histology report of the kidneys
In the renal tissue at low power, basophilic areas were evident, one of these in a subcapsular location. Cellular preservation was poor suggestive of a nephrogenic rest. The renal architecture was distorted due to the presence of ecstatic tubules with eosinophillic wispy material. Although the tubular basement membranes were not thickened Periodic Acid Schff (PAS) stain suggested tabular casts.

Some of the glomeruli had a foetal appearance and others showed an apparent increase in cellularity and possibly an increase of eosinophillic material. Some of the glomeruli did show increased (PAS) and silver staining within the eosinophillic areas in the glomeruli suggestive of sclerosis. No vascular lesions were identified. It was concluded that the appearances in the appropriate clinical context was consistent with CNF.

DISCUSSION

The two main causes of congenital nephrotic syndrome is the Finnish type and diffuse mesangical sclerosis which are both inherited in autosomal recessive fashion.[5]

CNF is the commoner form of the disease and in Finland where it was predominantly described in children (hence Finnish type), it occurs with an incidence of 1.2/10,000 live births.[6]

The gene was mapped to chromosome 19q13 in 17 Finnish families and other families around the world. The same gene causes the disease in non-Finnish children with CNF. The gene is called NPHSI encoding for a family of cell adhesion molecules called nephrin.[7] It is important to appreciate the clinical features in our setting, so that an earlier diagnosis may be entertained.

Both sexes are equally affected and are born early (at 35-38wks) and usually below gestational weight for age. The placenta is typically enlarged being more than 25% of the total birth weight.[8] Classically the newborn has widely separated cranial sutures, with large posterior and anterior fontanelles which was present in our index case. There may be flexion deformities of the hips, knees and elbow.[9]

Aggressive treatment is required including daily intravenous albumin, nutritional support via nasogatric tube feeding, prevention of infections (peritonitis, respiratory infections) and thrombi-embolic complications. In developed countries early bilateral nephrectomy to prevent massive protein loss, renal replacement treatment with dialysis and transplantation are further options.[10]

Pomeranz et al described two infants with CNF who responded to treatment with captopril (5mg/kg) and indomethacin (4mg/kg).[11] Subsequently, Heaton et al have also reported similar success.[12] This combination therapy led to a decrease in protein excretion and improvement in nutritional status and growth.

CONCLUSION

An infant with CNF has been described. Treatment is highly specialized. In our setting, a trial of both angiotensin converting enzyme inhibition (captopril) and indomethacin could have prolonged life. CNF is a rare but devastating cause of nephrotic syndrome in children.

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