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Congenital Nephrotic Syndrome: About A Case

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Abstract **Case Report**

Summary: Congenital nephrotic syndrome is a nephrotic syndrome present from birth or in the first three months of life, while infantile nephrotic syndrome is defined by a later onset but in the first year of life. Finnish-type congenital nephrotic syndrome and diffuse mesangial sclerosis represent the two main etiologies. Accurate diagnosis is based on clinical, histological and molecular biology criteria, and antenatal diagnosis is possible in some cases. We report the case of a female newborn, premature 35 WA + 9J, without particular pathological ATCDS admitted on D1 of life for a positive infectious assessment objectifying a bicytopenia made of thrombocytopenia and a neutropenia requested following an infectious anamnesis. positive in the mother, put on ATB, the evolution was marked by the appearance of edema of the two lower limbs on D6 of hospitalization taking the bucket in front generalized with puffiness of the face on D13 of hospitalization, a biological assessment was made and confirmed the nephrotic syndrome: hypoproteinemia at 20.3 g/l + hypoalbuminemia at 10.3 g/l + proteinuria for 24 hours at 3.3 g/24 hours proteinuria/creatinuria ratio 55. Associated symptomatic treatment nephroprotective treatment based on converting enzyme inhibitors was started with regular monitoring of renal function. In conclusion the congenital and infantile nephrotic syndromes are rare and generally have a poor prognosis whose evolution towards terminal renal insufficiency requires a program of dialysis and renal transplantationto the in the intensive Care Department A1 of the Hassan II University Hospital of Fez for the management of CT.

Keywords: nephrotic syndrome, mesangial sclerosis, diagnosis, thrombocytopenia.

INTRODUCTION

A congenital nephrotic syndrome is due to a hypoalbuminemia by loss of protein in the urine, the cause is usually genetic, sometimes infectious or alloimmune. The genetic forms are severe diseases, responsible for major edema requiring daily albumin infusions initially, and the evolution is towards renal failure. Infectious and nutritional complications are frequent due to the extent of protein leakage. Infant mortality remains high. The best known form is the Finnish nephrotic syndrome, linked to a double mutation of nephrin. The treatment is conservative, a uni- or even bi-nephrectomy may prove necessary to stop the protein leak. The disease may recur after kidney transplantation in the case of Finnish nephrotic syndrome (homozygous mutation Fin major), much more rarely in the other forms.

Through the observation of a D1 newborn and a review of the literature, we propose to take stock of the clinical, therapeutic and evolutionary particularities of the congenital nephrotic syndrome.

OBSERVATION

This is a newborn female, born on 10/26/22of a 26-year-old mother, 1st degree related marriage (paternal cousin), 4G4P, 2EV/VB (5-year-old girl, stillborn boy at 7 months, death at 4 months in a picture of anuria + urinary tract infection without document), grouping of the mother A+, with a history of hypothyroidism treated with Levothyrox for one year, monofetal pregnancy well monitored by a gynecologist, corticosteroid therapy not received, vaginal delivery at the of30 SA according to the mother and at 35 SA + 9J according to the FARR, cephalic presentation, PDN 1kg900, Apgar 9/10 go to 10/10, immediate cry, positive infectious anamnesis made of greenish amniotic fluid.

Patient admitted to D1 of life for positive infectious assessment made of neutropenia associated with thrombocytopenia. On clinical examination, the pink newborn reactive gesticulation spontaneously eupneic at 40 bpm normocardium at 133 bpm afebrile at 36.3 with disharmonious intrauterine growth retardation

(Height 44cm Weight 1kg 880 PC 31 cm), on neurological examination: good axial tone with slight peripheral hypotonia, sucking reflex and archaic reflexes present with a large bulging anterior fontanelle with disjunction of the sutures. The clinical malformative assessment notes bilateral slope feet with frenulum of the tongue. The rest of the somatic examination was unremarkable.

Bicytopenia on NFS: PNN 1400 PLQ 100,000, CRP was negative at 0.9; ECBU with sterile PL.

During his hospitalization, a transfantanel ultrasound objectified left frontal hyperechoic areas with minimal dilation of the ipsilateral horn in favor of periventricular leukomalacia, a complement by cerebral CT was made objectifying left cortical subcortical hemiatrophy associated with an area parieto-temporo-occipital hypodensity related to a secondary-looking porencephalic cavity: leucomalacia

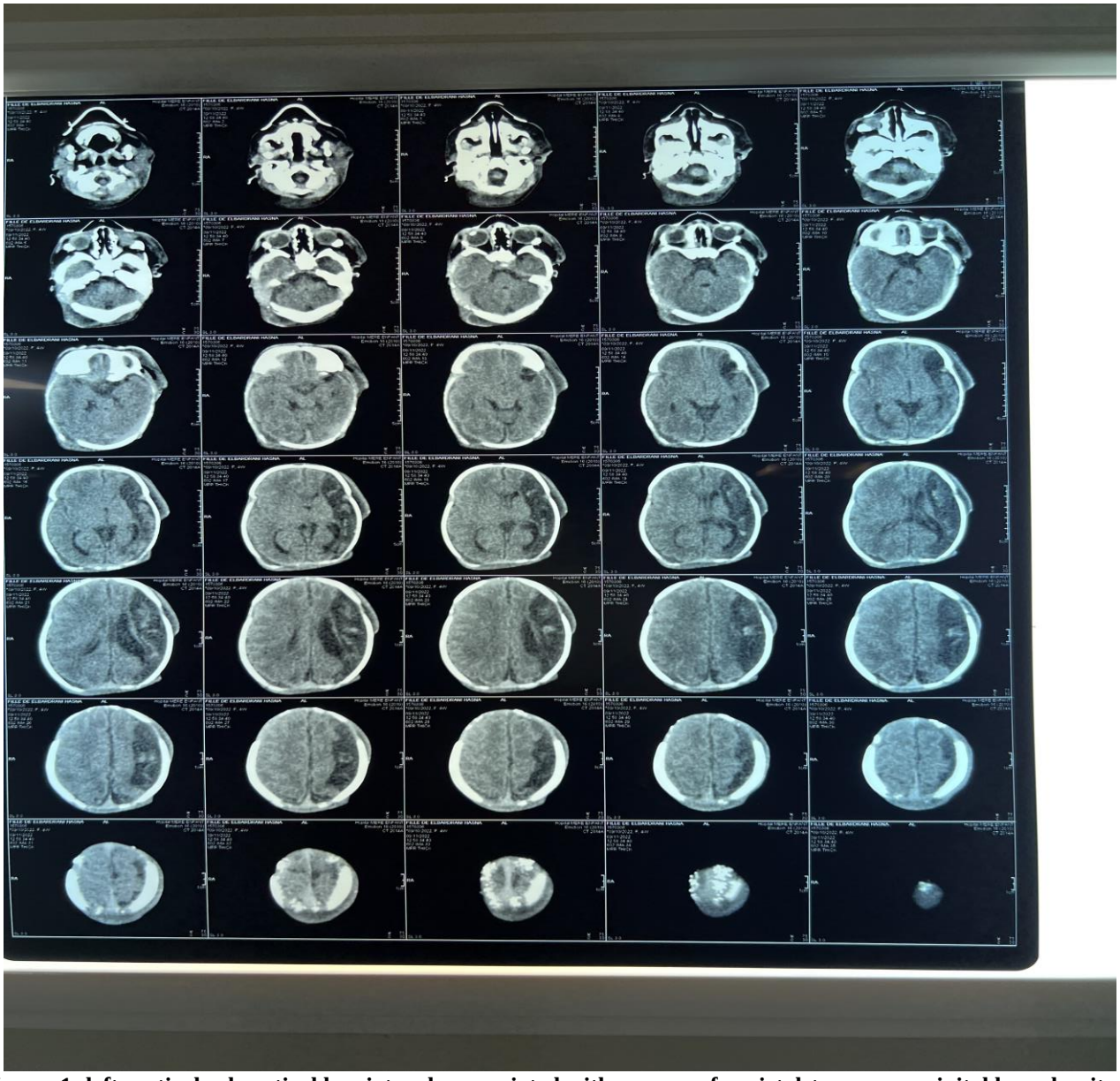
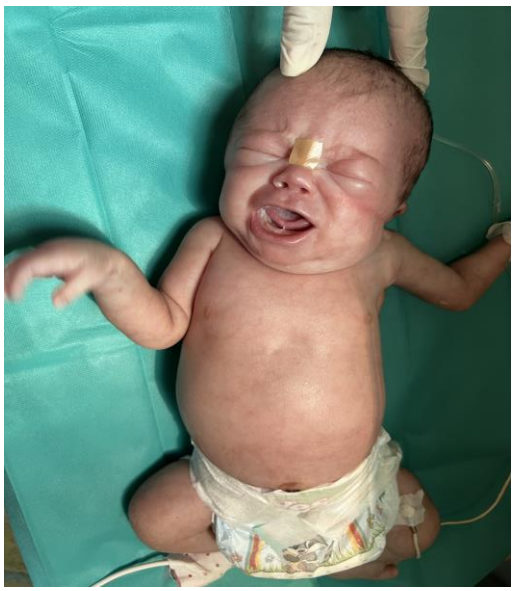
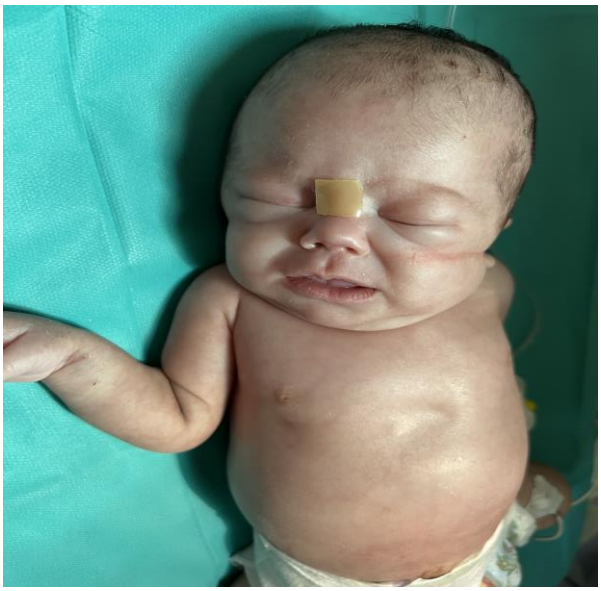


Image 1: left cortical subcortical hemiatrophy associated with a range of parietal-temporo-occipital hypodensity

The newborn was put on bi ATB: C3G associated with gentamycin.

The evolution was marked by the improvement of the biological assessment with the clinical appearance of edema of the two lower limbs on D6 of hospitalization taking the scoop in front generalized with puffiness of the face on D13 of hospitalization.

The biological assessment showed hypoprotidemia at 20.3 g/l, severe hypoalbuminemia at 10.3 g/l, proteinuria for 24 hours at 245 mg/kg per day. Renal function was normal: creatinine at 2 mmol/l. On the complete blood count (NFS), leukocytes were at 9610/mm3, hemoglobin at 12.8 g/dl, platelets at 195,000/mm3, serum potassium at 4.2 mmol/l and serum sodium at 136 mmol/l. The diagnosis of congenital nephrotic syndrome was thus retained.

Viral serology (Ag Hbs, HIV, CMV) and serology for syphilis and toxoplasmosis were negative. In addition, the renal ultrasound showed two kidneys of normal size and regular contours with a low-abundance peritoneal effusion, TSH us 10.6 uUI/ml +T4L 15.72pg/ml, the metabolic balance without anomaly with a genetic study not done for lack of means

Therapeutically, nephroprotective treatment was prescribed based on IEC 1mg/kg/d associated with symptomatic treatment with albumin infusion in the event of signs of hypovolemia with close monitoring of renal function.

The clinical course was favorable with regression of edema.

DISCUSSION

Congenital nephrotic syndrome is defined clinically by the presence of edema, massive albuminuria with hypoproteinemia, occurring at birth or appearing during the first three months of life [1], initially described by Hallman *et al.*, in 1959[1, 2] where a large series of cases was collected in Finland and by Vernier *et al.*, (1957) and Worthen *et al.*, (1959) in Minnesota, where many people live by extraction from Finland.

As its name suggests, it is in Finland that the incidence is highest because there is a focus of mutations. This is 1.2 per 10,000 births [3, 4]. It has also been observed in different ethnic groups around the world.

There are no data on the incidence and prevalence of the disease in Morocco. Family cases have been frequently described, in addition sporadic cases occurring in families with no notable history and no notion of consanguinity are not exceptional.

Premature birth is observed in 20% of cases [5, 6], with an average age of 36.5 weeks, and often complicated by acute fetal distress [7, 8].

The newborn in our study was born at the age of 35 +9 SA without any context of acute fetal distress.

The placenta is enlarged, weighing more than 25% of birth weight, and the amniotic fluid is often tinged with meconium, which is the case in our study.

Prenatal diagnosis is possible thanks to the determination of alpha-feto-protein (AFP) in the amniotic fluid, with a risk of false positives in the event of pathology of the nervous system. Intrauterine growth retardation is frequently found, which is consistent with the newborn in our study.

A non-specific poly malformation syndrome is often present at birth, such as talus feet, deformity in flexion of the hips, knees and elbows, arachnodactyly, wide fontanelles with disjunction of the sutures [8]. In our study, the newborn also presented with bilateral talus feet.

The term congenital nephrotic syndrome applies to patients whose disease is present at birth or appears during the first three months of life. When the nephrotic syndrome begins between the 3rd and the 12th month, it is an infantile nephrotic syndrome. In the

majority of cases, the prognosis is severe, the evolution is towards terminal renal failure. The precise diagnosis is based on clinical and histological criteria. Finnish-type congenital nephrotic syndrome and diffuse mesangial sclerosis represent the two main etiologies. However, there are rarer and possibly curable causes, such as congenital nephrotic syndrome secondary to syphilis or toxoplasmosis (Table 1).

Tableau 1 Classification des syndromes congénitaux et infantiles

Syndromes néphrotiques primitifs :
- syndrome néphrotique congénital de type finlandais ;
- sclérose mésangiale diffuse isolée ;
- syndrome de Denys-Drash ;
- syndrome néphrotique congénital avec malformations cérébrales ou d'autres organes ;
- syndrome néphrotique idiopathique ;
- glomérulonéphrite extramembraneuse.
Syndromes néphrotiques secondaires à une infection :
- syphilis congénitale ;
- toxoplasmose, rubéole, cytomégalovirus ;
- hépatite, VIH ;
- malaria ;
- lupus érythémateux disséminé.

VIH : Virus de l'immunodéficience humaine.

Finnish-type congenital nephrotic syndrome (SNCF) is a genetic disease transmitted in the autosomal recessive mode and therefore affects both boys and girls. The gene whose mutations are responsible for the disease has been located on chromosome 19 both in Finnish families and in families of other origins and there does not seem to be any genetic heterogeneity in the disease [9, 10]. This gene, called NPHS1, has been cloned [11]. Its size is 26 kb and it contains 29 exons. It codes for a transmembrane protein of 1,241 amino acids, nephrin, an adhesion protein of the immunoglobulin family. Several mutations have been identified, two of which predominate in the Finnish population [11]. These two mutations are present in 90% of Finnish patients either in the homozygous state or in the composite heterozygous state. This is a deletion of two base pairs in exon 2 (End major) responsible for a reading frame shift and a stoppage of translation at the level of this exon and a nonsense mutation in exon 26 (Fin minor). 8% of Finnish patients have the "Fin major" mutation on one chromosome while the mutation on the other allele has not been identified. Mutations in the same gene are responsible for the disease in non-Finnish patients, especially deletions, insertions, nonsense mutations, missense mutations distributed throughout the gene [12, 13, 9, 14, 15]. This is a deletion of two base pairs in exon 2 (End major) responsible for a reading frame shift and a stoppage of translation at the level of this exon and a nonsense mutation in exon 26 (Fin minor). 8% of Finnish patients have the "Fin major" mutation on one chromosome while the mutation on the other allele has not been identified. Mutations in the same gene are responsible for the disease in non-Finnish patients, especially deletions, insertions, nonsense mutations, missense mutations distributed throughout the gene [12, 13, 9, 14, 15]. This is a deletion of two base pairs in exon 2 (End major) responsible for a reading frame shift and a stoppage of translation at the level of this exon and a nonsense mutation in exon 26 (Fin minor). 8% of Finnish patients have the "Fin major" mutation on one chromosome while the mutation on the other allele has not been identified. Mutations in the same gene are responsible for the disease in non-Finnish patients, especially deletions, insertions, nonsense mutations, missense mutations distributed throughout the gene [12,13,9,14,15] 8% of Finnish patients have the "Fin major" mutation on one chromosome while the mutation on the other allele has not been identified. Mutations in the same gene are responsible for the disease in non-Finnish patients, especially deletions, insertions, nonsense mutations, missense mutations distributed throughout the gene [12,13,9,14,15] 8% of Finnish patients have the "Fin major" mutation on one chromosome while the mutation on the other allele has not been identified. Mutations in the same gene are responsible for the disease in non-Finnish patients, especially deletions, insertions, nonsense mutations, missense mutations distributed throughout the gene [12, 13, 9, 14, 15].

In our study the genetic confirmation of the nephrotic syndrome was not made for lack of means.

Malnutrition is favored by protein leaks and feeding difficulties in these anorexic infants. The set of disturbances secondary to severe nephrotic syndrome explains why children are very susceptible to bacterial infections and thromboembolic complications.

Hypothyroidism secondary to urinary leakage of thyroxine-carrying protein is common (16). Renal function is initially normal, but gradually deteriorates and end-stage renal failure occurs between the ages of 3 and 5 years.

The treatment of Finnish type nephrotic syndrome is symptomatic, it is always resistant to corticosteroid therapy and immunosuppressants and these treatments, which increase the risk of infection, are contraindicated. Only conservative treatment is recommended in order to maintain a satisfactory nutritional status, to control the edematous syndrome, to prevent thrombosis and infections, until a kidney transplant can be performed [17]. This conservative treatment consists of daily albumin infusions or every other day, gamma globulin infusions, a diet rich in protein (up to 3 to 4 g/kg) and calories (120 kcal/kg) but low in salt. Intravenous administration of furosemide is indicated after albumin infusions. Nutrition by gastric gavage or parenterally is often necessary. The prevention of thrombotic complications is discussed, some authors suggest a combination of low-dose aspirin and dipyridamole while others administer warfarin [17, 18]. Despite these measures, intercurrent complications are frequent.

In some patients, a bi-nephrectomy may be proposed before the stage of renal failure. Dialysis treatment is then necessary until the weight of the child has reached 8 or 9 kg [19], but it is necessary to insist on the need for intensive nutritional support, to carry out the vaccination schedule before transplantation and to set up rapid and effective antibiotic therapy in the event of suspicion of infection but not systematic antibiotic prophylaxis, before a kidney transplant was proposed.

Recurrences of the nephrotic syndrome are however possible after renal transplantation, particularly in homozygous carriers of the Fin-major mutation.

When the mutation of the gene responsible for the disease is identified in an affected child in a family, antenatal diagnosis is possible by studying the DNA on chorionic villus sampling.

CONCLUSION

Finnish-type congenital nephrotic syndrome is an early autosomal recessive condition. Currently, it is the genetic study that allows the diagnosis of certainty, it is a rare condition and overall poor prognosis due to infectious or thromboembolic complications whose evolution is towards end-stage renal failure require a dialysis program and kidney transplantation.

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