WCN24-AB-2676: Genetic variant in COQ8B, a potentially treatable cause of SRNS: First case reported in Chile

Carolina Garay[1], Paola Krall[1], Carolina Lizama[2,3], Eduardo Wolff[4,5]

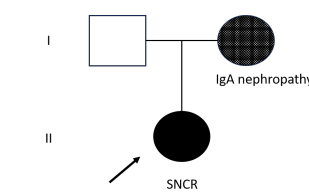
[1] Departamento de Pediatría y Cirugía Infantil Oriente, Facultad de Medicina, Universidad de Chile.[2] Servicio de Nefrología, Hospital Puerto Montt, Chile [3] Facultad de Medicina y Ciencias, Universidad San Sebastián Puerto Montt, Chile[4] Servicio de Pediatría, Hospital Luis Calvo Mackenna, Chile. [5] Servicio de Pediatría, Clínica Las Condes, Chile.

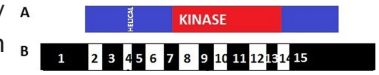
BACKGROUND

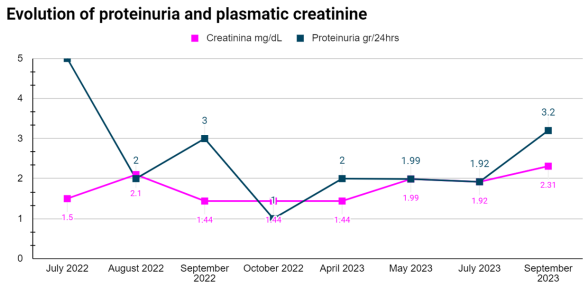
Steroid-resistant nephrotic syndrome (SRNS) is characterized by nephrotic-range proteinuria, hypoalbuminemia and edema that does not respond to steroid treatment. Its etiologies are diverse, including primary and secondary glomerulopathies, as well as genetic causes. It is noteworthy to highlight SRNS caused by variants related to coenzyme Q10 (CoQ10) biosynthesis, as this may be potentially treatable, in contrast to other SRNS causes that tend to progress to advanced chronic kidney disease (CKD) without therapeutic options.

CASE REPORT

- A **15-years-old** girl from Chiloé with a history of a mother with IgA nephropathy and CKD stage II-III. Nephrocalcinosis was detected at 8-9 years through renal ultrasound when studying enuresis. Since **2020**, the patient has had **non-nephrotic range proteinuria** and **enalapril** was prescribed with **partial response**.
- In **2022** she developed **nephrotic syndrome**, with nephrotic-range proteinuria (5 g/24 hrs), hypercholesterolemia, hypertriglyceridemia, hypoalbuminemia (2.8 mg/dl), increase in creatinine up to 1.5 mg/dl and mild hypertension. **Prednisone (60 mg/m2)** was prescribed with **partial response** after a month, maintaining proteinuria (2 g/24 hrs), hypoalbuminemia (2.8 mg/dl) and increase in creatinine up to 2.1 mg/dl. Renal ultrasound showed microcysts.
- Due to the suspicion of a genetic origin, a **panel of 401 genes** associated with nephropathies was requested, identifying 10 variants of uncertain significance (VUS), including a **homozygous deletion of exon 13 in the COQ8B (ADCK4) gene**, predicting loss of a segment of the kinase domain. Subsequent direct sequencing confirmed that deletion was inherited from both parents. Prednisone treatment continued for another month with a partial response. A **renal biopsy revealed 10 globally sclerosed glomeruli and 7 with segmental sclerosis, with 70% tubular atrophy**. The estimated glomerular filtration rate (eGFR) reached 43.9 ml/ min/1.73 m², with proteinuria of 3 g/24 h. **Treatment with CoQ10** (20 mg/kg/day), along with atorvastatin was initiated, and ACE inhibitors (ACEi) were suspended temporarily.
- During the **first 12 months of treatment**, her **renal function remained stable**, and her proteinuria decreased to 1 g/24 hrs. Subsequently, there was a **loss of function and an increase in proteinuria**.
- In the last months she transitioned from pediatric nephrology to adult nephrology.







Graphic 1. Evolution of proteinuria and plasmatic creatinine

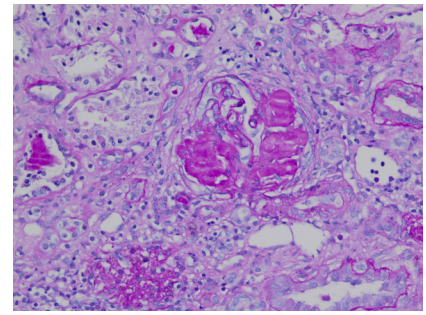


Figure 1. Histology: Glomerular sclerosis and segmental hyalinosis

CONCLUSIONS

- **SRNS poses a high risk of progression** to End-Stage Renal Disease (ESRD) and exhibits high **genetic heterogeneity**.
- Conducting a comprehensive **genetic panel** can quickly identify a genetic cause.
- The patient described represents the **first known case in Chile with a variant in COQ8B,** a gene associated with the mitochondrial biosynthesis of CoQ10.
- It manifests with proteinuria in adolescence and a biopsy compatible with global and segmental glomerulosclerosis. The timely initiation of **CoQ10 treatment can slow down the progression of ESRD**, and in the case of transplantation, recurrence is not expected.

Hospital de Niños Dr. Luis Calvo Mackenna
Hospital Autogestionado de Alta Complejidad Fundado en 1942

FACULTAD DE MEDICINA
UNIVERSIDAD DE CHILE