education in paediatrics. The rotation in PC allows students to acquire basic clinical skills while working with real-world patients, which are harder to acquire in the hospital setting, and get training in areas such as health prevention and promotion or the biopsychosocial approach to disease.

We believe that the rotation in PC paediatrics should be mandatory in the curriculum of every medical school in Spain and integrated with hospital-based rotations with specific goals. To this end, it is advisable that PC paediatricians be included in the teaching staff of university paediatrics departments. Our experience may provide a model for the development of the PC paediatrics rotation.

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Encephalopathy, kidney failure and retinopathy. CoQ10 deficiency due to COQ8B mutation*

Encefalopatía, fallo renal y retinopatía. Déficit de CoQ10 pormutación de COQ8B

Dear Editor:

Coenzyme Q10 (CoQ10) plays a crucial role in several cellular processes, such as such as energy production through the mitochondrial respiratory chain, β-oxidation of fatty acids and pyrimidine biosynthesis, and it is also one of the main cellular antioxidants. Its synthesis requires multiple enzymes encoded by different genes (*PDSS1*, *PDSS2*, *COQ2*, *COQ4*, *COQ6*, *COQ8A*, *COQ8B* and *COQ9*). Due to the ubiquity of CoQ10 and the fact that the tissue expression of enzymes needed for its synthesis is variable, the clinical spectrum of CoQ10 deficiency is very heterogeneous, with the disorder potentially manifesting with myopathy, psychomotor retardation (PMR), encephalopathy, cerebellar ataxia, retinopathy, pulmonary hypertension, myocardiopathy, steroid-resistant nephrotic syndrome (SRNS) and chronic kidney disease (CKD), depending on the involved gene.[1]

We present the case of a boy aged 6 years with a past history of febrile seizures and PMR of unknown aetiology admitted to hospital with hypertensive encephalopathy (blood pressure, 240/170 mmHg). The parents reported the child had experienced asthenia, polyuria, polydipsia and foamy urine lasting 6 months and palpebral oedema in the past few days. A head computed tomography (CT) scan was performed, with normal findings. The evaluation revealed the presence of microscopic haematuria, nephrotic-range proteinuria (urine protein/creatinine ratio, 23 mg/mg; normal range <0.2) and kidney failure with an estimated glomerular filtration rate of 4 mL/min/1.73 m^2 (KDIGO 2012 stage 3). The ultrasound scan revealed a small renal size for age, loss of corticomedullary differentiation and increased echogenicity, findings suggestive of long-term renal dis-

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Table 1 Previously described COQ8B variants and published case series.

Case series	*N*	Nucleotide change	Amino acid change	Ethnicity
Ashraf et al.	15	c.101G>A	p.W34*	European
		c.954_956dup	pT319dup	European
		c.532C>T	p.R178W	Arabic
		c.645delT	P.F215Lfs*14	Algerian
		c.1430G>A	p.R477Q	Algerian
		c.857A>G	p.D286G	Unknown
		c.1447G>T	p.E483*	Unknown
		c.958C>T	p.R320W	Tunisian
		c.1027C>T	p.R343W	Moroccan
		c.1199-1200insA	p.H400Nfs*11	Turkish
		c.1356-1362del	p.Q452Hfs	Indian
Korkmaz et al.	26	c.293T>G	p.L98R	Turkish
		c.929C>T	p.P310L	Turkish
		c.1493-1494CC>AA	p.A498E	Turkish
		c.1339dupG	p.E447Gfs*10	Turkish
Li et al.	2	c.625C>G	p.D209H	Chinese
Wang et al.	8	c.241G>T	p.E81*	Chinese
		c.1468C>T	p.R490C	Chinese
		c.448C>T	P.R150*	Chinese
		c.748G>C	p.D250H	Chinese
		c.737G>A	p.S246N	Chinese
Feng et al.	2	c.614C>T	p.S205N	Chinese
Current study	1	c.439T>C)	p.C147R	European
		c.1035+2T>C	p.(¿)	European

* The mutation does not result in an amino acid substitution but a stop codon.

ease. There was also evidence bilateral retinitis pigmentosa. Continuous venovenous haemodiafiltration was initiated to control hypervolemia and manage electrolyte abnormalities such as hyperphosphataemia and hyperkalaemia, and chronic haemodialysis was maintained for 3 months until the patient underwent transplantation of a kidney from a deceased donor, which was successful. Genetic testing for nephronophthisis (*NPHP1–4*) was negative. Later on, the evaluation was expanded with next-generation sequencing of 140 genes associated with renal diseases, which identified 2 novel compound heterozygous variants of gene *COQ8B* (ADCK4) (c.439T>C [p.Cys147Arg] and c.1035+2T>C [p.?]), one of the genes involved in the synthesis of CoQ10 (Table 1).

On account of the genetic diagnosis, the patient started treatment with ubiquinone (5 mg/kg/day), which improved psychomotor development and academic performance. At present, the patient is aged 12 years, the renal graft remains functional and his blood pressure is normal. The patient has not experienced any more seizures and treatment with anticonvulsants was discontinued successfully. In the physical examination, the patient continues to exhibit mild dysmetria in the finger-to-nose test and intention tremor in the hands despite normal findings of magnetic resonance imaging at age 11 years.

In CoQ10 deficiency, glomerular involvement, whether isolated or syndromic, is associated with changes in genes *COQ2*, *COQ6*, *PDSS2* and *COQ8B* (ADCK4). Between 1% and 1.9% of cases of SRNS are due to CoQ10 deficiency associated with variants of these genes.

COQ8B encodes a kinase (aarF domain-containing kinase 4, ADCK4)[2] expressed in mitochondria and in particular in pedicels, the proximal tubules and the collecting ducts. It also interacts with *COQ6* at the podocyte level.[3]

Changes in the *COQ8B* gene lead to loss of function in ACDK4, resulting in decreased levels of CoQ10 and decreased podocyte migration in absence of proliferation or apoptosis of fibroblasts or in podocytes. At onset, which typically occurs in adolescence, 44% of patients present with SRNS and 46% with advanced CKD (stage 3–5).[4] The renal histology is focal segmental glomerulosclerosis. Some patients also present with extrarenal manifestations, such as retinitis pigmentosa, convulsive seizures or PMR. Patients that have onset with SRNS may rapidly progress to terminal CKD and require a kidney transplant.

The administration of CoQ10 can improve symptoms, lower protein levels in urine and slow down the progression of CKD. Case series of CoQ10 deficiency caused by *COQ8B* variants (ADCK4) published to date have shown that 4 out of 43 patients had a partial or total response to this treatment.[3–5] In 3 of these patients, renal disease was in the early stages.

Genetic testing including investigation of genes involved in the biosynthesis of CoQ10 should be considered in patients presenting with SRNS or CKD of unknown aetiology with or without extrarenal manifestations such as retinitis pigmentosa, convulsive seizures or PMR. It offers multiple benefits: an unequivocal molecular diagnosis for patients and their families, knowledge of the genotype-phenotype association and delivery of treatment which, if initiated early, may partially or completely halt the progression of renal and extrarenal disease. Genetic testing through multi-gene next generation sequencing panels with subsequent confirmation by Sanger sequencing is the most cost-effective approach at the moment.[6]

The case presented here illustrates the added value of genetic diagnosis in paediatric patients with severe CKD of

unknown aetiology and the importance of identifying any associated abnormalities.

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Complete atrioventricular block associated with respiratory syncytial virus: Presentation of a case and a literature review☆

Bloqueo auriculoventricular completo asociado a infección por virus respiratorio sincitial: presentación de un caso y revisión de la literatura

Dear Editor:

Respiratory syncytial virus (RSV) is the most frequent causative agent of lower respiratory tract infections in children. In some cases, it can cause severe cardiovascular or central nervous system disease, such as myocarditis or necrotising encephalitis.[1] We present the case of a girl with acute myocarditis and complete heart block (CHB) associated with RSV infection.

The patient was a 1-month old female infant admitted to the paediatric intensive care unit (PICU) with severe bronchiolitis secondary to RSV infection and receiving noninvasive mechanical ventilation. A few hours after admission, the patient had an episode of prolonged bradycardia requiring intubation. After intubation bradycardia persisted (60–70 bpm) and the patient eventually develop-mend arterial hypotension. Infusion of adrenaline was initiated followed by performance of an electrocardiogram (ECG), which revealed a narrow complex bradycardia (Fig. 1). Each QRS complex was preceded by a P wave, but there seemed to be blocked P waves hidden in the T wave. An oesophagus ECG was performed that confirmed the presence of CHB (Fig. 1B). Intravenous infusion of isoproterenol was initiated at a dose of 0.2 μg/kg/min, achieving an increase of the heart rate (HR) to 120–130 bpm and resolution of hypotension. Twenty-four hours later, the patient developed ventricular dysfunction with a left ventricular ejection fraction (LVEF) of 42%, lactate elevation (3.8 mmol/L), pulmonary oedema and elevation of troponins (peak ultrasensitive cardiac troponin T, 27 ng/L), compatible with myocarditis. The patient required milrinone (0.5 μg/kg/min) and adrenaline (up to 0.3 μg/kg/min). A workup oriented to myocarditis was including a panel to identify anti-Ro and anti-La antibodies in the infant and the mother, serological tests for Lyme disease, blood, urine and cerebrospinal fluid (CSF) cultures, PCR tests for detection of viral and bacterial pathogens in blood, stool and nasopharyngeal aspirates, tests of serum amino acids and acylcarnitine profile analysis. The patient was treated with intravenous immunoglobulin (1 g/kg for 2 days), carnitine, ribavirin and palivizumab. She exhibited a quick haemodynamic recovery, allowing discontinuation of adrenaline and milrinone on days 3 and 5, respectively. However, the CHB persisted. The patient received 2 separate courses of intravenous methylprednisolone (2 mg/kg for 5 days), without response. The patient could tolerate a HR of 60–75 bpm, so she did not need placement of a pacemaker. The PCR test for detection of RSV-B was positive for the nasopharyngeal aspirate sample and the blood sample collected during the acute phase. The patient has remained asymptomatic during the follow-up. The ECG at 3 months showed recovery of atrioventricular (AV) conduction, with evidence of a residual first-degree AV block, which remained 9 months after the initial event.

CHB is an unusual manifestation in the course of acute myocarditis. A recent study in 31 760 adults found an incidence of 1.1%, and its presence was associated with longer lengths of stay and a higher mortality.[2] In 2014, Anderson

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