Sphingosine-1-phosphate lyase insufficiency syndrome presenting with oculomotor nerve paralysis

Ozpinar E[1], Kılıc B[1], Palaz M[1], Ayaz A[2], Topcu Y[1], Aydin K[1]

Istanbul Medipol Mega University Child Neurology Department, Istanbul Medipol Mega University Genetics Department

18TH ICNC 2024 Footprints to the future
INTERNATIONAL CHILD NEUROLOGY CONGRESS
Cape Town, South Africa I May 6-10, 2024

INTRODUCTION

Sphingosine–1–phosphate lyase insufficiency syndrome (SPLIS) is a rare metabolic disorder caused by a deficiency in SPL, final enzyme in sphingolipid degradative pathway. Biallelic SGPL1 gene mutations are associated with RENI syndrome (OMIM: 617575) which is an autosomal recessive form of steroid-resistant nephrotic syndrome with multisystemic findings. Most individuals have focal segmental glomerulosclerosis in infancy or early childhood. It also may be seen primary adrenal insufficiency, ichthyosis, acanthosis, immunodeficiency and neurological disorders. Neurological findings include sensorineural hearing loss, peripheral neuropathy, developmental delay, ataxia, epileptic seizures (1).

CASE

A 19-month-old female patient was admitted to the hospital with complaints of outward deviation and ptosis of right eye. She had no previous history of trauma and had infection. On examination, there were signs of right oculomotor nerve palsy but other neurological examinations were normal. Cranial MRI revealed pathological contrast enhancement in bilateral 3rd, 5th nerves and expansion in right 3rd nerve. Spinal MRI showed contrast enhancement on lower thoracic spinal cord and at conus level. Additionally, calcification was observed in the central parts of both adrenal glands. No pathology was found in cerebrospinal fluid tests and EMG. She had proteinuria in complete urinalysis. Infection panels, hormone and metabolic tests were normal. Steroids were given, and when steroid was tapered off, outward gaze and ptosis were observed in left eye. Autoimmune encephalitis panel was sent. She received IVIG due to both oculomotor nerve palsies. WES has been requested and resulted as biallelic SGPL1 gene mutation (p.L173Q c.518T>A).

DISCUSSION

Most recent systematic review showed that fifty-five SPLIS patients (54.9% male, 45.1% female) were identified. Most patients (54.9%) primarily manifested within the first year of life, nearly half of whom survived. The most prevalent clinical feature was endocrinopathies, including primary adrenal insufficiency (71.2%) and hypothyroidism (32.7%). Kidney disorders (42, 80.8%) were mainly in the form of steroid-resistant nephrotic syndrome and progressed to end-stage kidney disease in 19 (36.5%) patients at a median (IQR) age of 6 (1.4-42.6) months. Among 30 different mutations in SGPL1, the most common was c.665G > A (p.Arg222Gln) in 11 (20%) patients. Twenty-six (49.1%) patients with available outcome were deceased at a median (IQR) age of 5 (1.5-30.5) months, mostly following kidney disease (23%) or septic shock (23%) (2). Earlier diagnosis of SPLIS and prevention of end-stage kidney disease and other life-threatening complications are important for prognosis. In our case, she had kidney and adrenal manifestations with preceeding neurological findings.

CONCLISIONS

Because this form of nephrotic syndrome is multisystemic and progressive, genetic diagnosis is crucial for optimal treatment of the disease and appropriate screening for comorbidities. Since there is no case reported in literature that started with oculomotor nerve palsy, we wanted to emphasize this rare syndrome and this new finding we had with this case report.

REFERENCES

1. Choi YJ, Saba JD. Sphingosine phosphate lyase insufficiency syndrome (SPLIS): A novel inborn error of sphingolipid metabolism. Adv Biol Regul. 2019;71:128-140. doi:10.1016/j.jbior.2018.09.004
2. Pournasiri Z, Madani A, Nazarpack F, et al. Sphingosine phosphate lyase insufficiency syndrome: a systematic review. World J Pediatr. 2023;19(5):425-437. doi:10.1007/s12519-022-00615-4