Optic Neuritis in CD59 Deficiency: An Extremely Rare Presentation

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ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

INTRODUCTION

CD59 is a protein which regulates formation of membrane attack complex by preventing recruitment of C9 thereby keeping the cell lysis under control.[1] The relationship of the CS with both the central and peripheral nervous system demyelinating diseases has been shown in many studies.[2–4] But, to our knowledge, only two siblings have been reported to present optic neuritis, which was thought to be due to CD59 deficiency demonstrated in postmortem studies.[5] We present a patient with first two attacks of early-onset demyelinating peripheral neuropathy and third attack as ON.

Case presentation

First attack

An 8-month-old girl presented with a three-day history of generalized weakness and poor sucking. The patient was born at term by cesarean section without any complication and had age-compatible neurodevelopment. Parents were 2nd degree cousins with four children. The first child had recurrent episodes of weakness after febrile episodes which were responsive to intravenous immunoglobulin (IVIg) treatment and died at 12 months of age without a specific diagnosis. The mother's cousin was also under follow-up at another center with similar disease. Neurological examination revealed absent DTR and decreased muscle strength (Medical Research Council [MRC] grading system: 3/5) of lower extremities, normoactive DTR and decreased muscle strength (MRC: 4/5) of upper extremities and tongue fasciculation. The patient was unable to hold her head. Clinical features in each attack are shown in Table I. Complete blood count, biochemical tests, vitamin B12, creatinine kinase, contrast-enhanced brain MRI, contrast-enhanced spinal MRI, cerebrospinal fluid (CSF) examination, and extensive metabolic investigations were normal. Nerve conduction studies were normal but needle electromyography revealed diffuse neurogenic changes. With IVIg (1 g/kg/day for 2 days) treatment, sucking improved, head control was gained, but weakness in the lower extremities continued. Weakness episodes with neurogenic Electromyography suggested CD59 deficiency. Immunophenotypic analysis with flow cytometry showed CD59 deficiency. Sanger sequencing revealed a homozygous, pathogenic variant in the *CD59* gene (MIM: 107271), NM_203331: c146delA (p.Asp49Valfs*32) (rs587777149). Same variant was found in the mother's cousin. No hemolysis evidence was detected. Eculizumab treatment could not be given because parental consent could not be obtained. Seven days after IVIg treatment, sucking and other motor functions recovered without any sequelae.

Second attack

The patient who did not have any attacks in following four months and continued to gain the neurodevelopmental steps in time, presented with weakness in the legs and poor sucking. The patient had an upper respiratory tract infection 15 days ago and received oseltamivir and clarithromycin treatments. Neurological examination revealed absent DTR in upper and lower extremities, decreased muscle strength of lower and upper extremities (MRC: 3/5). IVIg was given at same dosage. On the 3rd day, the complaints regressed and the neurological examination findings improved.

Third attack

Eight months after the second attack, the patient presented with sudden vision loss and dilated pupils noticed by the mother. Detailed ophthalmological examination revealed loss of light fixation with fixed dilated pupils and no light reflex; however, dilated fundoscopy was totally normal (Figure 1A and B). The patient was diagnosed with bilateral ON, since remainder of the neurological examination and CSF assessment were normal. Orbital MRI showed increased signal intensity on T2 weighted sequences and increased enhancement on contrast enhanced T1 images at the bulbar and retrobulbar level of the bilateral optic nerves, more prominent on the right, increased thickness of chiasm, heterogeneity in the orbital fatty tissue on the right and suspicious enhancement in the bilateral olfactory nerves. CSF MOG-Ab and aquaporin 4 antibody (AQP4-Ab) were negative. Pulse steroid (30 mg/kg/day for ten days) and intravenous immunoglobulin (1 g/kg/day for two days) was given without any benefit. After the parental consent, eculizumab treatment was planned biweekly. Five days after the steroid therapy, the patient was uncomfortable with the light and avoided objects while walking. Ophthalmological examination revealed bilateral optic disc pallor with the lack of optokinetic nistagmus (OKN). Subjective complaints about vision disappeared. The neuro-ophthalmological examination revealed bilateral normoisochoric pupils with central, steady, and maintained fixation on the 30th day of the beginning of symptoms (15th day of the end of steroid treatment). Radiologic examination after one month revealed regression of optic and olfactory nerve findings but new three cerebellar demyelinating small lesions on T2 images without clinical correlation. The first dose of eculizumab (300 mg, intravenous) was administered on the 35th day of the symptom onset. Detailed ophthalmological examinations after the sixth dose of eculizumab revealed positive OKN, bilateral central, steady, and maintained fixation with normoisochoric pupils and positive light reflexes on both eyes; however, dilated fundoscopy depicted bilateral optic atrophy (Figure 2A and B). Cycloplegic refraction was found as -1.75 diopters (D) of myopia with -3 D of astigmatism in the right eye and -3.5 D of astigmatism in the fellow eye. The patient is still followed-up with no further attacks.

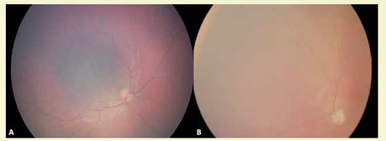

Figure 1 A-B. Dilated fundoscopy revealed normal findings

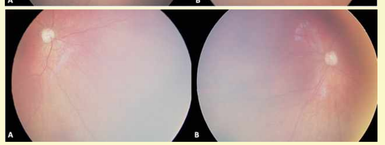

Figure 2 A-B. Bilateral optic atrophy was diagnosed by dilated fundoscopy

Conclusion

CD59 deficiency may be a relatively common autosomal recessive disease in Turkey. Child neurologists should know classical findings of the disease because the attacks are preventable with eculizumab. Optic neuropathy may be a manifestation of CD59 deficiency.

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