A rare neurodegenerative disorder induced by COVID-19: CONDSIAS

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OBJECTIVES

Stress induced childhood onset neurodegeneration with variable ataxia and seizures (CONDSIAS) is a very rare childhood onset severe neurodegeneration syndrome associated with episodic, stress-induced seizures, ataxia, and axonal neuropathy. It is an autosomal recessive disorder. The ADP-Ribosylhydrolase Like 2 (ADPRHL2) gene that encodes the protein reverses ADP-ribosylation is defected (1). In this study, we introduce a case of CONDSIAS with severe clinical presentation.

CASE

A three-years-old female patient, born to a nonconsanguinous family, was referred with various clinical symptoms including variable ataxia, torticollis and gradual onset of truncal hypotonia within one year. Her neurological development was normal until the age of 2 and she had COVID-19 infection 3 weeks ago. She developed complete motor and speech regression, infrequent seizures, and loss of consciousness. On follow up, abnormal movements mostly myoclonic and choreiform types were seen. An electroencephalogram was performed and showed epileptic encephalopathy (Fig2). Our patient developed a severe septicemia and had cardiac arrests several times. Serial magnetic resonance imaging (MRI) showed mild cerebral and cerebellar atrophy (Fig1).

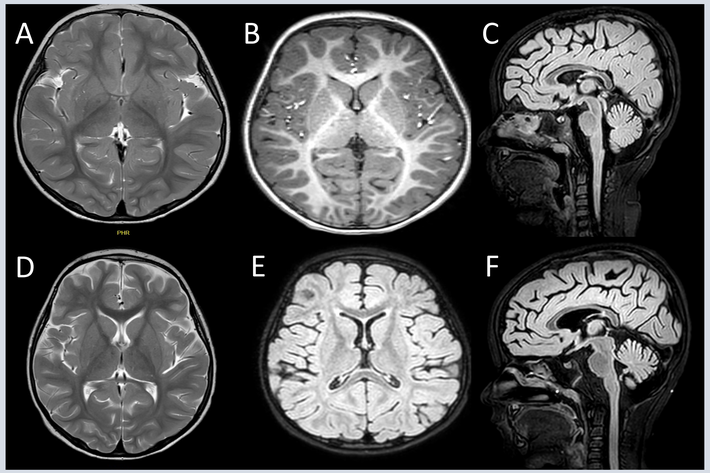

Fig. 1. Brain MRI shows mild cerebral and cerebellar atrophy. A-B-C at 2 years, D-E-F at 3 years of age

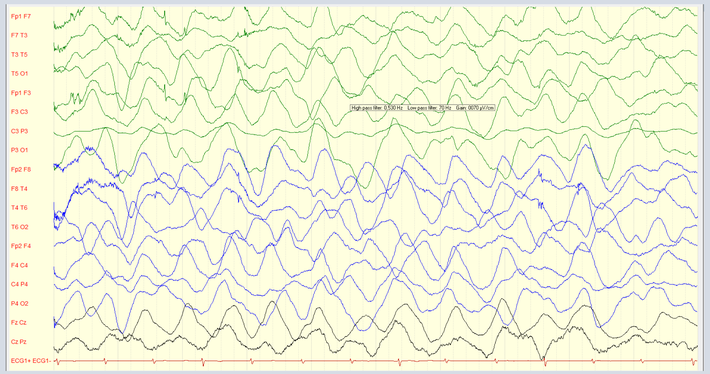

Fig. 2. EEG shows epileptic encephalopathy

Neurodegenerative disorder especially neurotransmitter deficiency disorders and autoimmune encephalitis were in our differential diagnosis and intravenous immunoglobulin, neurotransmitter precursors were administered. All basic metabolic tests and tests for autoimmune encephalitis were normal. To differential diagnose, whole-exome sequencing (WES) was performed on the proband. A homozygous frameshift variant in the ADPRHL2 (NM_017825.3; c.529_530del, p.S177Gfs*48) was identified by WES analysis.

CONCLUSIONS

The ADP ribosylation (ADPr) is a reversible post-translational modification in which PAR is added to proteins in response to stress, involving a variety of physiological and pathological processes. In response to stress, excessive accumulation of PAR-modified protein can trigger a cascade of cell death responses leading to progressive neurodegeneration (1). CONDSIAS has broad phenotypic spectrum, have been reported as neurodegeneration, variable ataxia, seizures, tremor, nystagmus, balance problems, cerebellar, spinal cord and cerebral atrophy, hearing impairment and occasionally hearing loss, ptosis, ophthalmoplegia, dysarthria, muscle weakness, axonal neuropathy, dysmetria, and tongue fasciculation (2).

Approximately, one-third of the reported patients died from acute cardiac arrest (1). Symptoms and severity of the disorder appear to be different in patients and sometimes lead to early childhood death (2). In the present study, we introduced a female child with a variation in the ADPRHL2 gene presented with ataxia, abnormal movements, seizures, progressed with severe clinical findings such as septicemia and cardiac arrest after COVID-19.

REFERENCES

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