P 1-56

Alexander Disease mimicking Cerebral Palsy : A Case report

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Introduction

Alexander disease is a rare degenerative disorder and leukodystrophy caused by dominant missense mutations in the gene encoding the glial fibrillary acidic protein. The characteristic signs of Alexander disease are developmental delay, megalencephaly, seizures, spasticity and psychomotor deterioration. Four types can be distinguished based on the age at clinical presentation: neonatal, infantile, juvenile, and adult. Especially, the juvenile type, with an onset in childhood, shows a variable clinical course; slowly progressive paresis, bulbar signs, and brisk reflexes, but often with an intact mental state. This is a case in which an adeolescent presented with developmental delay, history of seizures, and progressive paresis.

Case presentation

A 17-years old boy visited our outpatient clinic with a history of progressive paresis. The boy was born with a full-term pregnancy. Postnatally, he showed global developmental delay and was able to walk at about 24 months. He was diagnosed as cerebral palsy and intellectual disability. He had crouched gait but was able to stair up and down. But, He began to fall down when he was fifteen and has been unable to walk at all since the slip down injury of August 2017 even if he had no evidence of fracture. He seemed to have a progressive paresis and was not able to even sit to stand alone. Based on the progressive paresis, neurodegenerative disease, cerebral infarction, leukodystrophy, etc. were considered. We did several diagnostic evaluation. Brain MRI showed bilateral confluent T2 high signal intensity in periventricular and subcortical white matter of bilateral cerebral hemispheres and central white matter of cerebellum which. The exome sequencing test showed mutation of the gene encoding glial fibrillary acidic protein (GFAP) which is known to be the cause of Alexander disease. In the exon 1 of the GFAP gene (17q21.3) mutation was found in which the 79th amino acid, arginine, was substituted with cysteine. Gene study about parents and siblings were all negative, so the patient was concluded to have de novo mutation of GFAP gene.

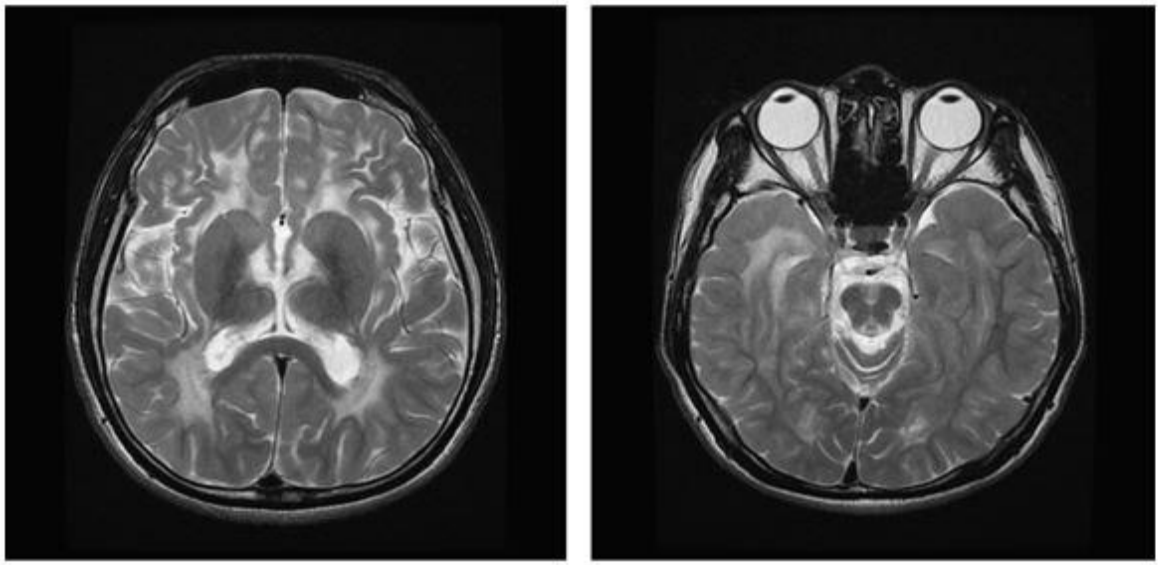
Discussion

Alexander disease is a slowly progressing neurodegenerative disease. Children with infantile form do not survive past the age of 6, and the juvenile onset do not live until child-bearing age and do not reproduce, indi¬cating that the majority of cases are sporadic. In this case, the boy was incorrectly assumed as cerebral palsy until the 17 years-old. So It is inevitable to get the regular follow-up in children with developmental delay of unknown origin and the accurate diagnosis will be helpful to give appropriate palliative care.

Table1. Exome sequencing report

Gene	Mutation	Mutation effect	Hetero/ Homo	HGMD/ OMIM	Inheritance	Classification
GFAP	c.235C>T [p.Arg79Cys]	Missense	Hetero	ALXDRD	AD	Pathogenic

Reference sequence : NM_002055.4
Abbreviations : ALXDRD [Alexander disease], AD [Autosomal dominant]



[Figure 1. Bilateral confluent T2 high signal in periventricular and subcortical white matter]