Col6 diseases among patients with CP in Kazakhstan

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Introduction

It is known that under the label of cerebral palsy, other neuromuscular disorders may be hidden, which are characterized by a progressive course and require a different management approach than cerebral palsy.

Collagen VI-related myopathies represent a group of disorders that cause muscle weakness and joint contractures with a significant variability in disease severity among patients.

Objective:

Detection of neuromuscular disorders among patients with cerebral palsy among Kazakhstan patients.

Materials and Methods

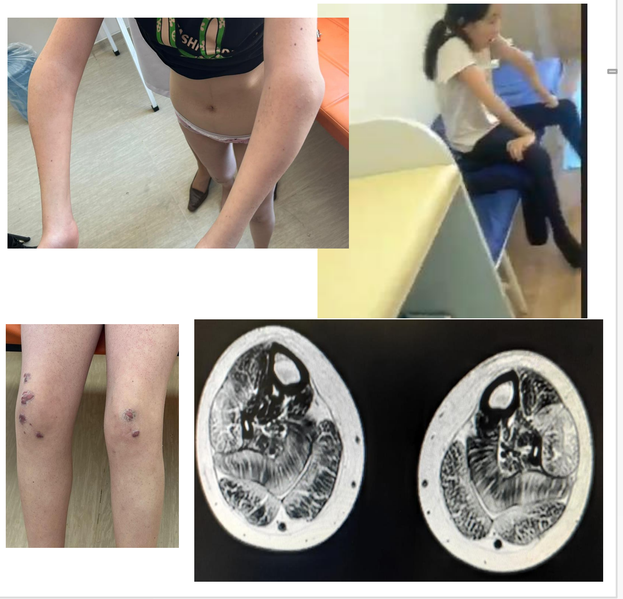
During the period of 2022-2023, over 300 patients with cerebral palsy (CP) were examined, among whom 9 patients with genetically confirmed collagenopathies were identified. The majority of children were identified at the pediatric rehabilitation center. All patients exhibited a clinical presentation associated with mutations in the COL6A1 and COL6A3 genes. Three patients were found to have a heterozygous mutation in the COL6A1 gene, while the remaining six patients had mutations in the COL6A3 gene.

Phenotype of the patients: increased muscle weakness, inability to jump, climb stairs, myopathic gait, hypermobility of small joints, and contractures in large joints. (Table with phenotypes attached)

Case №1

by sequencing by Sanger MORC2c.260C>T (p.Ser87Leu). pathogenic

Case №2



№	sex	age	gene	type	variant coordinates	Contractures	Stiffness
1	m	11	COL6A3	Splicing	c.6156G>A	no	in the ankle joints
2	m	7	COL6A3	Splicing	c.6156G>A	no	in the ankle joints
3	**m**	**10**	**COL6A3**		**c.4912G>A**	**UL(fingers) and LL(knee joints)**	
4	**f**	**14**	**COL6A1**	**Missense**	**c.788G>A**	**LL(ankles) and UL (elbow)**	
5	f	8	COL6A1	Splicing	c.1056+1G>A	no	
6	f	7	COL6A1	Missense	c.850G>A	no	in the ankle joints
7	m	11	COL6A3	Splicing	c.6210+1G>A	LL(knee) and UL (elbow)	in the ankle joints and restriction of movement in the left hip joint
8	m	12	COL6A3		c.6158G>A	LL(ankles)	
9	m	8	COL6A3		c.1597C>T	no	in the right ankle joint.

Results:

More splicing mutations than missense mutations were identified in the analysis. Additionally, 66.7% of patients had mutations in the COL6A3 gene, and 33.3% had mutations in the COL6A1 gene. It is worth noting that these mutations are more commonly found in Kazakhstan compared to mutations in the COL6A2 gene.

Based on the analysis results conducted on children from Kazakhstan, it can be observed that certain point mutations, such as 1056+1G>A, 850G>A, and 850G>A, were detected in this population and have been previously documented in Japan and China as well. These point mutations exhibit similar phenotypic characteristics in both Kazakhstan children and children from China and Japan. The remaining point mutations found in Kazakhstani children are unique and were first identified in this population.

Conclusion:

We obtained data indicating that genetic progressive disorders requiring careful diagnosis, which can mimic cerebral palsy, may be present. This has implications for the management approach of patients.

References:

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