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JOURNAL	World Science
p-ISSN	2413-1032
e-ISSN	2414-6404
PUBLISHER	RS Global Sp. z O.O., Poland

ARTICLE TITLE	EARLY PHYSICAL THERAPY MEF2C HAPLOID DEFICIENCY SYNDROME (5Q14.3 MICRODELETION)
AUTHOR(S)	Eliso Murvanidze
ARTICLE INFO	Eliso Murvanidze. (2023) Early Physical Therapy MEF2C Haploid Deficiency Syndrome (5q14.3 Microdeletion). *World Science*. 2(80). doi: 10.31435/rsglobal_ws/30062023/8017
DOI	https://doi.org/10.31435/rsglobal_ws/30062023/8017
RECEIVED	25 May 2023
ACCEPTED	29 June 2023
PUBLISHED	30 June 2023

EARLY PHYSICAL THERAPY MEF2C HAPLOID DEFICIENCY SYNDROME (5Q14.3 MICRODELETION)

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DOI: https://doi.org/10.31435/rsglobal_ws/30062023/8017

ARTICLE INFO

Received: 25 May 2023
Accepted: 29 June 2023
Published: 30 June 2023

KEYWORDS

MEF2C, MEF2C haploinsufficiency, mutation, gene, deletion.

ABSTRACT

MEF2C haploid deficiency syndrome is caused by a mutation of the MEF2C gene, which causes dysfunction of a protein essential for the proper functioning of the musculoskeletal, cardiovascular, neurological, craniofacial, and immune systems. A deletion mutation occurs when part of a chromosome is missing. Signs and symptoms vary widely and usually first appear when the patient is between 5 months and 2 years old. This is mainly a review and partly research article. The mentioned syndrome is still in the process of research, since the patients with this syndrome are very few worldwide, and there are 2 patients in Georgia, one of them started treatment from the age of 7 months, when a delay in the stages of development was noticed, namely physical therapy, which was carried out 5 days a week, the improvement started from the first month. This also confirms that before anomalous movements become dominant, intervention should take place and be tailored to the areas that need it at that stage; along with gross motor function, fine motor skills improved, as well as eye-hand coordination; if we evaluate the general condition, this observation led to purposeful movements of the patient. I think this article will help physical therapists and the patient's parents to focus on early intervention in terms of gross motor function, as a result of which the general condition of the patient improves.

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Introduction.

MEF2C haploid deficiency syndrome was first described in 2009. MEF2C deficiency is an extremely rare genetic disorder caused by a change (mutation) in the MEF2C gene. This mutation, often a deletion, causes dysfunction of the MEF2C protein, which occurs in the 5q14.3 band, in most cases, the MEF2C deficiency is de novo, which means that it is caused by spontaneous changes in the DNA sequence and is not inherited from the patient's parents [5, 6].

MEF2C (myocyte enhancer factor 2C) is a coding gene of protein. Problems associated with MEF2C include neurodevelopmental disorders with hypotonia, stereotypic hand movements, speech problems, and autism spectrum disorders [7, 6].

Today, there are 117 MEF2C gene mutation patients in the world, 2 children with MEF2C haploid deficiency syndrome (9 years old and 2 years old) are registered in Georgia. Characteristics of patients with MEF2C gene mutation are identified (as of 2021).

- Developmental delay - 96/97 (99. 0%);
- Epilepsy - 89/102 (87. 3%);
- Intellectual disability - 83/85 (97. 6%);
- Hypotonia - 58/59 (98. 3%);
- Lack of speech over 3 years old - 65/70 (92. 9%);
- Social and behavioral disorders - 62/71 (87. 3%);

- Dysmorphic signs - 68/69 (98. 6%);
- Stereotyped movement - 46/55 (83. 6%);
- Damage MRI - 58/86 (67.4 %);
- Disorders of eating and digestion system - 35/36 (97. 2%);
- Damage EEG - 50/73 (68. 5%);
- Vision problem - 24/24 (100. 0%);
- Inability to walk after 18 months - 31/55 (56. 4%);
- Sleep disorders - 20/28 (71. 4%);
- Heart problems - 17/17 (100.0%).

Methodology: Since there are a total of 2 children with MEF2C haploid deficiency syndrome in Georgia, only 1 patient who started treatment with physical therapy at the age of 7 months was observed. The patient was born in 2021, on the 40th week; the child was evaluated by a geneticist in October 2022 and diagnosed with following: "MEF2C gene chromosome 5q14.3 deletion syndrome" (MEF2C haploid deficiency syndrome/5q14.3 microdeletion syndrome). After the diagnosis, he was referred to the rehabilitation specialists whose help he needed (age 19 months). There is no approved therapy that specifically targets MEF2C deficiency. A multidisciplinary approach to treatment is needed.

Physical development of the patient by the age of 7 months (gross motor functions):

- Head control
- Turns from a pronated position to a supinated position
- Small stereotyped movements in the hands
- He did not bring his hands to his mouth
- He did not want to start movement.

Of the above-mentioned symptoms, which are characteristic of MEF2C gene mutation, the patient described by us had only the following:

- Delay in developmen;
- Social disorders;
- Stereotyped movements;
- Lack of speech above 3 years (at this stage, only sounds are pronounced for 2 years and 2 months of age).

Table 1. Assessment of patient's gross motor skills from 2021 to present (2023).

Abilities	**7 months before treatment**	**7-10 months**	**11-13 months**	**14-16 months**	**17-19 months**	**20-22 months**	**23-25 months**	**2 years and 2 months**	**2 years and 5 months**
1	2	3	4	5	6	7	8	9	10
Head control	+	+	+	+	+	+	+	+	+
Turns (S>P)	-	-	-	+	+	+	+	+	+
Turns (P.S)	-	+	+	+	+	+	+	+	+
Sitting with support	-	-	+	+	+	+	+	+	+
Independent sitting	-	-	+ (1 min)	+ (3 min)	+	+	+	+	+
Standing on all fours	-	-	-	-	-	+	+	+	+
To stand with the support	-	-	-	-	+	+	+	+	+

Table 1. (continuation)

1	2	3	4	5	6	7	8	9	10
To move with the support	-	-	-	-	-	+	+	+	+
Independent standing	-	-	-	-	-	+	+ (5 min)	+	+
Independent walking	-	-	-	-	-	-	-	+ (10 steps)	+

Physical therapy was mainly aimed at the problems of the stages of the child's physical development, the perception and sensations of the movements of individual parts of the body and the entire body.

Conclusion:

1. We can positively evaluate the effectiveness of early and goal-oriented physical therapy during the **mentioned syndrome**, since the improvement of large motor functions really took place and at the age of 24 months he was able to take 10 to 15 steps independently;

2. Early intervention during MEF2C prevented the formation of incorrect/anomalous movements and patterns, which would then hinder his physical development;

3. Hand-eye coordination has improved considerably, hand function has partially improved (picking up small things, taking food and bringing it to the mouth);

4. As his physical condition improved, it helped him initiate and complete purposeful movements.

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