Case Study

Neuro Motor Development in a Girl with SERAC 1 Gene Dysfunction from Kingdom of Saudi Arabia. A case study

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Abstract

Background & Purpose: The SERAC1 gene mutation is rare disorder related to deficits in mitochondrial metabolism. Neuromotor development was not studied in literature for this type of patients based on physical therapy perspectives. However, in this case report, we described the Neuromotor development in a child with SERAC1 mutation at 18 months of age in order to plan for better rehabilitation care in pediatrics physical therapy profession. **Case Description**: A girl child with SERAC1 mutation (18 months old) presented to the physical therapy clinic with delay in Neuromotor development. During physical therapy evaluation, hearing and vision are intact, Able to distinguish her parents voice and able to recognize them. Speech is impaired, Head control and sitting was perceived at six months of age, and became very dependent at 18 months of age. Grasping and reaching is not completely developed. **Outcomes**: The child was evaluated at the age of 12th and 18th month for normal development by using Alberta infant motor scale. The total score at 12 months was 17/58, and at 18th month was 13/58. We observed that the child development was less than 5th percentile of normal at both the measurements. We evaluated her neuromotor development by using Infant Neurological International Battery (INFANIB). The child was under abnormal category for neuro motor systems by having the total score 36/100. We used these two outcome measures as primary measure since they are the most common measures that used among pediatric physical therapists **Discussion**: This indicates that the abnormality in motor development was due to the nature of the disease, which is consistent with clinical manifestations presented in the literature. Both the scales have good reliability and validity. INFANIB scale has good predictive validity, by seeing definite abnormality at the 18th month we can assume that child may not

الملخص:

الهدف من الدراسة: الطفرة الجينية SERAC1 هو اضطراب نادر متعلق بقصور في وظيفة الميتوكوندريا داخل الخلية. حتى هذه اللحظة لم يُدرس التطور الحركي العصبي في الأبحاث الطبية السابقة لهذا النوع من المرض من منظور مهنة العلاج الطبيعي. في هذه الدراسة، قمنا بوصف التطور الحركي العصبي في طفلة مع طفرة SERAC1 في ١٨ شهرا من العمر من أجل تحسين الخطة العلاجية والرعاية التأهيلية للأطفال.

وصف الحالة: قدمت طفلة مع طفرة SERAC1 (١٨ شهرا من العمر) إلى عيادة العلاج الطبيعي مع تأخير واضح في الحركة والعضلات. أثناء التقييم المبدئي للعلاج الطبيعي، كانت وظائف السمع والرؤية سليمة، ولديها القدرة على تمييز صوت والديها وأيضا قادرة على التعرف عليهما. لا يوجد تواصل لفظي لديها، السيطرة على الرأس والجلوس كانت سليمة في اول ستة أشهر من العمر، وأصبحت غير قادرة على ذلك في عمر ١٨ شهرا. الوظائف الدقيقة لليد لم تصل لمرحلة التطور تماما.

النتائج: تم تقييم الطفلة في سن ١٢ و ١٨ شهرا للتطور الطبيعي باستخدام مقياس Alberta infant. وكانت النتيجة الإجمالية في ١٢ شهرا ٥٨/١٧، وكانت النتيجة في الشهر الثامن عشر ٥٨/١٣. لاحظنا أن نمو الطفلة كانت أقل من ٥ في المئة من الطبيعي بالمقارنة مع اقرانها. وأيضا قمنا بتقييم تطورها العصبي باستخدام مقياس (INFANIB) وكانت النتيجة الكلية ١٠٠/٣٦. لقد استخدمنا هذين المقياسين في دراستنا كمقياس أساسي لأنهما من أكثر المقاييس شيوعا بين مختصو العلاج الطبيعي للأطفال

المناقشة: بعد الاطلاع على النتائج وجدنا هناك تدهور في الحالة الطبية للطفلة وذلك يرجع إلى طبيعة المرض، وهو ما يتفق مع الدراسات السريرية السابقة. هناك حاجة لعمل دراسات مستقبلية لاستكشاف فعالية التأهيل الطبي (بما في ذلك العلاج الطبيعي، وعلاج النطق والتخاطب) في تحسين المهارات الوظيفية او المحافظة لمنع اي تدهور قد يحصل مستقبلا. وبالإضافة إلى ذلك، هناك حاجة إلى مزيد من الاختبارات السريرية اللازمة مثل اختبارات السمع لضمان نتائج أفضل اثناء برنامج التأهيل الطبي.

الكلمات الرئيسية: INFANIB، طب الأطفال، التأهيل الطبي، التطور الحركي العصبي

have normal development in future also. Future studies are required to explore the effectiveness of intensive rehabilitation therapy (including physical therapy, occupational therapy, and speech pathology services) in improving neuromotor development also to prevent any neuromotor regression for this type of disease. In addition, further investigations are required such as hearing test for better rehabilitation outcomes.
Keywords: Infanib, Pediatrics, Rehabilitation, Neuromotor Development.

Introduction

Serine active site containing 1 is a gene protein found in humans and it is encoded as SERAC 1 gene. [1] The SERAC1 plays a key role in phosphatidylglycerol remodeling which is essential for intracellular cholesterol trafficking and mitochondrial function. [2] Abnormality in SERAC 1 gene leads MEGDEL (3-*me*thylglutaconic aciduria with *d*eafness, *e*ncephalopathy and *L*eigh-like) syndrome. [3] The SERAC1 gene mutation is rare disorder related to deficits in mitochondrial metabolism. [4]

The children with SERAC 1 gene dysfunction had shown following clinical features like hypotonia and hypoglycemia at neonatal stage, in infancy, there was failure to thrive, feeding difficulties, recurrent infections and developmental delay. After the first year the clinical features are severe progressive sensory neural deficit, hearing loss, spasticity, extra pyramidal signs like dystonic movements, episodes of respiratory insufficiency and developmental regression. [5–7] Lab analysis of these children had shown mitochondrial hepatopathy, lactic acidosis, elevated serum transaminase levels, elevated serum γ-glutamyl transpeptidase, hyper ammonia and elevated serum α-fetoprotein. [7] MRI shows brain atrophy, leigh like findings, small corpus striatum and progressive dysfunction of the basal ganglia. [7]

Case description:

The case described here is a girl child with age 2 years and 6 months. She was born in the United States of America, but she is of Saudi nationality and currently residing in the Kingdom of Saudi Arabia. The parents of the child have step first degree consanguinity the full pedigree was mentioned in (Figure.1). The informed consent form was obtained and fully explained to her guardian.

The child was full term born through normal vaginal delivery to a $G_1P_1L_1$ mother. The birth weight of the child was 2.6 kilograms, birth length was 46.9 centimeters and head circumference was 32.5 centimeters. APGAR score was 9 at the first minute and 10 at fifth minute. First 24 hours' child was on normal breast feeding after that child developed metabolic crisis and respiratory distress with rapidness and difficulty in breathing, the food intake and urine output were decreased, increase in drowsiness, no eye contact and no sucking. On lab examination child had hypoglycemia with sugar levels at 37 mg/dl, elevated ammonia at 271 umo/l and elevated lactate at 13.5 mmol/l. As an emergency the

child was shifted to Neonatal Intensive Care Unit (NICU). During this time child Complete Blood Count (CBC) was normal no signs of bone marrow suppression were found. Next three weeks' child was in the NICU on oxygen support and underwent one session of dialysis to decrease the ammonia levels. After three weeks she was discharged during this time she was on intravenous hydration, carnitine, bolus of ammonul, arginine and glucose infusion. Four weeks after the birth the child underwent whole exome sequencing tests for detecting genetic abnormality. At 4 weeks her development was 3.1 kg in birth weight (2ndpercentile), body length 50 centimeters (4th percentile), head circumference was 36.7 centimeters (37thpercentile), muscle tone was normal and there was no clonus. At 3 months of age lab examination showed lactate at 5.8 mmol/dl, serum ammonia 72 umo/l, alkaline phosphate 1386 u/land elevated liver enzymes that is Alanine Aminotransferase (ALT) at 76.7 u/l and Aspartate Aminotransferase (AST) at 97.5 u/l.At 6 months of age she was diagnosed with deleterious mutations in SERAC 1 gene. She was diagnosed with 3-methylglutaconic aciduria with deafness, encephalopathy and Leigh-like syndrome (MIM: 614739) Confirmed Sanger sequencing identity's mother and father as heterozygous. Examination of urine revealed significant elevation of 3 – methylglutaconic acid. Before the evaluation, the child was hospitalized only once with lactic acidosis and hyper ammonia.

During the current general evaluation, hearing and vision are intact, Able to distinguish her parents' voice and able to recognize them. Speech is impaired, head control and sitting was perceived at six months of age, but it is deteriorating and become very dependent by 18 months of age. Grasping and reaching is not completely developed. There is only mass grasp. She shows fluctuating tone with athetoid kind of movements.

The child was evaluated at the age of 12th and 18th month for normal development by using an Alberta infant motor scale. [8] The total score at 12 months was 17/58, and at 18th month was 13/58. We observed that the child development was less than 5th percentile of normal at both the measurements and there is deterioration in normal motor development. At 18 months we evaluated her Neuro-motor development by using the Infant Neurological International Battery (INFANIB). [9,10] The child was under the abnormal category for Neuro motor systems by having the total score 36/100. At the age of 2 years and 3 months the Gross Motor Function Measure (GMFM 66) was done. The total score was 6.24 %, which is very poor for that age. Out of the 5 sub components of GMFM child was able to perform some activities in the first two components only that is lying-rolling and sitting.

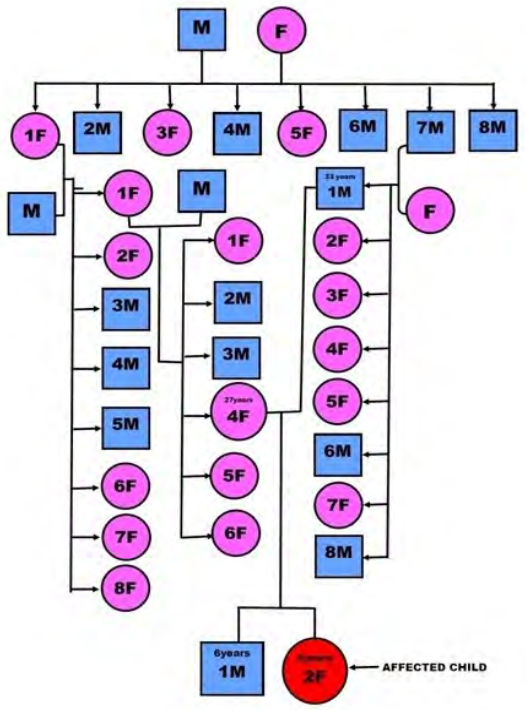

Figure legend

Figure -1: Full Pedigree of the affected child Note for figure one: M means male and F mean female

Discussion

Based on case description, it indicates that the abnormality in motor development was due to the nature of the disease, which is consistent with clinical manifestations presented in the literature. Similar cases were reported in the past, [1–4,12] but they did not describe about the developmental aspects of the child in a quantitative manner. All the scales used to measure the development have good reliability and validity. [13–20] By seeing definite abnormality at the 18th month and 2 years we can assume that child may not have normal development in future also. There are limited studies in litruture regarding this kind of disorder. Thus, cohort studies are required to make a concrete clinical picture about the complete development of these children. Future studies also are required to explore the effectiveness of intensive rehabilitation therapy including physical therapy, occupational therapy, and speech pathology services in improving neuromotor development also to prevent any neuromotor regression for this type of disease and to provide preventive and management measures for this type of genetic disease. Physical therapist working with pediatrics patients need full picture regarding neuromotor development in order to assess and manage similar conditions.

Conclusion

This girl child with SERAC 1 gene dysfunction had shown severe abnormality in motor development by three standard scales. She even showed deterioration in the motor development on Alberta Infant Motor Scale.

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