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Case Report / Olgu sunumu

Copy Number Alterations Associated with Schinzel-Giedion Syndrome: Case Report

Schinzel-Giedion Sendromu ile İlişkili Kopya Sayısı Değişiklikleri: Olgu Sunumu

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Abstract

Schinzel-Giedion syndrome (SGS) is a highly recognizable syndrome characterized by severe mental retardation, distinctive facial features, multiple congenital malformations, and higher-level neurological deficits. Comprehending SGS is essential for customized medical treatment, genetic counseling, and furthering developmental problem research. Enhanced understanding leads to better assistance for impacted people and their families, which improves results overall. In this study, we present a case of SGS associated with 2q35-q37 duplication, 4q34.1 duplication, and 9p24.3-24.1 deletion.

Keywords: Schinzel-Giedion syndrome, case report, 2q35-q37 duplication, 4q34.1 duplication, 9p24.3-24.1 deletion

Öz

Schinzel-Giedion syndrome (SGS) is a highly recognizable syndrome characterized by severe mental retardation, distinctive facial features, multiple congenital malformations, and higher-level neurological deficits. Comprehending SGS is essential for customized medical treatment, genetic counseling, and furthering developmental problem research. Enhanced understanding leads to better assistance for impacted people and their families, which improves results overall. In this study, we present a case of SGS associated with 2q35-q37 duplication, 4q34.1 duplication, and 9p24.3-24.1 deletion.

Anahtar Kelimeler: SGS, olgu sunumu, 2q35-q37 duplikasyonu, 4q34.1 duplikasyonu, 9p24.3-24.1 delesyonu

INTRODUCTION

Schinzel-Giedion syndrome (SGS) was initially identified by Schinzel and Giedion. Severe mental retardation, characteristic facial features, multiple congenital malformations (such as skeletal abnormalities, genitourinary and renal malformations, and heart defects), and higher-order neurological deficits are the hallmarks of this highly identifiable syndrome.[1]

Another account cited a tiny, tilted nose, macroglossia, a short neck, a large and wide forehead, enormous fontanelles, ocular hypertelorism, and bilateral hydronephrosis. Anomalies include aberrant fundus, cerebral ventricle enlargement, splenopancreatic fusion, enlarged and dense long bone cortices, and heart problems.[2]

The facial phenotype, which includes the broad forehead, retraction of the midface, and tiny, turned-up nose, together with one of two additional key differentiators (typical skeletal abnormalities or hydronephrosis), can be used to make a clinical diagnosis. Broad ribs, significant supraoccipital-exoccipital synchondrosis, sclerotic skull bases, and increased cortical density or thickness are examples of common skeletal deformities. Hypertrichosis, brain abnormalities, and neuroepithelial cancers (17%) are further strongly supporting characteristics. Among the cases that have been recorded, severe developmental delay and poor survival are constants.[2]

The same clinical findings, including megacalycosis, progressive neurodegeneration with infantile spasms, and

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hypsarrhythmic activity, were reported in two infants. Together with ocular hypoesthesia, tuning fork malformation of the stirrup bone, and alacrimia. These characteristics might help define SGS as an additional clinical criterion in the future.[3]

Research has indicated that the duplication of 2q35-q37 has been linked to several conditions such as growth failure, dysmorphic findings, cardiovascular abnormalities, genitourinary system anomalies, and global developmental delay.[4] Global developmental delay, complete/partial gonadal dysgenesis, and autistic spectrum disease have all been linked to the 9p24.3 deletion.[5] Furthermore, renal hypoplasia, microcephaly, growth retardation, epilepsy, and dysmorphic features have all been linked to 4q duplication.[6]

CASE REPORT

The male patient was 2 years old when he applied to Umraniye Training and Research Hospital in Istanbul. His seizures began at 4.5 months old, and he has both epilepsy and a developmental disability. Two months before being admitted to the hospital, he suffered his final seizure. At 34 weeks gestation, he was born as G2Y2 and weighed 3740 grams. Due to his respiratory discomfort and feeding issues, he spent a month in the incubator. The mother and father are not consanguineous.

Necrotizing enterocolitis was identified at admission and optic disc hypoplasia in the left eye was found during the newborn eye examination. After doing an echocardiography, atrial septal defect (ASD) was diagnosed. The karyotype is 46, XY. The arachnoid space expanded. Frontal atrophy was taken into consideration (**Figure 1**). SGS was identified by the genetics department's findings. Molecular karyotyping revealed the presence of 2qdup-9pdel. The size of the head measured 45.5 cm. In addition to having severe hypotonia in the axial and extremities, he was dysmorphic and lacked head control. There was simply seeking eye movements and no eye tracking.

Chewing was absent, as well as assisted sitting. Meals must be consumed in puree form for him. He was seen to be seizure-free. A left ear issue was discovered during a hearing test, but it was not investigated. The results of an array study at an external facility showed deletion at 9p24.3-24.1, duplication at 2q35q37, duplication at 4q34.1, and partial trisomy. On chromosome 9, a heterochromatin region was found by karyotype analysis. The results of the karyotype studies for the mother and father were normal. His sibling is in good health, and his karyotype is similarly determined to be normal.

His height was 84 cm, head circumference was 46.5 cm, and his body weight was 9,770 g during his subsequent examination. Gray sclera and hypertelorism were determined to be positive. The hands were little, the upper lip was slender, and the philtrum was lengthy. The bilateral fifth fingers showed signs of clinodactyly and hypospadias, and the scrotum was unable to palpate either testicle.

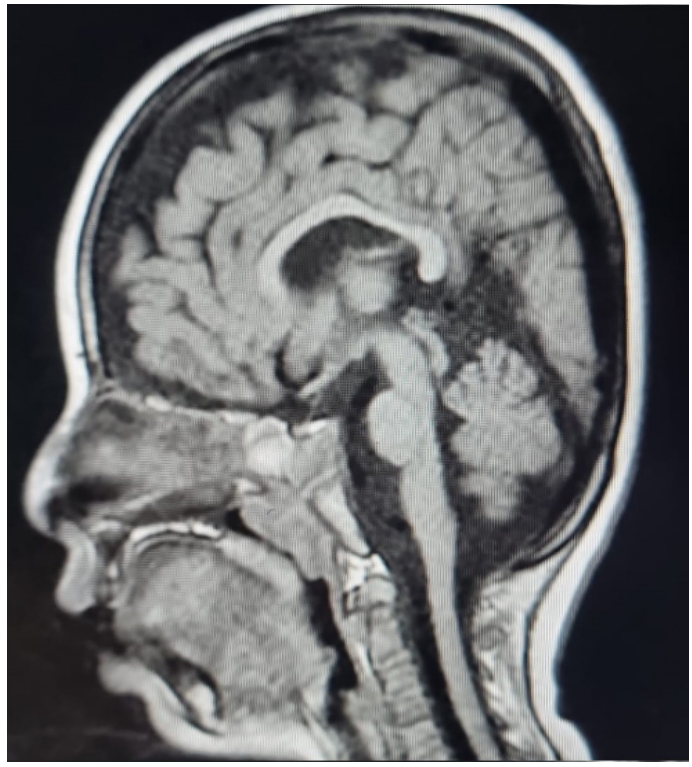

Figure 1. MRI image showed that the arachnoid space was enlarged in the bilateral frontotemporal parietal region.

Both testicles in the scrotal USG were of normal size. The inguinal canal revealed both testicles. The glandular prepuce was missing, and the penis was slightly twisted on the right. The size of each epididymis was normal. Each testicle's echo structure was uniform. Both the waking and sleep electroencephalogram showed widespread epileptiform abnormality.

DISCUSSION

Our case presents a compelling array of challenges, encompassing various malformations affecting the limbs, urogenital system, and facial features. Beyond the evident physical anomalies such as a large philtrum, hypertelorism, and other facial characteristics, our patient also exhibited a spectrum of concerning symptoms including visual and auditory impairments, growth retardation, and muscle hypotonia. These phenotypic abnormalities have been strongly associated with the duplication of the 2q35-q37 region, a significant finding that underscores the complexity of our case.[7]

Furthermore, the implications extend beyond mere physical abnormalities. Heart abnormalities, an issue of critical concern, have also been linked to the duplication of the 2q33-q37 region. Remarkably, our case exhibited a duplication in the 2q35-q37 region, suggesting a potential association with ASD, a condition demanding urgent attention and specialized care.

Epilepsy and neurodevelopmental delay are distressingly common among patients with similar genetic duplications, categorizing our case within the spectrum of epileptic and developmental encephalopathies.[9] The onset of epileptic seizures in our patient aligns with prior studies correlating seizures with specific genetic duplications, such as the 4q34.1 duplication.[4] Notably, our patient began experiencing seizures at a young age, emphasizing the urgency of intervention and comprehensive care.

Compounding these challenges, our patient's MRI scans revealed frontal brain atrophy, mirroring observations from previous studies,[9] and highlighting the progressive nature of the condition. These neurological manifestations underscore the critical need for ongoing monitoring and intervention to mitigate potential complications and optimize outcomes.

Additionally, our patient exhibited a constellation of symptoms reminiscent of monosomy 9p syndrome, further complicating the diagnostic landscape. The presence of developmental delays, craniofacial abnormalities, and cardiac issues aligns with the characteristic features of this syndrome, necessitating a holistic approach to management.

CONCLUSION

Our case presents a compelling narrative of complex genetic anomalies with profound implications for both physical and neurological health. By elucidating the intricate interplay between genetic duplications and clinical manifestations, our findings underscore the pressing need for multidisciplinary intervention and ongoing research to enhance our understanding and management of such conditions.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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