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Gingival Hipertrofisi veDental Anomali
Noonan Sendromunun Nadir Bir Görüntüsü

Gingival Overgrowth and Dental Anomaly
An Unusual Presentation of Noonan's Syndrome

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Özet

Noonan Sendromu doğumda tipik dismorfik anomalilerin görüldüğü otozomal dominant bir hastalıktır. Etkilenen bireylerde kardiyak defektlerle birlikte farklı bir yüz görünümü mevcuttur. Bu olgumuzda özellikle gingiva hipertrofisi ve dental anomali ile seyreden Noonan Sendromunu'nun farklı bir varyantını tartışmayı amaçladık. 15 yaşında kız hasta aile hekimliği polikliniğimize, gelişme geriliği nedeni ile başvurdu. Fenotipik bulguları ile hastaya Noonan Sendromu tanısı kondu. Noonan Sendromu, Turner benzeri fenotipik özelliklerle seyreden kromozomal anomalilerle ilişkili olmayan sendromlardan biridir. Bizim olgumuzda Noonan sendromuyla ilişkili oral bulgulara ek olarak gingiva hipertrofisi ve dental anomali birlikteliği aynı anda mevcuttu. Özellikle ağız, diş muayenelerindeki gingival hipertrofisi, dental anomali olan vakalarda eşlik eden semptom ve bulgular var ise noonan sendromu düşünülebilir.

Anahtar kelimeler: Noonan sendromu, dental Anomali, gingiva hipertrofisi

Abstract

Noonan syndrome is an autosomal dominant disorder that is typically dysmorphic anamolies at birth. In many affected individuals, this syndrome is associated with cardiac defects and a distinctive facial appearance. We aimed to discuss a different variant of Noonan Syndrome progressing especially with gingival overgrowth and dental anomaly in our cases. A 15-year-old female patient presented to our family medicine outpatient clinic with the complaint of growth retardation. The patient was diagnosed with Noonan Syndrome with phenotypic symptoms. Noonan Syndrome is one of the syndromes without any chromosomal anomalies developing with Turner-like phenotypic features. Gingival overgrowth and dental anomaly coexistence in addition to the oral symptoms that are likely to be related to the Noonan Syndrome was present in our case.Specifically, if there are accompanying symptoms and findings in cases with gingival overgrowth and dental anomalies as seen in patients' mouth and teeth examinations, Noonan Syndrome may be taken into consideration.

Key words: Noonan's syndrome, dental anomaly, gingiva overgrowth

INTRODUCTION

Nooan Syndrome is one of the syndromes without any chromosomal anomalies that may progress with short stature, web neck, dysmorphic face, hypertelorism, pitosis, epicantus, downward slating palpebral fissures, low set backward rotated ears, triangular face, small maxilla, micrognathia, high arched palate, dental malocclusion, congenital cardiac anomalies, chest deformity, pathologies of skeleton and lymphatic system, delay in puberty, hearing loss, bleeding diathesis, cryptorchidism, lymphedema, and mild mental retardation (1-3). Noonan Syndrome may be confused with the typical phenotypical features of Turner syndrome. Therefore, it is also called Turner-like syndrome, female pseudo-Turner syndrome, male Turner syndrome, and Ulrich Noonan syndrome. While about half of the Noonan Syndrome cases are sporadic, autosomal dominant inheritance is detected in some of them. Specifically, characteristic facial features are key to diagnosis. Facial symptoms may change by age and especially diagnosing newborns may be complicated because of edema (4). Affected individuals may have normal chromosomal structures. Among the mouth findings of patients with Noonan Syndrome, high arched palate with 55-100%, dental malocclusion with 50-67%, articulation difficulties with 72%, and micrognathia with 33-43% may frequently be seen (1). Growth retardation in Noonan Syndrome is one of the most frequent reasons of presentation during childhood. The reason for growth retardation is not clear. Although it has been reported that IGF-I level was low or at the lowest border, frontal hypophysis function tests and growth hormone secretion were found to be within normal bounds. Some studies have reported dysfunction in Growth Hormone (GH) secretion that might characterize short stature in Noonan Syndrome. It has been stated that GH secretion in these cases is at low amounts and at low amplitude (5). Other endocrinal disorders defined in Noonan Syndrome are hypognathism and autoimmune thyroid (2, 6).

Noonan Syndrome is one of the syndromes without any chromosomal anomalies developing with Turner-like phenotypic features and was first defined by Noonan and Ehmke in 1963. Its incidence

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Figure 1. Short stature

was found to be one in between 1000-2000 live births (1). Noonan Syndrome, which is generally seen as sporadic, can also be inherited by autosomal dominance. It has been reported that some genes cause the Noonan Syndrome (PTPN 11, NS 1, NF 1, NF 2). More than 50% of the cases were brought about by a "missense mutation" in the PTPN 11 gene. The NS 1 gene is found in the 12q24 localization; it can be seen with neurofibromatosis and NS(NFNS) as a result of the mutation in the neurofibromin gene (NF 1) located in the long arm of the 17th chromosome (7,8). It frequently coexists with cardiac pathologies. The most frequent cardiac malformation seen in the Noonan Syndrome is valvular pulmonary stenosis, hypertrophic cardiomyopathy caused by pulmonary valve dysplasia has an incidence of 37.9-39% (9). Burch M. et al reported that out of 118 patients diagnosed with phenotypic Noonan Syndrome, 69 (58%) had cardiac pathologies (10).

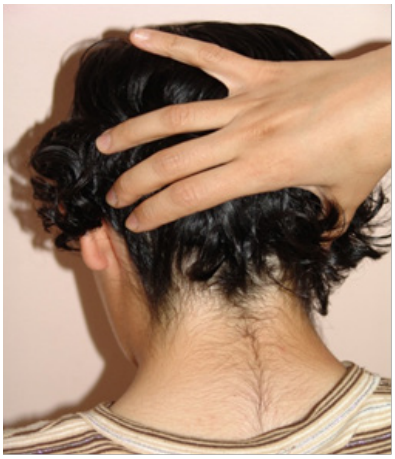

Figure 2. Low-set hair line, Web neck

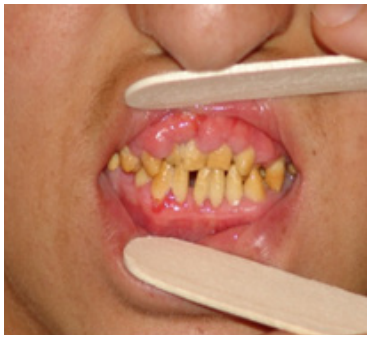

Figure 3. Gingiva overgrowth and dental anomaly

We aimed to discuss a different variant of Noonan Syndrome progressing especially with gingival overgrowth and dental anomaly in our cases.

CASE

A 15-year-old female patient presented to our family medicine outpatient clinic with the complaint of growth retardation. The patient's anamnesis revealed that she was born on time by normal vaginal course with 1900 gr of birth weight and that meconium aspiration and polyhydramnios developed and cleft palate and scoliosis at her birth. Apart from these, she had no history of disease, accident, or medication. Our patient was the oldest of 3 siblings. The other siblings of the patient were healthy and had normal height and weight percentiles. The mother's 4th pregnancy resulted in an abortus in the 5th month. The mother was 36-year-old and she was 155 cm tall and weighed 49 kg, while the father was 39-year-old and he was 170 cm tall and weighed 64 kg.

The physical examination of the patient revealed that she was 135 cm tall (<%3 percentile) (Figure1) and weighed 44 kg (between 3-10% percentile). Our patient's pulse was 76 beats/min., her blood pressure was 120/80 mm Hg, and respiratory rate was 20/min. The patient's head-neck examination showed that her uvula was deviated towards the right; she had low set hair line on the neck (Figure 2), had short neck and

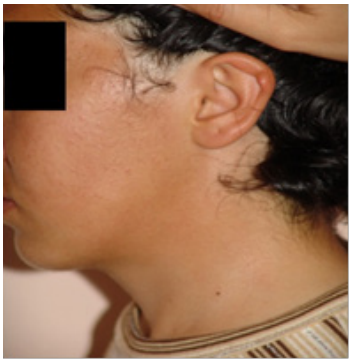

Figure 4. Hypoplastic ear

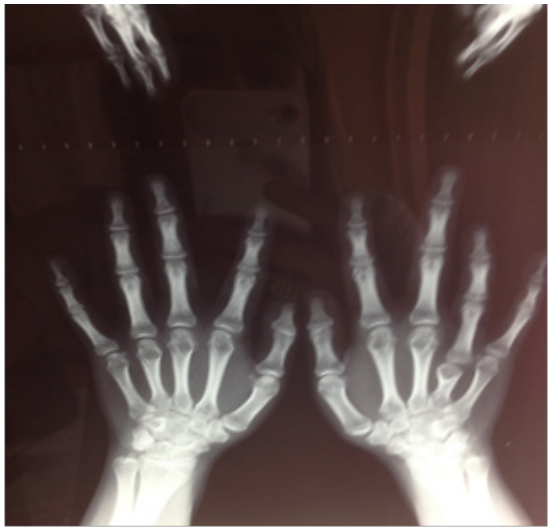

Figure 5. Shortness of the 4th finger of her right hand

hair development on her neck. Her mouth examination showed nasal speaking. She had dental anomaly (Figure 3), decayed and yellow teeth, gingival overgrowth at birth (Figure 3), and surgical scars in the upper lip and palate of a previous cleft palate surgery. The patient's respiratory system examination revealed normal respiratory sounds and there was no rale or rhoncus. There was no sensitivity or rebound in her abdominal examination. The patient's ear, nose, and throat consultation revealed that her audiometer and hearing test results were normal but her both ears were dysplasic (Figure 4). Her ophthalmologic examination results were normal except the presence of pterygium in her right eye. No cardiac pathologies were seen in her cardiology consultation. S1 and S2 were natural; no additional sound or murmur was detected. Further, her electrocardiography, telegraphy, and echocardiography results were found to be normal. The patient's genital system examination was externally natural and her thelarche, menarch, and adrenarche stages were in line with her age. The WISC-R test conducted by a psychologist revealed a slight mental retardation (total score=62) in comparison with her peers. The patient had shortness of the 4th finger of her right hand (Figure 5) scoliosis , and extensive brown pigmentations on her back.

The patient's lab analyses revealed that her hemogram, urine and feces tests, biochemical parameters bleeding time results, TSH, FSH, LH, and IGF1 values were within normal bounds. Her genetics consultation results showed that her genogram was normal. Her caryotype was found to be 46 XX. Our patient's case was regarded as sporadic inheritance (Figure 6). Her radiography results revealed that her bone age was in line with 17 years of age and her radiological results revealed shortness of the 4th finger of the right hand. Her abdominal ultrasonography was normal. The patient was diagnosed with Noonan Syndrome with phenotypic symptoms.

DISCUSSION

We diagnosed our patient with the Noonan Syndrome based on phenotypic features like short stature, growth retardation, history of cleft palate-lip, nasal speech, gingival overgrowth, dental anomaly, decayed and yellow teeth, right-deviated uvula, low set hair line on the neck, dysplasia of the right and left ears, scoliosis and brown pigmentations on the back, short 4th metatarsus of the right hand, pterygium in the right eye, and slight mental retardation. Oral symptoms like high arched palate and gap in the front teeth, and macroglossia in the Noonan Syndrome have been previously reported by literature. Alongside with these symptoms, bilateral taurodontism, missing teeth and distinctive ruga formation as novel oral symptoms have also been reported (11-13). Another study has described missing teeth in addition to oral symptoms seen in the Nooan Syndrome (14). Gingival overgrowth and dental anomaly coexistence in addition to the oral symptoms that are likely to be related to the Noonan Syndrome was present in our case. Sugar et al. defined the coexistence of front teeth gap and prognatism in patients with the Noonan Syndrome (13). Gingival overgrowth may be a symptom of some genetic diseases caused by changes in the proteins of the RAS-MAPK pathway regulated by the activities of the SOS-1 protein and it is a symptom especially seen in individuals with Noonan Syndrome having this gene (15). In a study by Ekvall et al. (16), the authors reported that hoarseness, osteoporosis, gingival hyperplasia, spinal neuroblastoma, and hepatic hemangioma may additionally be seen in Noonan Syndrome cases with mutations in the SHOC2 gene (p.S2G) and PTPN11 gene (p.G409A). In our case, however, no genetic mutations were detected although there was the coexistence of gingival overgrowth and dental anomaly. Turner Sydrome, Shprintzen-Goldberg and Leopard syndrome are similar disorders which are sometimes difficult to distinguish from Noonan Syndrome (11,17-21).

Noonan Syndrome cases should be examined carefully. Specifically, if there are accompanying symptoms and findings in cases with gingival overgrowth and dental anomalies as seen in patients' mouth and teeth examinations, Noonan Syndrome may be taken into consideration. Although the early diagnosis of the disease does not change the clinical progress, it is important that the patients' families are offered genetic consultation. Our patient who was diagnosed with Noonan Syndrome was referred to the Periodontology Department of our university's Faculty of Dentistry for the treatment of her oral complaints and symptoms. Further, the patient's necessary examinations and controls continue at our university's Department of Pediatrics regarding growth retardation.

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