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Coexistence of Klippel Feil syndrome, Poland syndrome and mirror movements: A genetic case study

Klippel Feil sendromu, Poland sendromu ve ayna hareketlerinin birlikteliği: Bir genetik olgu çalışması

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ABSTRACT

Coexistence of Klippel Feil syndrome, Poland syndrome and mirror movements have not been reported before. We aimed to report a patient with such coexistence and examined whether there is a possible genetic background of this association. A 19-year-old male patient presented with the absence of right thumb and deformity at the elbow. Right pectoral muscle mass was markedly smaller than left. There was a high scapula on the right side. Mirror movements were observed in neurological evaluation. Right radial head was dislocated. On magnetic resonance images, a syrinx was observed at the level of C6-C7 fusion. A high-resolution chromosome microarray (CMA) testing was performed. Small segmental de novo variations were detected. The largest gene spanning variation did not exceed 287 kb and none of the detected variations was known to be disease-associated or candidate to explain the phenotypic features according to The International Standard Cytogenomic Array (ISCA) criteria. Since our case is sporadic with multiple congenital abnormalities, we performed high-resolution chromosome microarray analysis to rule out genomic imbalance and did not find any significant deletion or duplication that could be associated with phenotypic characteristics.

Keywords: *Klippel Feil syndrom, Poland syndrom, mirror movement*

ÖZ

Klippel Feil sendromu, Poland sendromu ve ayna hareketlerinin tek olguda bir arada bulunması daha önce literatürde bildirilmemiştir. Çalışmamızda, bu antitelerin birlikte bulunduğu bir hastayı rapor edip; bu birlikteliğin genetik bir arka planı olup olmadığını inceledik. On dokuz yaşındaki erkek hasta, dirsek deformitesi ve sağ başparmak aplazisi ile başvurdu. Sağ pektoral kas kitlesi sola göre belirgin şekilde küçüktü. Sağ tarafta yüksek skapula görünümü vardı. Nörolojik değerlendirmede ayna hareketleri gözlendi. Sağ radius başı disloke idi. Manyetik rezonans görüntülerinde, C6-C7 füzyonu ile birlikte bu seviyede syrinks gözlemlendi. Yüksek çözünürlüklü kromozom mikrodizisi (CMA) testi gerçekleştirildi. Küçük segmental de novo kopya sayısı varyasyonları belirlendi. Değişikliği kapsayan en büyük gen 287 kb'yi aşmamaktaydı ve saptanan varyasyonların hiçbirisi, Uluslararası Standart Sitogenomik Array (ISCA) kriterlerine göre fenotipik özellikleri açıklamakta bilinen bir hastalıkla ilişkili değildi. Bilgimize göre literatürde tek olan olgumuzda çok sayıda konjenital anomali mevcudiyeti nedeniyle yüksek çözünürlüklü kromozom mikroarray analizi uyguladık ve fenotipik özellikler ile ilişkili olabilecek önemli bir delesyon veya duplikasyon bulamadık.

Anahtar kelimeler: *Klippel Feil sendromu, Poland sendromu, ayna hareketleri*

INTRODUCTION

Klippel-Feil syndrome is a genetic disorder characterized by multigenic inheritance, congenital fusion of cervical vertebrae and accompanying pathologies[1,2]. It is generally thought that anomalies in the formati-

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on or segmentation of cervical somites develop after 3 to 8 weeks of gestation[3]. Although the syndrome is associated with congenital scoliosis, Sprengel deformity, renal anomalies, congenital heart diseases, deafness, basilar invagination, and atlantoaxial instability, the main finding is cervical vertebral fusion anomalies, which may be of varying degrees[4,5]. Poland syndrome is a congenital malformation affecting the chest wall on the same side with hand or forehand[6]. In general, it is characterized by the absence of the pectoralis major muscle. Symbracydactyla, hand / forearm hypoplasia / agenesis, and Sprengel deformity and thumb agenesis may be associated with this syndrome[6,7].

Mirror movement is known as the involuntary and simultaneous movement of homologous muscles on the other side of the extremity because of the activation of certain muscle groups performing specific functions in voluntary movements on one side of the extremity. It is most commonly seen in upper extremity, although it can be seen in all limbs; especially in the hands. Although it can be seen as isolated movements, it has been shown to be associated with various syndromes.

Although it has been reported in the literature that the Klippel-Feil and Poland syndromes[8] or Klippel-Feil syndrome and mirror movements can be seen together[9,10], to the best of our knowledge, a patient with all three anomalies has not been reported so far. We hypothesized that;Klippel-Feil syndrome, Poland syndrome, and mirror movements are different forms of the same disease, and it is examined whether there is a possible genetic background of this association.

CASE PRESENTATION

A 19-year-old male patient presented with the absence of right thumb (Figure 1) and elbow deformity. It has been learned that the patient's complaints have existed since birth. There was no history of similar illness in the family.

Physical examination: There was an image of a mane neck with a hairline extending to about C6. There was no limitation on cervical spine range of motion. Right pectoral muscle mass was markedly smaller than its left counterpart (Figure 2). There was a high scapula / Sprengel deformity on the right side. Right thumb was absent. There was no restriction of range of motion of the right wrist and 2-3-4-5th fingers There was bilateral camptodactyly of the fifth fingers. There was deformity in the right elbow, but there was no limitation on elbow range of motion. The hands, wrists, and elbows were neurovascularly intact.

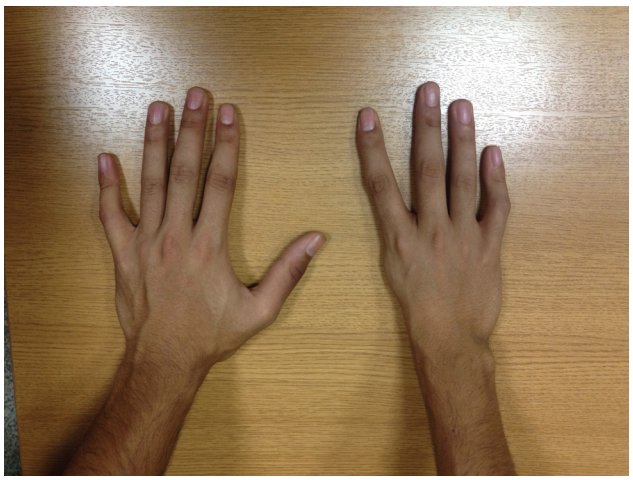

Figure 1. Photograph of the patient showing absence of right thum.

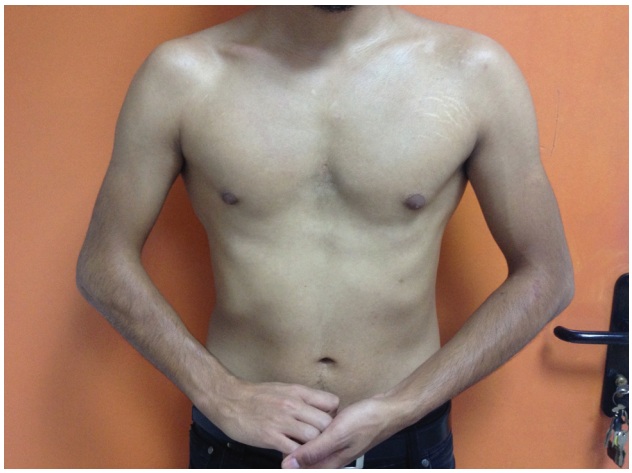

Figure 2. Photograph of the patient showing right pectoral muscle mass was markedly lower than left.

Neurological evaluation: Mirror movement was observed. When the patient was asked to abduct only the left arm, he abducted both left and right arms. Similarly, when the patient was asked to bend his elbow, he bent both his right and left elbows. There was no other neurological disorder.

Radiological evaluation: On X-ray, absence of the thumb including metacarpal and phalanges and trapezium was observed (Figure 3). Right radial head was dislocated (Figure 4). C6 and C7 vertebrae were fused (Figure 5). On magnetic resonance images (MRI), a syrinx was observed at the level of C6-C7 fusion.

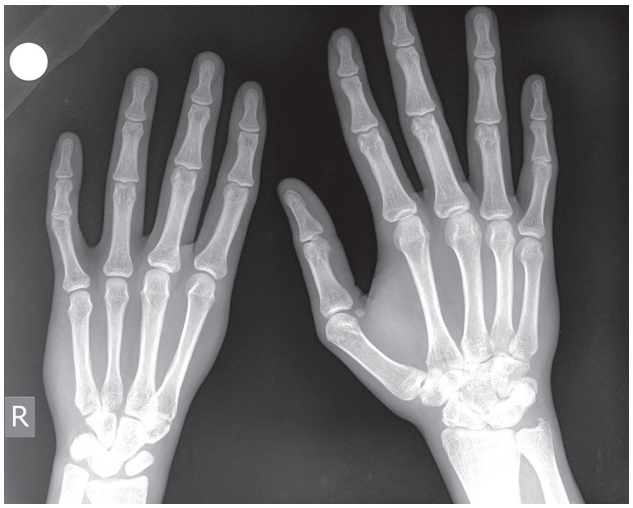

Figure 3. X-ray of the patient showing absence of the thumb including metacarpal, phalanges and trapezium.

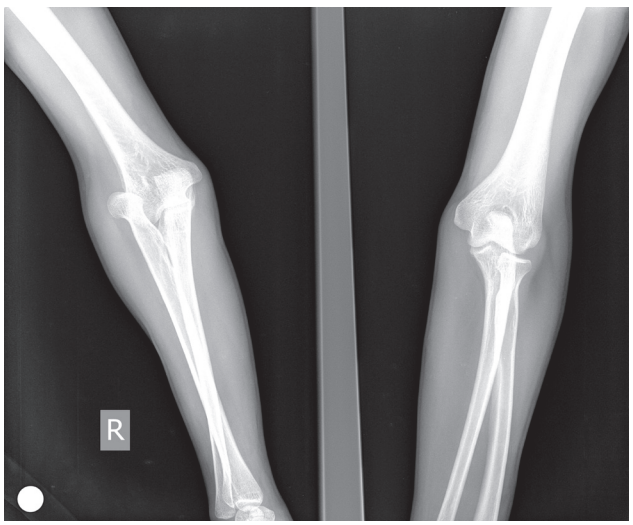

Figure 4. X-ray of the patient showing radial head dislocation.

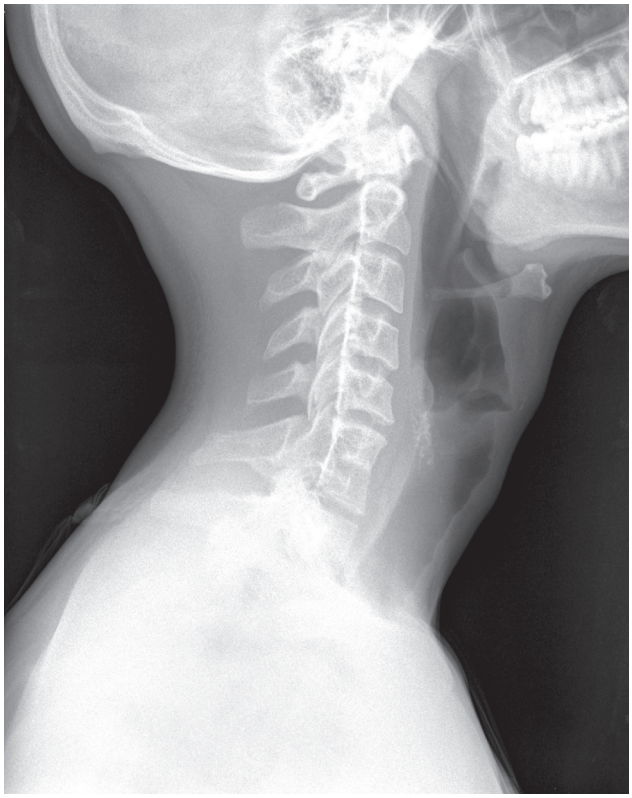

Figure 5. X-ray of the patient showing C6 and C7 vertebrae fusion.

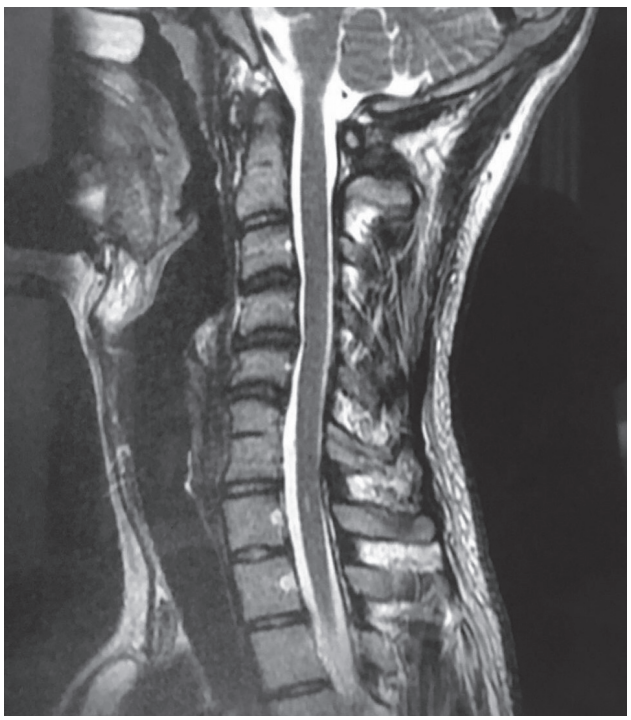

Figure 6. Sagittal MR image of the patient showing syrinx.

Genetic evaluation: Due the occurrence of multiple congenital anomalies in the case, we decided to perform a high-resolution chromosome microarray (CMA) testing. Informed consents and ethical approval were obtained from the index case and his parents and genomic DNA was extracted from the lymphocytes of each individual with DNAeasy Blood & Tissue Kit (Qiagen, Venlo, the Netherlands; Cat. No.: 69504). The genome wide analysis was carried out to detect the copy number status in the index case and the two healthy parents with the use of Agilent GenetiSure CGH+SNP Array, 2 x 400K (Agilent Technologies, Santa Clara, California, USA; Cat No. G5974A). The array platform contains 300,000 CGH and 103,000 SNP probes, the median probe spacing being approximately[10] Kb. Gains and deletions are measured using three or more CGH probes for almost 90% of the covered exons, providing resolution at the single exon level. Small segmental de novo variations were detected. The largest gene spanning variation did not exceed 287 kb and none of the detected variations was known to be disease-associated or candidate to explain the phenotypic features according to The International Standard Cytogenomic Array (ISCA) criteria[11].

DISCUSSION

The present study was the first study in the literature reporting coexistence of Klippel-Feil and Poland syndromes and mirror movements, according to our knowledge.

Kim et al.[12] reported a 4-year-old case with coexistence of axial mesodermal dysplasia complex, Goldenhar syndrome, Poland syndrome, Sprengel deformity and mirror movements. In addition, there are numerous studies on Klippel-Feil syndrome with Poland syndrome[8,9], or mirror phenomenon[10,13]. However, due to lack of data in the literature about coexistence of such syndromes we performed a genetic analysis, hypothesizing such findings were different manifestations of the same disorder. Klippel-Feil syndrome (KFS) is a genetically heterogeneous condition. De novo chromosomal aberrations associated with KFS have previously been reported in a few sporadic case reports[14,15]. Tassabehji et al.[16] identified a recurrent missense mutation of GDF6 gene in two cases among 121 sporadic KFS individuals. Mutations of DCC, RAD51, and DNAL4 have previously been identified in non-syndromic, hereditary congenital mirror movements[17-19]. Since our case is sporadic with multiple congenital abnormalities, we performed high-resolution chromosome microarray analysis to rule out genomic imbalance and found no significant deletion or duplication that could be associated with phenotypic characteristics.

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Conflict of Interest: Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained. There is no conflict of interest regarding publication of this manuscript.

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