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CASE REPORT
OLGU SUNUMU

Pallister-Killian Sendromu: Olgu Sunumu

Pallister-Killian Syndrome :A case Report

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ÖZ

Pallister killian sendromu (PKS) 12.kromozomun p kolunun tetrazomisi ile karakterize ve çok nadir rastlanan bir kromozom anormalisidir. Etkilenmiş bireylerde 12. kromozomun kısa kolunda dört kopya bulunur. Hastalarda 12. kromozomun kısa kollarının izokromozomundan oluşan bir mozaizm vardır. Bu vakalarda Ekstremite deformitesi, kısa ense ve alında belirginlik (frontal bossing) gibi anatomik anomaliler, pigmentasyon bozuklukları ,kardiyak ve renal patolojileri, mental retardasyon,nöbetler ve hipotoni görülebilen bir sendromdur. Bu yazıda böbreklerde gelişen anormalları ve fonksiyonları etkilenmesiyle başvuran Pallister- Killian Sendromu tanısı alan bir olgu, bu sendroma dikkat çekmek amacıyla sunulmuştur

Anahtar Kelimeler: Pallister-Killian sendromu, bebek, böbrek anomalisi

ABSTRACT

Pallister-Killian syndrome (PKS) is an extremely rare medical condition characterized by tetrasomy of P arm in 12th chromosome Individuals with this condition have also isochromosomic mosaicism. Pigmentation disorders mental retardation, seizures and hypotonia are common features of the syndrome. Anatomic malformation such as limbs deformities, short neck, frontal bossing, cardiac and renal anomalies are hallmark of clinical presentation in PKS. Here, we present a two-month-old boy with PKS and prenatal diagnosis of renal anomalies, and would like to draw attention of our colleagues toward Pallister-Killian Syndrome.

Keywords: Pallister-Killian Syndrome, Infant , Renal Anomaly

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INTRODUCTION

Pallister-Killian syndrome, is a developmental disorder that affects many parts of the body. Due to the distinct nature of the chromosomal damage, different variants of clinical presentations of PKS can be present [1.2,3]. PKS is not inherited; the disorder is the result of a random event during the formation of reproductive cells, it usually occurs in the mother. Typically, an error in cell division (nondisjunction) causes a reproductive cell to contain an isochromosome 12p, It is a very rare disorder that affects males and females in equal numbers [3,4]. PKS had been first identified in 1977 in adult, as an extremely rare condition however, in a population-based study in Britain estimated the birth incidence of Pallister-Killian syndrome to be 5.1 per million live births [5]. . PKS is characterized by tetrasomy of P arm in 12th chromosome with, some distinct clinical features such as rough facial appearance, abnormal auricles, local alopecia, pigmented skin lesions, diaphragmatic hernias, cardiovascular anomalies and widely spaced nipples [3-8]. Seizures and mental retardation are characteristics. For the diagnosis of an individual with PKS, fibroblast culture from skin biopsy or occasionally from lymphocytes is required [9-15]. Once PKS is diagnosed a multidisciplinary approach is necessary for management. We present herein a case of PKS with its clinical and laboratory features.

The Case (Symptoms& Sıgns)

A two-month-old boy who was diagnosed antenatally with bilateral renal enlargement has been referred to our facility for further investigations. Prenatal and natal history was unremarkable. But postnatally was admitted to Neonatal Intensive Care Unit for indirect hyperbilirubinemia Family history was unremarkable. On physical examination the infant's general health was fine. He was active and alert. His body weight was 5.600 Kg (above 25th percentile), with a length of 57cm (50th percentile) and head circumference of 38 cm (50th percentile). However, he has had an abnormal facial appearance which includes hypertelorism, epicantus, wide and flattened nasal root, anteverted nostrils, long-simple philtrum, dysmorphic ears, thick lower lip, micrognathia and webbed neck. The patient also had wide halluces, polydactyly, and syndactyly in toes. There was an audible 3/6 systolic murmur over ULSE. Echocardiograpy showed mild pulmonary hypertension, bicuspid aortic valve, secundum type atrial septal defect with 3 mm diameter and grade-2 tricuspid regurgitation as shown in fig.3. On abdominal examination; an umbilical hernia and increased hair growth on the sacral area have been observed. Neither complete blood count nor biochemical laboratory assessment showed any abnormality. Ultrasonographic evaluation of urinary tract has revealed; increased echogenicity of the left kidney parenchyma, dilatation of pelvi-calyceal system and a parapelvic cyst in middle pole of right kidney measuring 14mm X10mm. as shown in fig.2 .MAG3 renal scintigraphy has been performed for further investigation and showed that contribution of the left kidney to total renal functionality was 72% whereas its right counterpart's contribution was 28%. Left kidney's perfusion and concentrating ability and the response of the collecting system to diuretics has been found to be normal. However, there was a significant urinary retention problem. The right kidney was smaller compared to the other side, and its parenchyma was thinner. In addition its ability to concentrate urine was reduced compared to its left counterpart. Audiological evaluation has also shown a moderate to severe sensorineural hearing loss.

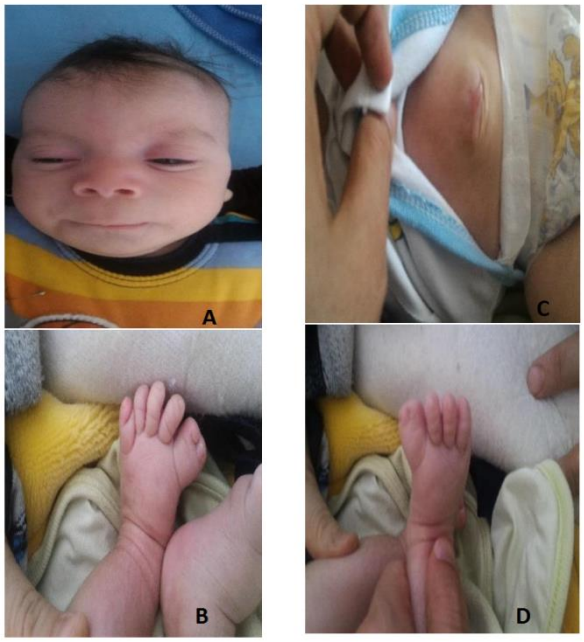

Figure.1 :Two month old infant with PKS (A, B, C, D)

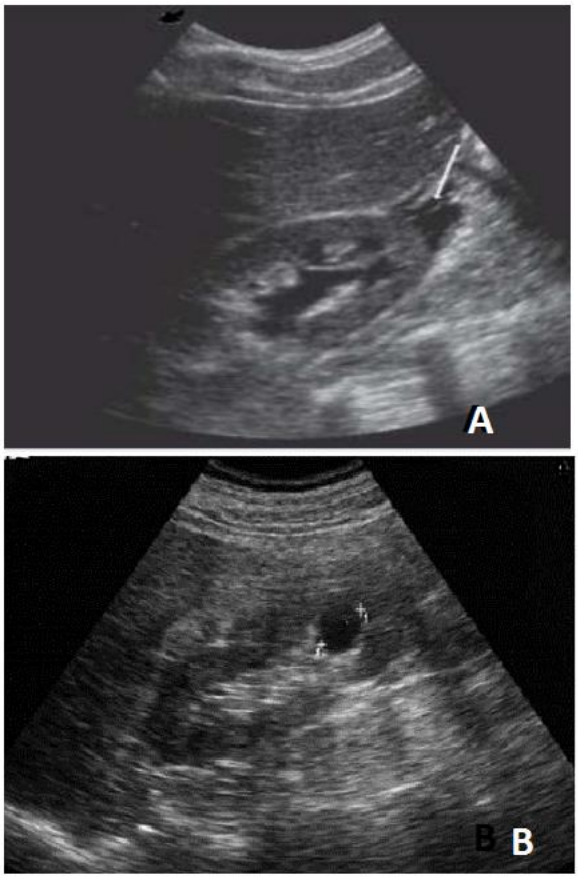

Figure.2 :Shows ultrasound findings in two months old infant with pks: ***(a: increased echogenicity of the left kidney parenchyma, b: parapelvic cyst in middle pole of right kidney)***

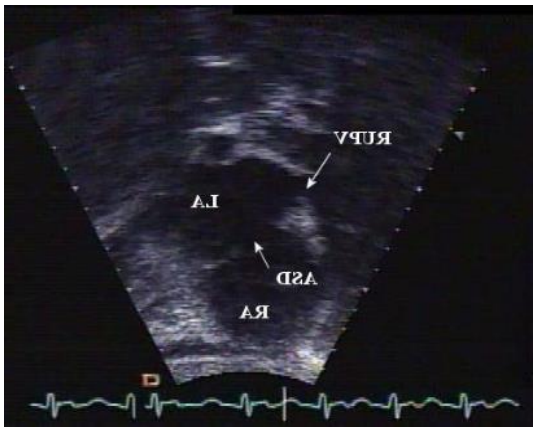

Figure.3: echocardiography of two months old infant with pks showing asd secundum type

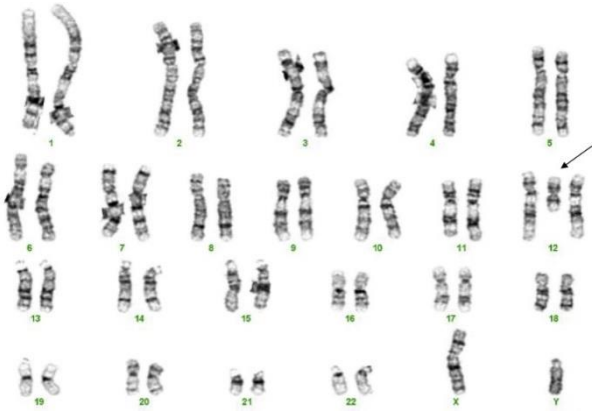

Fig .4: Karyotype of the two months old infant with PKS Tetrasomy 12 P chromosome using basic staining technique indicated by an arrow and labelled i12p

Diagnosis: Together with clinical findings, the patient was sent for cytogenetic analysis of skin fibroblast .which showed tetrasomy of chromosome 12p . There are different ways of writing a PKS karyotype. The simplest is: 47,XY,+i(12p)/46,XY, as shown in fig.4

Management; The patient has been managed by a multidisciplinary team approach that included pediatric nephrology, cardiology, neurology and ENT departments.

Outcome; The ınfant was discharged home in stable condition for proper follow up

DISCUSSION

Pallister-Killian syndrome is a rare genetic disorder diagnosed occasionally in pediatric practice. Even though this syndrome had been first identified by Pallister and his colleagues in 1977, Techler-Nicola and Killian have also identified the same syndrome in 1981 independently [(2)] .The current evidence shows that the main reason behind pathologic features of PKS originates from chromosome P_{12} tetrasomy. In the past, many PKS cases were thought erroneously as a mosaic pattern of tetrasomy 21 [(3,4,5)]. The extra-chromosome containing metaphases can be seen in cell cultures from amniotic or bone morrow cells. However, it could be observed in majority of the fibroblasts and lymphocytes [(12.14.15)]. Due to tetrasomy in PKS, the clinical presentation are heterogeneous. However, recent studies did not show a significant correlation between the rate of tetrasomic lymphocytes-fibroblasts and the severity of the congenital malformations, neurological impairment, and life expectancy [(6.8.9.12.16)]. The prevalence of PKS is unknown, and only 150 cases of PKS have been reported so far, the incidence of PKS increases with increasing maternal age [(4.13)]. Antenatal ultrasonographic evaluation might be helpful to reveal many clues about PKS such as diaphragmatic hernia, congenital heart and renal abnormalities, frontal bossing, and an absence of one of the umbilical arteries [(9.14.15.17)]. The majority of the children with PKS die at prenatal or early postnatal period of the life .The causes of death may be due to respiratory and renal failure. Nevertheless, average life expectancy is around 11 to 16 months [(2,10)]. Facial features such as high hairline, frontal bossing, local alopecia on the temporo-frontal area, absent or sparse eyebrow and eyelash, low-set and dysplastic ears, hypertelorism, flattened and relatively wide nasal bridge, exophtalmus are some components of the typical facial appearance of PKS. In addition, patients with PKS can also show features of upturned nose, small nostrils, long and thin upper lip, large and angled/downwarded mouth, high arched palate with pronounced lateral ridges. Early in life the mandible is short but as the time passes it tends to get to the forefront. Patients generally have a short neck and they likely to have patch-like, rarely diffuse, hypo-hyperpigmented skin lesions. These lesions only can be seen with Woods light examination [(9)]. Disproportionally short upper and lower limbs are seen in almost every patient with PKS. Their hands and feet are small and enlarged as well as polydactyly and syndactyly can be seen [(11)]. Rhizomelic brachimelia is quite often [(12).] In addition, atlantooccipital fusion and the absence of second ribs might accompany these features [(4, 13).] In our report, the patient has had polydactyly and syndactyly. Ocular malformations such as microophtalmia, cataract, keratoconus, pinpoint pupils and aniridia can also be observed in patients with PKS although our patient did not have any of these aforementioned pathologies [(2, 10, 14, 15).] Cardiovascular anomalies have been reported in the majority of the cases [(7)]. The most frequent cardiovascular malformation is the atrial septal defect in PKS patients. In addition, coarctation of aorta, aortic stenosis, PDA, hypertrophic cardiomyopathy has also been reported [(10,14).] Echocardiographic evaluation of our patient has shown secundum atrial defect by 3mm diameter; mild pulmonary hypertension, bicuspid aortic valve, and grade-2 tricuspid regurgitation. Bicuspid aortic valve and tricuspid regurgitation in PKS has not been reported before. Among all gastrointestinal (GIS) anomalies in PKS patients, diaphragmatic hernias are the most frequently observed lesions and is quite specific finding for PKS [(3).] If pulmonary hypoplasia is severe the shorter average life span is expected. Another common GİS pathologies in PKS patients are anal malformations such as anal atresia, anal stenosis and anterior ectopic anus [(12, 13, 14).] Fortunately

our patient had an umbilical hernia only. Although it is not quite often, some other pathologies such as dysplastic kidneys, renal cystic malformations, and cryptorchidism, small scrotum in boy, ambiguous genitalia, hypoplasia of labia major, the absence of upper vagina and uterus in girl can be observed as well [4, 10, 15].Our patient has, dilatation of pelvi-calyceal system of the left kidney and a parapelvic cyst in middle pole of right kidney but fortunately the renal function generally was normal. Following the delivery; hypotonia, severe global developmental delay, and seizures occur.. In addition, most patients have speech disorders. Even though the mechanism of the speaking disorder is being explained by sensorineural hearing loss, the main reason of this problem is assumed to be the severe neurological impairment [9],

In conclusion, physicians must be suspicious about PKS, in the patient who has multiple congenital anomalies such as frontal bossing, heart malformations, diaphragmatic hernia during the antenatal or postnatal periods. These patients require a multidisciplinary approach for their treatment and follow-up.

Conflict of Interest; The authors have no financial or other conflict of interests to disclose**.**

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