

Trisomy 8 Mosaicism Syndrome with Pigmentation Anomalies: A Case Report

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Abstract

Trisomy 8 Mosaicism syndrome, also known as Warkany syndrome 2, is a rare genetic event with an estimated frequency of about 1:25,000 to 1:50,000 births. Complete trisomy 8 is usually lethal, causing 0.70% of first-trimester abortions. However, mosaic trisomy 8 syndrome has extremely variable phenotypes, with a wide range of clinical manifestations, including cranio-facial dysmorphism, mild to severe intellectual disability, multiple skeletal abnormalities, deep palmar-plantar creases, and cardiac-renal abnormalities. A few cases of skin pigmentary anomalies have also been reported. We report on a 36 year old male case with mosaic trisomy 8. He has mild clinical findings and palmo-plantar hypopigmentation, which appears as a demarcating line between his hands' dorsal and palmar regions. We report this case to investigate palmo-plantar pigmentation anomalies.

Keywords: Trisomy 8; Palmar hypopigmentation; Mosaicism

Introduction

Trisomy 8 mosaicism syndrome, also known as Warkany syndrome 2, is a rare genetic event with an estimated frequency of about 1:25000 to 1:50000 births. Males are more frequently affected than females (M/F=5/1) [1]. Complete trisomy 8 is usually lethal, causing 0.70% of first-trimester abortions [2]. However, mosaic trisomy 8 syndrome has extremely variable phenotypes, with a wide range of clinical manifestations, including cranio-facial dysmorphism, mild to severe intellectual disability, multiple skeletal abnormalities, deep palmar-plantar creases, cardiac-renal abnormalities and skin pigmentary anomalies [3,4]. We report the case of a 36 year old male with mosaic trisomy 8 and palmo-plantar hypopigmentation.

Case Report

The reported patient was a 36 year old man from Turkey. He was the first child born to healthy, non-consanguineous parents. He was married to a third-degree relative over 12 years ago. They had a healthy, 10 year old son. After this delivery, their next four pregnancies ended as spontaneous abortions. There were no important features in the family history. The patient's childhood developmental process was normal. However, the patient had dysmorphic features, including androgenic alopecia, hypertelorism, deep set eyes, a high nasal bridge, down-slanted palpebral fissures, anteverted nares, a wide nose base, a long philtrum, a thin upper lip, a high-arched palate, a bifid uvula, widely spaced nipples, and deep palmar and plantar creases (Figures 1a-1c).

On his skin, there was a marked difference in pigmentation between the palmoplantar region and other skin regions. There was a demarcating line in the merger zone (Figure 2). He also had skeletal anomalies, including cubitus valgus, mild scoliosis, ulnar deviation in the right second finger and left third finger, radial deviation in the left second finger, and a thin elongated trunk (Figures 3a-3d). He has an

ectopic right kidney that it was detected due to abdominal ultrasound imaging. The patient had undergone surgery due to right cryptorchidism when he was 10 years old. The patient's intelligence and cardiological examination results were normal. He was not experiencing any complaints.

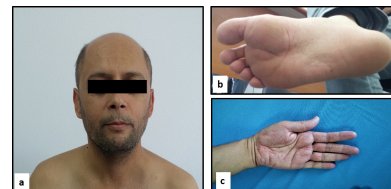


Figure 1: Dysmorphic features and deep palmo-plantar creases.

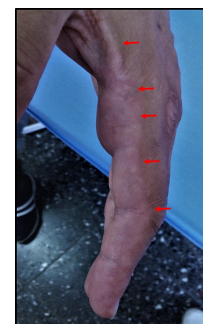


Figure 2: Palmar hypopigmentation and demarcation line (red arrows).

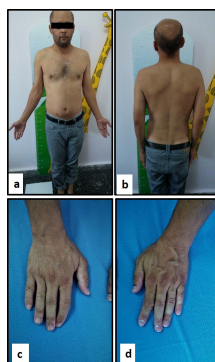


Figure 3: a. Skeletal anomalies including cubitus valgus, b. mild scoliosis, c. ulnar deviation in right second finger and left third finger, d. radial deviation in left second finger and elongated thin trunk.

Due to the presence of dysmorphological findings, skeletal anomalies, palmoplantar pigmentation changes, and a parental history of lost pregnancies, conventional chromosomal analysis was applied to the patient's peripheral blood cultures. The result of the chromosome analysis was 47 XY+8 [50]/46, XY, [8] (mosaic trisomy 8) (Figures 4a and 4b).

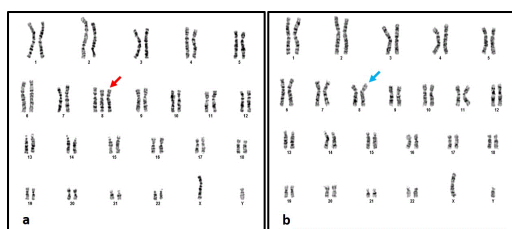


Figure 4: a. Karyotype 47,XY,+8 (red arrow), b. Karyotype 46,XY (blue arrow).

Fluorescence in-situ hybridization studies were performed using chromosome enumeration probe 8 (CEP 8) (Aquarius). Two hundred metaphase and interphase nuclei were scored (Figure 5).

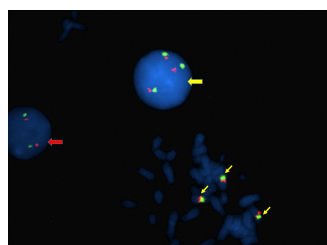


Figure 5: Green arr: 8p11.1-q11.1, Red: 8q12.1-q12.2.

Three signals were observed in 75% of the scored cells [nuc.ish. (CEP8) X 3[150/200]. The results were normal for both parents. Genetic counselling was provided to the patient.

Discussion

Trisomy 8 mosaicism syndrome is a rare chromosomal disorder defined by the presence of three copies of chromosome 8 in some cells of the organism [5]. It is thought that complete trisomy 8 is not compatible with survival [2].

Mosaic trisomy 8 is the result of a post-zygotic event. Other autosomal mosaic trisomies are associated with increasing maternal age and meiotic errors. In these other autosomal trisomies, normal euploid cell lines are the result of mitotic trisomy correction [6]. However, most mosaic trisomy 8 cases are caused by post-zygotic mitotic nondisjunction. The mitotic origin of mosaic trisomy 8 may help to explain the wide variation in phenotypes between these cases because the distribution of the trisomic cells in fetal tissues may begin in the embryonic stage [7].

The features of trisomy 8 mosaicism syndrome are extremely variable [8]. Common findings include peculiar facial dysmorphism; mild to severe intellectual disability; and joint, urinary, cardiac, and skeletal anomalies. Cranio-facial findings include scaphocephaly, prominent forehead, hypertelorism, deep-set eyes, a broad upturned nose, micro-retrognathia, low-set ears, large dysplastic ears, corneal opacity, and strabismus. Additionally, patellar aplasia-hypoplasia, corpus callosum agenesis, restricted articular function, vertebral fusions, bilateral camptodactyly, deep palmo-plantar creases, long and slender body habitus, narrow shoulders and pelvis, hypospadias, bilateral undescended testis, small penis, and diffuse hyperpigmentation with hypopigmented patches are also described [1,5,8-12]. In our case, the patient had a dysmorphic facial appearance, widely spaced nipples, deep palmar and plantar creases, an ectopic right kidney, mild skeletal abnormalities, and hypopigmented appearance in the palmo-plantar regions, with a demarcation line. A patient with linear brown blotches that followed Blaschko's lines has been previously reported [5]. However, to our knowledge, such a case of palmo-plantar hypopigmentation has not been reported before.

Patients with mosaic trisomy 8 syndrome can vary from phenotypically normal individual to those with severe malformations. In our case, the patient had mild clinical findings, and his life expectancy is normal. However, patients with mosaic trisomy 8 syndrome are at an increased risk of developing leukaemia and myelodysplastic syndrome [13]. Therefore, this patient should be followed up on periodically.

In conclusion, mosaic chromosomal disorders should be considered in patients with multiple congenital abnormalities and patchy pigmentation changes.

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