ORIGINAL RESEARCH PAPER VOLUME-6 | ISSUE-8 | AUGUST - 2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

An Unusual Case of Mosaic Trisomy 13 with Hemihypertrophy and Cutaneous Changes

Pediatric

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ABSTRACT

Patau syndrome (trisomy 13) was first described by Patau in 1960. It is a rare chromosomal anomaly with severe physical and developmental abnormalities. The mosaic type does not present with the same phenotypic features and children with this type live longer because of the less severe affection of the body organs. Hypomelanosis of Ito was first described by Ito in 1952. Hypomelanosis of Ito is sporadic, however some case reports highlighted the disorder as a non-specific expression of chromosomal mosaicism including mosaic trisomy 13. We present a case of mosaic trisomy 13 with hypomelanosis of Ito and hemihypertrophy as an unusual combination of signs for the diagnosis and counseling of chromosomal aberrations.

KEYWORDS:

Trisomy, Mosaic, Cutaneous, hypomelanosis, hemihypertrophy

Introduction

Patue syndrome or trisomy 13 is the third most common trisomy succeeding trisomy 21 and trisomy 18 with a reported prevalence ranging from 1 in 10000 to 1 in 21700 live births (1). It occurs when some or all of the cells of the body comprise superfluous genetic material from chromosome 13 that can either be a full extra copy, partial or a mosaic of chromosome 13. The mosaic form of trisomy 13 syndrome is caused by non-disjunction during mitosis resulting in two karyotypically distinct populations of cells with discrete genotype in the same individual. Mosaic trisomy 13 is not inherited and in addition, it mitigates the degree of severity of affection by the change in the genetic material and thus results in phenotypically and physically challenging cases for diagnosis and genetic counseling. (2) Majority of infants affected by full trisomy 13 die within the first year of life, however the mosaic form of the syndrome grants them few more years of survival with less physical and mental disability. Intrauterine growth restriction, along with craniofacial, heart, and limb anomalies are the most striking features in children with trisomy 13. (3) Here we describe an uncommon constellation of signs that lead to the diagnosis of a mosaic trisomy 13.

Case report

A 2-year-old Somalian boy was admitted to the pediatric ward at King Abdulaziz University Hospital with history of fever and difficulty of breathing for 2 days that was associated with decreased activity and poor oral intake. The child was admitted and treated as a case of pneumonia. Further history confirmed that the boy was born at term and did not attend pediatric follow-up or vaccination clinics afterwards. At the age of 5 months, he was admitted and treated for afebrile seizures and was discharged on valproic acid after which his seizures were under control. Developmental history revealed a child functioning at the age of 5 months. Family history was unremarkable for consanguinity, a similar condition, metabolic diseases, or early death in infancy or childhood. The child has 7 other healthy siblings. Physical examination revealed fever 38°c and mild to moderate respiratory distress requiring supplemental oxygen. His weight and head circumference were on the 50th centile. He had some dysmorphic features including, frontal bossing, sparse eyebrows, microphtalmia, wide nasal root, depressed nasal ridge, bulbous nose tip, bifid and tied tongue, small teeth with caries and wide gaps, bilateral postaxial polydactyly in both hands, incomplete palmer crease, tapering fingers, flexion contracture of wrist and polydactyly in feet bilaterally. (Figure 1) He also had evidence of hemihypertrophy involving the right leg. (Figures 1) Skin examination showed hypo/hyperpigmented skin lesions mainly on the trunk, neck, axilla and inguinal area. (Figure 2) Cardiovascular examination was normal as well as his echocardiography. Ophthalmologic examination revealed bilateral colobomas. Abdominal examination revealed hepatomegaly, which was confirmed by abdominal ultrasound. Brain CT SCAN showed findings suggestive of hypogenesis of cerebellar vermis and well-defined cystic structure noted posterior to the cerebellum measuring 1.6x2x7 cm likely an arachnoids cyst. Electroencephalogram showed grade 4 right mid-temporal dysrhythmias. Skeletal survey revealed reduced antero-posterior diameter of the skull suggesting possible brachycephaly and coxa valga of the right hip. The Chromosomal analysis was consistent with a male karyotype with two cells lines (47, XY,,+13 [18]/46,XY[32], 36% showed male karyotype, with trisomy 13 and 46% showed normal male).

Discussion:

To our knowledge, this is the first reported case of a patient who has trisomy 13 mosaicism with both hemihypertrophy and cutaneous manifestations. Trisomy 13 is a severe and rare disorder. In a population-based study in United Kingdom ascertaining all cases of trisomy 13 over 5 years from 1997 to 2001, 18% of affected fetuses were live-born, 7% were stillborn, and 7% were spontaneously aborted.(4) Only 6% of patients with trisomy 13 present with mosaicism. (5) Survival beyond the first year is rare in complete trisomy 13; however, those with mosaicism can survive longer. Some reported survival until adolescence and adulthood. (6, 7) The characteristic features in patients with complete trisomy 13 are rarely present in patients with the mosaic form of trisomy 13. (8) Although cutaneous manifestations are rare in patients with complete trisomy 13, case reports of their association with mosaic trisomy 13 are referenced in this paper. (2, 9, 10) Abnormal skin pigmentation and hemangiomas were the most commonly reported cutaneous manifestations. Some reports described patients with trisomy 13 mosaicism to have skin pigmentary abnormalities in a phylloid pattern accompanied by hypopigmentation or hyperpigmentation (11-13) and others with hypomelanosis of Ito (10) as it is the case in our patient. The abnormal skin pigmentary patterns associated with trisomy 13 mosaicism may be due to the differential expression of pigmentary genes encoded on chromosome 13 (ATP7B, EDNRB, DCT, EFNB2) (9), but this remains unclear. (10)

Hemihypertrophy is a condition in which one side of the body or a part of one side is larger than the other. Isolated hemihypertrophy, now called isolated hemihyperplasia, is a congenital overgrowth disorder associated with an increased risk for embryonal tumors, mainly Wilms tumor and hepatoblastoma (14) In our case, hemihypertrophy was confined to the middle aspect of the right thigh. As far as we are aware, no other reports mentioned trisomy 13 with hemihypertrophy. However, Wilms tumor, which is one of the associations with overgrowth syndromes, was reported in a 4-year-old boy with trisomy 13. (15)

Conclusion

Cutaneous manifestations in mosaic trisomy 13 are not uncommon, however we reported a new association of mosaic trisomy 13 with hemihypertrophy. The skin manifestations do not present in a homogenous pattern and most of the cases present either as vascular anomaly or pigmentary changes. Cutaneous manifestations in presence of hemihypertrophy and other subtle findings may give a clue to the diagnosis of mosaic trisomy 13.



Figure 1: Polydactaly and flexion contracture of wrists



Figure 2: Hemihypertrophy of right thigh and hypo/hyperpigmenttaion of the skin

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