Case Report

Hypomelanosis of Ito - A Case of Pigmentary Mosaicism Associated with Partial Trisomy of Chromosome 20

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Abstract

Introduction: Hypomelanosis of Ito is characterized by hypopigmentation along the lines of Blaschko, evident at birth or during childhood, in combination with variable extra cutaneous findings, mainly affecting the central nervous system, musculoskeletal system and eyes. Most commonly caused by chromosomal mosaicism associated with a variety of changes in structure or number of autosomes or X chromosome.

Case report: Female patient, 8 years old, with a history of left renal agenesis, congenital strabismus, bone malformation of the first two left ribs with fusion of their anterior arcs, kyphoscoliosis, and delayed psychomotor development with learning and language difficulties. Referenced for hypopigmented linear bilateral macules and patches along the lines of Blaschko, on the trunk and limbs, since the age of 4. No change of hair, nails, palms, soles and mucous membranes. No previous personal or family history of skin condition, namely vesiculobullous, verrucous or pigmentation lesions. The karyotype of hypopigmented skin fibroblasts revealed the existence of partial trisomy of chromosome 20 in mosaic (mos47, XX, +20 /46,XX).

Discussion: We emphasized this case by the presence of neurocutaneous pathology associated with partial trisomy of chromosome 20 detected on cytogenetic analyses of skin fibroblast cultures. This chromosomal mosaicism is often associated with renal and sometimes psychomotor changes, although in some publications the psychomotor development is considered normal. The prognosis is mainly determined by the associated extracutaneous manifestations so a multidisciplinary approach to these patients is imperative.

ABBREVIATIONS

HI: Hypomelanosis of Ito

INTRODUCTION

Hypomelanosis of Ito (HI) is a cutaneous expression (phenotype) for hypopigmentation along Blaschko lines rather than being a distinct entity. Some authors reserve this designation for patients with extracutaneous abnormalities, mainly affecting the central nervous system, musculoskeletal system and eyes in 50% cases[1,2].

The streaks and swirls of hypopigmentation along Blaschko may be present at birth or become evident during childhood, especially in those with fair skin. Sun exposure can precipitate the development or extension of clinically apparent lesions by accentuating contrast with background skin.

HI almost always occurs sporadically, and it seems to be caused by a de novo mutation in early embryogenesis. Most common is caused by chromosomal mosaicism associated with a variety of changes in structure or number of autosomes or X chromosome. Almost any chromosoma can be affected, hence the wide heterogeneity of systemic manifestations in HI [3].

Trisomy 20 mosaicism is the commonest prenatally detected mosaic autosomal trisomy identified on amniocentesis [4]. Most (90–95%) of these cases appear normal at birth, although the trisomy 20 mosaicism is seldom confirmed postnatally in certain specific fetal organs or tissues such as kidney, skin, rectum, esophagus, lung and in blood [5].

Trisomy 20 mosaicism has previously been described in six patients with blaschkoid skin pigmentary abnormalities [6-9] although one was the first demonstration in keratinocytes [10]. A significant number of affected individuals also show: intrauterine
growth retardation, dysmorphic features, facial asymmetry, microcephaly, hypotonia, deaf lip and palate, renal anomalies, congenital heart disease, occipital and cervical meningecele, anencephaly, and various minor anomalies including epicanthal folds, abnormal ears, 'non-mobile' tongue, clinodactyly, abnormal dermatoglyphics, delayed closure of the fontanelle, and micro-retrognathia [5].

However, with such a small number of reported cases and high variability in clinical expression, it is difficult to definitely state the true prevalence of associated problems.

**CASE PRESENTATION**

Female patient, 8 years old, caucasian, phototype III referenced to dermatology department for linear hypopigmentation, insidious onset, on the trunk and limbs, since the age of 4. Lesions were asymptomatic but cosmetically disfiguring.

No maternal exposure to medications or other agents. No reference to pregnancy complication. Newborn of term (39 weeks) with Apgar 9/9. No previous personal or family history of skin condition, namely vesiculobullous, verrucous or pigmentation lesions. With a history of left renal agenesis, congenital strabismus, bone malformation of the first two left ribs with fusion of their anterior arcs and kyphoscoliosis. In particular, there was no history of urinary tract problems or hospitalizations.

Clinical examination revealed hypopigmented linear diffuse, bilateral, symmetric macules and patches along the Lines of Blaschko on the trunk and limbs. On the trunk lesions were patchy whorls which did not cross the midline (Figure 1). On the forearms it was present equally on the left and right, primarily on the flexor surface. The hypopigmented streaks on the legs extended from the superior thigh down towards the ankles. It was more marked on the thighs, with more streaks on the left than the right (Figure 2). There were no facial lesions. No change of hair, nails, palms, soles and mucous membranes. Some evidence of social interaction although mild left kyphoscoliosis. In particular, there was no history of urinary tract problems or hospitalizations.

The karyotype of hypopigmented skin fibroblasts revealed the existence of partial trisomy of chromosome 20 in mosaic (mos47, XX, +20 /46,XX) consistent with Hypomelanosis of Ito.

Hemogram and metabolic profile presented no abnormalities.

The benign nature of the dermatosis was explained to the patient’s family. It was recommended sun protection.

**DISCUSSION**

Hypomelanosis of Ito refers to hypopigmentation along the Lines of Blaschko that is characterized by a clone of skin cells with a decreased ability to produce pigment. The characteristic pattern of streaks and whorls can occur unilaterally or bilaterally and is seen most commonly on the trunk and limbs.

Probably the pigmentary anomaly is controlled in expression or function by many genes. Co-localization of the cytogenetic abnormality with several candidate pigmentary genes (attract in, agouti signalling protein, endothelin 3, SOX18) on chromosome 20 suggests that copy number effect of any one or more of these genes may explain the pigmentary abnormalities in our and previously reported patients [3].

A wide range of cytogenetic abnormalities has been reported including aneuploidy, polyploidy, chimerism, and balanced and unbalanced translocations although chromosomal mosaicism is found in only 20–30% [10]. It is possible that in the reminder the genetic abnormality is submicroscopical (point mutations, microdeletions, microinsertions) undetectable by cytogenetic techniques [10]. More sensitive techniques such as microarray-based comparative genomic hybridization or fluorescent in-situ hybridization might be useful.

In addition, mosaicism cannot always be shown using conventional karyotyping of blood lymphocytes or skin fibroblasts (cell lines from mesoderm). Because the mosaic abnormality along Blaschko’s lines is an ectodermal origin, analysis of keratinocytes (not available as most cytogenetics laboratories), would likely be of higher yield as well as more sensitive and biologically relevant [10].

In patients with trisomy 20 mosaicism and pigmentary abnormalities, learning difficulties, facial dysmorphism, cardiac defects and other abnormalities have also been reported although in one series had normal development (71%) [5].

We emphasized this case by the presence of neurocutaneous pathology associated with partial trisomy of chromosome 20 detected on cytogenetic analyses of skin fibroblast cultures consistent with Hypomelanosis of Ito and described in 2005 [9].

Chromosomal mosaicism in tissues of mesodermal origin may explain some of the associated features in patients with...
pigmentary mosaicism such as skeletal abnormalities [10] and might be associated with a better prognosis neurologically.

Based on survey data of 144 reported cases, the risk for a serious birth defect in a patient with prenatally detected trisomy 20 is less than 10 per cent although long-term studies are not available [11]. Regarding the ongoing care of these children, authors suggest a renal ultrasound because some of the cases examined at birth have renal anomalies and some have trisomy 20 mosaicism detected in kidney cells and/or urinary sediment [5].

Our finding expands the case reports of trisomy 20 mosaicism trisomies associated with variations of skin pigmentation. The skin lesions require no special treatment beyond sunscreen. Cosmetic camouflage does offer some promise. For individuals without additional neurologic manifestations, an annual follow-up appointment is recommended [12].

Hypopigmentation along Blaschko lines are suggestive for pigmentary mosaicism. Cutaneous manifestations can alert for underlying neuropediatrics diseases. Hipomelanosis of Ito is a rare neurocutaneous disorder and the prognosis is mainly determined by the associated extracutaneous manifestations so a multidisciplinary approach to these patients is imperative.

REFERENCES