An Interesting Coexistence of Multifocal Hypertrichosis and Hirsutism in Hypomelanosis of Ito

Abstract
Hypomelanosis of Ito (HOI) is a sporadic disorder characterized by naevoid hypomelanosis in association with neurological, musculoskeletal, and other systemic defects. Localized hypertrichosis has been reported in HOI, however, multifocal hypertrichosis along with hirsutism in HOI are rare. We report an interesting coexistence of multifocal hypertrichosis and hirsutism in a 7-year-old girl with HOI.

Keywords: Generalized hypertrichosis, hirsutism, hypomelanosis of Ito

Introduction
The term “Hypomelanosis of Ito” (HOI) is used to describe hypopigmentation of the skin along the Blaschko’s lines.1 Hypomelanosis of Ito (HOI) is a sporadic disorder characterized by naevoid hypomelanosis in association with neurological, musculoskeletal, and other systemic defects. Localized hypertrichosis has been reported in HOI, however, multifocal hypertrichosis along with hirsutism in HOI are rare.

Case Report
A 7-year-old girl, product of non-consanguineous marriage, first born child was brought with a history of progressively increasing, asymptomatic hypopigmented patches over forearms, hands, and feet since birth with excessive hair growth over back, face, and thighs for the past 2 years. There was history of learning difficulties in school; however, there were no seizures, hearing/visual impairment, dental abnormality, or any visible limb deformity. Family history was insignificant. Physical examination showed head circumference as 45 cm, weight 15 kg, and height 108 cm (height and weight <3rd centile). Body mass index (BMI) was 5th centile. Clinical examination showed short stature, microcephaly, small triangular face, low set ears, high arched palate, bifid uvula, and webbed fingers. General physical examination was normal. Cutaneous examination showed generalized xerosis, streaky hypopigmentation over both axillary folds, which extended medially over forearm and arm upto the wrist with sparing of elbows in a blaschkoid pattern [Figure 1]. Hypopigmented macules were also present over extensor aspect of arms, dorsal aspect of hands and feet extending over shin, and anterior aspect of thigh and right inguinal area. There were patches of hypertrichosis in the midline, scapula, right and left lumbar area, and posterolateral aspect of both thighs (notably sparing the streaky, hypopigmented patches both in upper and lower limbs) and pubic hair [Figure 1]. Thick, coarse, terminal hairs were also observed over the forehead and zygomatic area. She had bushy eyebrows and thick eyelashes along with presence of hirsutism over upper lip and chin [Figure 2]. Keratosis pilaris was noted over thighs and knees. Yellowish discoloration and roughness of the nail plate were noted in the 3rd and 4th toenails bilaterally. Scalp was normal. Laboratory investigations showed insufficient vitamin D, and MRI brain showed empty sella and polymicrogyria and pachygyria. Intelligence quotient assessment showed borderline intellectual level (IQ-73, SQ-65). Her endocrinial evaluation was normal. Skin biopsy from hypopigmented patches revealed an epidermis showing
flattening and keratotic plugging and mild perivascular chronic inflammatory infiltrate. On Masson Fontana stain, presence of basal layer pigmentation was normal.

**Discussion**

The term “Hypomelanosis of Ito (HOI)” is used to describe hypopigmentation of the skin along the Blaschko’s lines. These lines represent the streams of growth of cutaneous cells derived from a limited number of precursors and are expression of highly varied genetic mosaicism because of the presence of different clones of cells in early embryogenesis. Prevalence is unknown, but incidence has been estimated between 1/10 000 and 1/8500. We report an interesting case of HOI with multiple anomalies including multifocal hypertrichosis, hirsutism, empty sella and polymicrogyria, and pachygyria. In our patient, multiple naevoid hypertrichosis spared areas of blaschkoid hypopigmentation. The coexistence of these two entities has been reported in very few cases. Naevoid hypertrichosis usually presents as an isolated, solitary defect, but the occurrence of partial lipoatrophy and bony abnormalities has been reported. Presence of multiple patches of naevoid hypertrichosis in a patient is relatively uncommon. Our patient showed multiple areas of hypertrichosis. Khurana et al. reported a 3-year-old female of HOI over left side of trunk, upper and lower limb with patches of hypertrichosis over scapulae, buttocks and linearly along flexor aspect of both lower limbs to mid-calf and extensor aspect of both arms since birth. The underlying skin was normally pigmented at the sites of hypertrichosis, and there was no overlap with the hypopigmented lesions anywhere. Lestringant et al. described two cases of HOI with hypertrichosis. In the first case, achromatic patches and streaks along Blaschko lines were present on trunk, limbs, and face with patches of hypertrichosis equally distributed over both normally and hypo-pigmented areas since the age of 10 weeks. Hypertrichosis was also present over the genitilia. Other features included dysmorphic facies, additional nipple, webbing of anterior fold of axilla, clinodactyly of 5th finger, and capillary hemangioma on thigh. The second case was a 21-month-old female with generalized HOI and hypertrichosis of cheeks, arms, back, and thighs that was strictly present over streaks of normally pigmented skin along with presence of dysmorphic facies, digital anomalies, mental retardation, and partial absence of corpus callosum. Lopes-Barrantes et al. described multiple lesions of HOI with naevoid hypertrichosis involving left arm, right side of trunk, and both legs in a 2-year-old girl. In our patient, hypertrichosis was multifocal in the form of excessive terminal hair growth, diffusely
involving the midline, scapula, right and left lumbar area, and posterolateral aspect of thigh notably sparing the streaky, hypopigmented patches. Hypertrichotic patches with thick, coarse, terminal hair were also observed over forehead and zygomatic area. She had bushy eyebrows and thick eyelashes along with presence of hirsutism over upper lip and chin. There was no clinical evidence of precocious puberty or any other cause of hypertrichosis such as congenital hypertrichosis, lanuginosa, porphyrias, hypothyroidism, or Cornelia de Lange, Hurler’s, Gorlin’s or Lawrence–Seip syndromes.\[5\] The coexistence of multifocal hypertrichosis and HOI has been reported in very few cases. López-Barrantes and colleagues have proposed that this combination of findings may be explained by concept of twin spotting, according to which, in an organism heterozygous for two different mutations located on either of two homologous chromosomes, a somatic recombination may result in two different daughter cells homozygous for either mutation, giving rise to two different mutant clones of cells that form paired mutant spots.\[7\] It is noteworthy that all the affected cases have been female, and this could be more than a chance association. Her endocrinal evaluation was normal. Thus, in all probabilities, cause of hirsutism could be central in origin. It is a novel finding, which is hitherto unreported in HOI. Our patient showed empty sella and polymicrogyria and pachgyria in MRI brain, which has also not been reported before. We conclude that hypertrichosis should be added to the list of the various known associations with HOI.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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