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Hypomelanosis of Ito and Asymmetric Crying Facies: A Rare Case Report From West Africa

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ABSTRACT

Hypomelanosis of Ito is a neurocutaneous disorder characterised by areas of hypomelanosis that follow the lines of Blaschko. It has multisystemic/ extracutaneous manifestations, predominantly in the nervous and musculoskeletal systems. This condition has no racial predilection, but skin lesions are better seen in darker complexion individuals. Because of the similarities with other cutaneous conditions, there are proposed criteria for a presumptive or definitive diagnosis. Our case fits a proposed definitive diagnosis for Hypomelanosis of Ito.

We describe a 6-week-old child born at term with patches of hypopigmentation on the body and face with other associated congenital anomalies. A unilateral lower lip palsy on the left is notable among the associated congenital features. This child is the last of 3 children born to native Ghanaians with no consanguinous relationship. This report examines the clinical presentation of the case and includes a literature review on the incidence, diagnosis, associated features, and management of Hypomelanosis of Ito. Like any child with a congenital anomaly, a comprehensive physical examination should be performed, as there could be other related or entirely different anomalies. We present a case we report of Hypomelanosis of Ito and asymmetric crying facies in a 6 week old.

Keywords
Hypomelanosis of Ito, Asymmetric Crying Facies, Neurocutaneous, Congenital Anomalies.

Introduction

Hypomelanosis of Ito (HI) was first described in a Japanese woman in 1952 by Ito [1] as depigmented spots arranged similarly to the pigmentation in incontinentia pigmenti and thus named the condition incontinentia pigmenti achromians. However, in 1972, Jelinek, after studying three cases of incontinentia pigmenti achromians, stated that the name suggested one would have to have true incontinentia pigmenti that would undergo a process of decolourising and thus in the patient may have both hypermelanosis and hypomelanosis. The three patients he studied had no features of hyperpigmentation and therefore felt the name inappropriate and named the condition Hypomelanosis of Ito [2]. It was later discovered that HI is not only a cutaneous disease but affects other systems, predominantly the central nervous and musculoskeletal systems [3,4]. Some theories state that Hypomelanosis of Ito is a non-specific manifestation of chromosomal mosaicism; however, this has not been documented in every case of HI [5,6]. The incidence and prevalence are estimated to be between 1in 7540 and 1 in 82,000 [6]. Hypopigmented lesions, which may appear as whorls, linear streaks, or patches following the lines of Blaschko, are the characteristic feature of HI. They are predominantly found on the trunk but may also be present on the extremities, face, and Scalp [7]. The lesions may be present at birth or within the first 18 months [8]. Herein, we report a case of HI with multiple congenital anomalies and no family history of HI.

Case Report

A 6-week-old female presented to the plastic surgery outpatient clinic for evaluation of syndactyly on the left hand and right foot. The child was born at a government hospital at 38 weeks gestation age with a birth weight of 2.1kg. The child was said to have been born with multiple hypopigmented lesions. The mother attended regular antenatal visits, took the prescribed medications, and had no complications throughout her pregnancy. She did not smoke nor take alcohol during her pregnancy.

The child is the last of three children, and none of the siblings have been noted to have any anomalies. There is no family history of similar anomalies. The mother is a prison officer, and the father is a police officer. The parents are not in consanguinity. The child was alert and active during the physical examination and was not in respiratory distress.

Generalised hypopigmented lesions appearing as patches were noted on the trunk, upper and lower limbs, and the soles of the feet and the head.

Head

1. Has a patch of Alopecia (Figure 3).
2. The mouth deviates to the right when the baby cries but is symmetrical at rest (Figure 2).
3. He has low-set ears bilaterally, with the left ear missing the superior crus of the antihelix and a prominent tragus (Figure 3).

Ophthalmic Examination Findings

Patient's visual acuity -Fixating and Following Light (FFL), no nystagmus, blepharoptosis, or hypertelorism. The lens is transparent. On fundoscopy, cup to disc ratio is 0.2, pink neuro-retinal rim, normal macula, normal peripheral retina.

Trunk

Respiratory- vesicular breath sounds with no added sounds.

Cardiovascular- S1 and S2 are normal with no murmur.

Abdomen- reducible umbilical hernia with a hypopigmented patch in the centre, no organomegaly.

Upper Limb

Right hand- all fingers fully developed.

Left hand- Incomplete simple syndactyly of the middle and ring finger (Figure 1).

Figure 1: Baby with features of Hypomelanosis of Ito.

A- Syndactyly of left middle and ring fingers.

B- Hypopigmented patches.

C- Umbiical hernia.

D- Syndactyly of right 1st and 2nd toes.

Lower Limb

Right lower limb- Complete, simple syndactyly of the first and second toes (Figure 4).

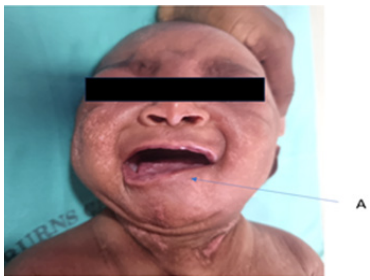

Figure 2: Baby with an asymmetric crying face.

A- Impaired depressor anguli function on the left.

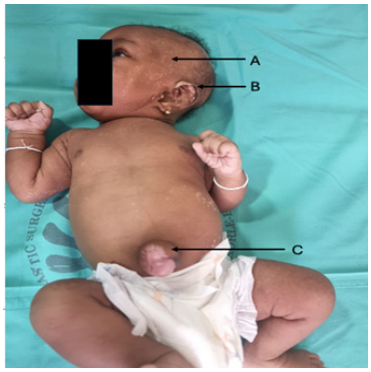

Figure 3: Baby exhibiting scalp and umbilical irregularities.

A- Alopecia.

B- Low-set ear.

C- Umbilical hernia.

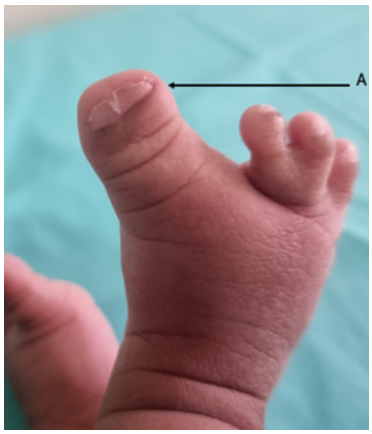

Figure 4: Close-up of the patient's foot.

A- Syndactyly of first two toes.

Discussion

Minor Ito wrote about three patients he had observed, one being a woman of 26 years with distinctive patterns of hypopigmentation on the trunk and extremities [1]. Hypopigmentation, or pigmentary mosaicism, occurs as patches, whorls, or streaks and usually follows the lines of Blaschko [9-11]. It used to be called incontinentia pigmenti achromians, characterised by inflammation and blistering with hyperpigmentation and eventual hypopigmentation [6,11,12]. It has been shown there is no such inflammation with Hypomelanosis of Ito. Hypomelanosis of Ito was formerly considered a purely cutaneous entity, but recent publications have demonstrated several extracutaneous manifestations, chiefly neurological and musculoskeletal presentation [6]. As a neurocutaneous entity that is now identified, it is said to be the third most common, following neurofibromatosis type 1 and tuberous sclerosis [13-15]. Its incidence is said to be higher than Sturge-Weber Syndrome [13].

It is thought to be more common in non-white populations, but very few cases are reported in Africa [14]. Ruggieri et al. estimated a frequency of 1 in 7540 births and 1 in 82,000 individuals in the general Sicilian population [6]. This somewhat ties in with the frequency reported by Pascual-Castroviejo to be 1 per 1000 new patients consulting a paediatric neurological service or 1 per 8,000-10,000 unselected patients in a children's hospital [13]. Some studies have shown a female-to-male ratio of about 0.7:1, whereas others show only a slight female preponderance [4,6,13]. The pathogenesis of the condition is unclear and likely to be multifactorial [4]. The pathogenetic basis of many cases of hypomelanosis of Ito was identified as chromosomal mosaicism, which provided a hint to explain the condition's variable clinical presentations and their frequently asymmetric expression. Although some reports have claimed familial occurrence and single gene inheritance, none of these reports have been proven [6]. Patients who show chromosomal alteration could show mosaicism for almost any autosome or sex chromosome or a balanced, constitutional X; autosome translocation, with a cytogenetic breakpoint in the pericentromeric region of the X (seen mostly in female patients) [5,6,9,11]. Mosaicism occurs when two distinct cell populations occur during embryologic development, usually due to chromosomal nondisjunction in one cell line or mutation. The neural crest-derived pigmentary cells that exhibit the whorled pattern of hypopigmentation observed in HI are thought to express mosaicism [9].

According to Chamli et al. and other reports, histopathology of the affected skin usually reveals no extracellular melanin in the dermis and no indication of inflammation. The epidermal basal layer also has reduced melanocytes and melanosomes, with a selective decrease in eumelanin without pigmentary incontinence [4,6,9,11].

Clinical presentation is variable but usually has a constant skin manifestation in affected individuals. The hypopigmentary pattern on the skin may be whorls, patches, or linear streaks on the trunk, usually stopping in the anterior or posterior midline, on the shoulders or hips, or even on the extremities. Sometimes, these patterns may be seen on the face, palms or soles of the feet. These patterns are said to follow the lines of Blaschko [4,6,10,11,14]. These lines of Blaschko are lines on the skin that represent the developmental growth pattern during epidermal cell migration. They follow a V-shape over the upper spine, an S-shape over the abdomen, an inverted U-shape from the breast to the upper arm, and perpendicular lines up and down the arms and legs. They also appear on the head and neck in a less well-defined manner [4,6,7,11,17]. Hypopigmentation may be more noticeable in the early months of life or following the first sun exposure due to its increased contrast with healthy skin. It usually fades by adulthood but rarely in childhood [7,11].

Other minor pigmentary lesions may be present, including Mongolian blue spots, ichthyosis, morphea, angiomatous nevi, nevus of Ota, cafe-au-lait spots, and cutis marmorata [6,16]. Extracutaneous manifestations include mostly neurological (seen in 90% of cases), musculoskeletal presentations (seen in 70% of cases), and abnormal features from other system [11]. In a study by Pascual-Castroviejo et al. (Hypomelanosis of ITO), neurological complications in 34 cases showed that mental retardation, autism, and seizures of various types were present in most of the children seen [16]. A case report from East Africa also revealed that the child was delayed in achieving her developmental milestones [14].

Neuropathology findings typically include dysmyelination of the corticospinal tracts, heterotopic areas, pachygyria, laminar or band heterotopia, focal or generalised brain atrophy, brainstem and cerebellum hypoplasia, abnormal neurons in the white matter and periventricular regions, and a notable astrocyte reaction [16]. These findings are caused by the coexistence of neural cells undergoing regular migration and cells exhibiting migration arrest or even complete absence of migration [4,6]. Asymmetry in limb length or size, joint contractures, kyphoscoliosis, pectus excavatum or carinatum rudimentary ribs, small hands and feet, pes valgus or varus or cavus, genu valgus, or congenital hip dislocation, polydactyly or syndactyly, short stature, and delayed skeletal maturation are the most common skeletal abnormalities observed [4,16]. Our patient had syndactyly in both upper and lower limbs (Figure 1).

In their series of 34 patients, Pascual-Castroviejo et al. found ophthalmologic, dental, cardiac, and genitourinary presentations [16]. Ophthalmic presentations and cardiac manifestations are said to occur in 25% and 10% of cases, respectively [11]. Some of these include strabismus, nystagmus, exotropia, myopia, heterochromia of the irides, coloboma of the iris, orbital hypertelorism, congenital heart defects like Tetralogy of Fallot, atrial or ventricular septal defects. Other anomalies noted are genitourinary anomalies-ureteral and renal agenesis, horse-shoe kidneys, bilateral urethra duplication, renal tubular acidosis, hypospadias, and vaginal skin tags and craniofacial anomalies such as low-set ears, small nose and inner epicanthic folds, microcephaly, brachycephaly, turricephaly, large fontanels, late closure of fontanels, frontonasal and midfacial

hypoplasia, triangular face, prognathism or hypotelorism [11]. The patient could also present with an umbilical or inguinal hernia [11,16]. It is important to note that though there have been few reports of associated tumours with hypomelanosis of Ito, there is generally a lack of evidence of a predisposition to the development of these tumours [9].

An essential feature in our patient is the deviation of the lower lip to the right when crying and a symmetric face when quiet (Figure 2). This is a feature consistent with cases with congenital unilateral lower lip palsies. The pathology with asymmetric crying facies could be due to congenital hypoplasia or insufficiency of the depressor anguli muscle [18-20] on the side that does not go down when crying, a facial nerve compression, or a faculty facial muscle or nerve development [20,21]. Liu et al. described a 26-month-old girl with an asymmetric crying face who had other associated congenital abnormalities, mainly in the cardiorespiratory system [20].

In the case we report hypomelanosis of Ito, the asymmetric crying facies is most likely one of the neurological manifestations of the condition, as previously mentioned. While there are no universally accepted criteria for diagnosing Hypomelanosis of Ito, Ruiz-Maldonado et al. proposed criteria for presumptive and definitive diagnoses after conducting a 20-year prospective review of 41 paediatric patients [3,14].

They devised these criteria:
The sine qua non: Congenital or early acquired nonhereditary cutaneous hypopigmentation in linear streaks or patches involving more than two body segment [3]
Major: 1 or more nervous system anomalies; 1 or more musculoskeletal anomalies [3]
Minor: 2 or more congenital malformations other than nervous system or musculoskeletal; chromosomal anomalies [3].

For a definitive diagnosis, a patient must fulfil the sine qua non and one or more features of the major or two or more minor criteria [3]. For a presumptive diagnosis, the sine qua non must be present alone or in association with one feature of the minor criteria [3]. Our patient fulfils the sine qua non with a musculoskeletal anomaly (syndactyly) and other congenital anomalies, including an umbilical hernia, low-set ear, and left ear anomalies.

Patients with hypopigmentation or any lesion in the distribution of the Blaschko lines should have their skin thoroughly examined and their nervous, musculoskeletal, ophthalmologic, cardiac, and genitourinary systems. Patients with neurologic symptoms should undergo a skeletal survey, CT, and MRI, and those with seizures should undergo an electroencephalogram [11].

The treatment of Hypomelanosis of Ito is mainly symptomatic and requires an interprofessional team, including dermatologists, neurologists, paediatricians, orthopaedic surgeons, ophthalmologists, dentists, and geneticists [11]. The skin lesions require no special interventions. Make up can obscure the areas of hypopigmentation. Patients must also be monitored for complications arising in any system with anomalies. Genetic counselling should be part of the patient's overall management [11]. Differential diagnoses include incontinentia pigmentosi, other neurocutaneous conditions, vitiligo, piebaldism, and systematised nevus depigmentosus. Complications that occur are referred to the areas with anomalies and managed accordingly. These anomalies and their complications often determine the prognosis, and according to Chiamli et al., death is rare [11]. If the described skin lesions are seen on a patient, a complete physical exam and investigations must be performed to identify extracutaneous findings. Patients should be followed up frequently to assess their mental development and the progression of the lesions.

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