CASE REPORT

Hypomelanosis of Ito - case report

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Abstract

Objectives: the authors report a case of hypomelanosis of Ito (HI), a rare neurocutaneous syndrome with neurological and chromosomal alterations associated with cutaneous involvement and recurrent pneumonia.

Case report: a male patient, age 1 year and 11 months, was admitted with bilateral bronchopneumonia to the São Vicente de Paulo Hospital. Examination revealed hypochromic maculas on the skin, compatible with HI, and a delay in neuropsychomotor development. The patient was submitted to incisive biopsy of the abdominal skin lesions, electroencephalogram, magnetic resonance, and cytogenetic evaluation.

Results: histology and immunohistochemistry evinced absence of melanin and reductio of melanocyte in focal areas of the epidermis. The electroencephalogram revealed diffuse cortico-subcortical dysfunction. Encephalic magnetic resonance imaging was compatible with arachnoid cyst in the temporal region. Karyotype showed chromosome mosaicism (46, XY) and interstitial deletion of bands 22.2 to 24.4 of the long arm of chromosome 10 (25%).

Conclusions: analysis of skin lesions is important for the etiologic definition of neuropediatric disorders.


Introduction

Since 1952, when Ito described the syndrome of incontinentia pigmenti achromiens, dermatologic, genetic, and neurologic findings have been the object of detailed reports.1 This name was chosen because the cutaneous lesions of the syndrome, as seen on a negative, were similar to those of incontinentia pigmenti of Bloch-Sulzberger. In 1973, Jelinek and colleagues suggested that the syndrome be named hypomelanosis of Ito, which is currently the most widely used nomenclature.2

The hypomelanosis of Ito (HI), or incontinentia pigmenti achromiens or, still, achromic and systematized nevi is a rare neurocutaneous syndrome possibly related to autosomal dominant inheritance and that is more frequent among women. It is characterized by hypopigmented areas with irregular borders, streaks, whorls, or patches and it is commonly associated with neurological abnormalities.3,4 HI is usually present at birth and, at times, repigmentation can occur with time. Moreover, others have described HI as a neuroectodermal disorder that appears to be a nonspecific manifestation of chromosome mosaicism.5 According to Williams and Elster, there are approximately 95 cases of HI reported in the literature until 1990.6

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Our objective is to report a case of a child with hypomelanosis of Ito who presented with chromosomal and neurological abnormalities associated to cutaneous involvement and recurrent pneumonia. It is also our objective to review the current literature on HI.

Case report

Male patient with dark-brown skin color, age 1 year and 11 months (02.17.1998), born and residing in the city of Passo Fundo, state of Rio Grande do Sul, southern Brazil. Patient presented with suspected bilateral bronchopneumonia that was confirmed by chest X-ray. It was the third episode of bronchopneumonia reported since 4 months of age. Patient was born from normal delivery, term gestation, and with congenital club foot.

At admission, patient was submitted to physical examination and the following casual findings were observed: hypochromic, asymmetrical, bilateral maculae with irregular borders, distributed in stripes and in the form of streaks, whorls, and patches following Blaschko’s lines and affecting mainly the trunk and limbs, but not the face, palm, planta, and mucous membranes (figures 1 and 2). According to the mother, the patient had presented these lesions from birth. In addition, it was also observed that patient presented delayed development of teeth. Patient has 4 siblings and there are no references of similar lesions in other members of the family.

We carried out incision for biopsy of the lesions on the abdomen. The histologic findings, following Fontana-Masson staining, and the immunohistochemical assay, by means of avidin-biotin method, indicated, respectively, absence of melanin and of melanocyte in focal areas of the epidermis (figures 3 and 4).

Neurological evaluation indicated a delay in neuropsychomotor development for age according to the Denver Developmental Screening Test. Electroencephalogram (EEG) examination indicated diffuse cortex and subcortex dysfunction. Brain magnetic resonance imaging (MRI) was compatible with arachnoidal cyst in left anterior temporal region (Figure 5).

Patient presented with chromosome mosaicism and normal karyotype (46, XY) and interstitial deletion of bands 22.2 to 24.4 of the long arm of chromosome 10 (karyotype 46,XY/46XY, del(10)(q.22.2 - 24.2), as shown in Figure 6.

Discussion

The hypomelanosis of Ito is a leukoderma whose pathogenesis is unknown\(^2\) and that is characterized by hypopigmented cutaneous lesions with linear or irregular,\(^3\) and unilateral or bilateral form. HI lesions can present progression or regression with time. They can also be associated with other complications, that consist of ocular, musculoskeletal and oral alterations, hypotonia, macrocephalia, microcephalia, congenital cardiac malformations, urological and genital malformations.\(^7\) According to Hermida and colleagues, non-cutaneous abnormalities, particularly of the central nervous system, eye, teeth and skeleton, have been reported in 76-94% of patients.\(^8\)
The pigmentation of the skin depends on a series of factors, among which the content of melanin is the most important. Fontana-Mason staining is used to make the pigmentation more evident for microscopy. Moreover, the number of melanocytes on the skin can be either normal or reduced. The anti-S\textsubscript{100} autoantibodies are markers for the S\textsubscript{100} protein in melanocytes. In the case presented, we observed absence of melanocytes in focal areas of the skin with no immunomarkers for anti-S\textsubscript{100}. Also, other histologic studies have shown that hypopigmented areas have normal melanocytes with reduction of intracellular content of melanin. Conversely to incontinentia pigmenti, in HI there are no melanophage found on the skin, and that is why the nomenclature hypomelanosis of Ito is preferred over incontinentia pigmenti achromiens.

Neurologic complications are more frequent and, also, more severe. Ross postulated that brain anomalies with a migration disorder and a disorder in cells of the neural crest, during embryo life, would be the reason for cutaneous hypopigmentation and, also, the gray matter heterotopias found in the autopsy of these patients. Neither a specific type of brain abnormality nor an associated involvement of the central nervous system have been described for HI patients. Neurologic alterations include seizures, delayed psychomotor development, alterations of tonus, gait disorders, and so on. Out of these alterations, mental retardation and seizures are more common and have been described in over 50% of cases. Approximately 10% of HI patients have presented seizures during the first year of life, and another 10% have presented autistic behavior. The only evident neurologic alteration observed in our patient, until the present moment, was the delay in neuropsychomotor development.

As described by Glover and colleagues, there are no definitive alterations at EEG for hypomelanosis of Ito. Findings of abnormal rhythmic EEG can be an indication of neuronal migration defects. In this sense, it is possible that there may be a distinctive sub-group of patients with Ito’s syndrome who present with an early onset of intractable seizures and have poorer prognosis.

Cranial MRI findings in patients with HI include hemimegalencephaly, medulloblastoma, cortical malformations, dilated Virchow-Robin spaces, brain atrophy,
small discrete bilateral periventricular cysts, abnormal white matter signal, and gray matter heterotopias and other neuronal migration defects.\textsuperscript{6,11} Our patient presented with arachnoidal cyst at MRI, which is a relatively common abnormality. Some cysts present asymptomatic, such as in the case of our patient. In case symptoms are present, they are usually secondary to the compression of adjacent structures following hydrocephalus, and to visual symptoms.\textsuperscript{12} We did not find a direct association between arachnoidal cysts and HI in the literature; thus, the cyst may be a casual finding and not related to HI.

HI is a clinically well-characterized syndrome in which chromosomal instability may be a component.\textsuperscript{13,14} Chromosome abnormalities, particularly those of translocation and mosaicism, have been reported in approximately 50\% of cases;\textsuperscript{7} which supports the hypothesis that HI is the result of migration of two primary melanocyte clones, each with a different pigmentation potential. According to Lenzini and colleagues, the X-chromosome was involved in 53\% of cases with chromosomal abnormalities.\textsuperscript{15} Our patient presented alteration in the chromosome 10, which, until this moment, had not been described in the literature.

It is important to include the hypomelanosis of Ito in differential diagnosis of incontinentia pigmenti, depigmented nevi, focal dermal hypoplasia, segmental vitiligo, and linear and whorled nevoid hypermelanosis.\textsuperscript{3}

Finally, it was our intention to underscore the importance of skin lesions for the etiologic definition of neuropediatric disorders.

\textbf{References}


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