

Dyschromatosis symmetrica hereditaria with neurological abnormalities

Sir,

Dyschromatosis symmetrica hereditaria (DSH) is a pigmentary genodermatosis of autosomal dominant inheritance which is characterized by a combination of hyperpigmented and hypopigmented macules on the face, back of the hands, and feet.^[1] The condition primarily affects the skin and has rarely been associated with neurologic manifestations.

A 2-year old boy, born to non-consanguineous parents presented with hyperpigmented and hypopigmented spots on his hands and feet that began at 3 months of age. Till 18 months of age, he achieved normal developmental milestones but 6 months prior to presenting to us, the parents noted regression in language development and

behavioral problems like unaccustomed laughing and crying. There was no history of associated seizures or jaundice and his perinatal history was uneventful. No one else in the family had similar skin lesions or any neurological abnormality. Examination revealed freckle-like pigmented macules on his face. In addition, hyperpigmented and hypopigmented macules arranged in a reticulate pattern were present over the dorsa of hands and feet [Figure 1]. The surface of skin lesions did not show telangiectasia, atrophy, or scaling. Palms, soles, and mucosa were spared. There were no similar lesions elsewhere on his body. He was able to stand without support and walked with an abnormal gait with inverted feet. A dystonic (hypertonic) posture was observed in both upper and lower limbs (right more than left) along with brisk deep tendon reflexes. Rest of the systemic examination including ophthalmological examination was normal. Laboratory investigations, including routine blood and metabolic screening, calcium, phosphorus, magnesium, serum lactate, thyroid and parathyroid function, hepatic function, and serum ceruloplasmin level, TORCH screening [Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), and Herpes infections], and urine examination was normal. Histopathological examination of a 4 mm punch biopsy specimen of a hyperpigmented area showed increased pigmentation of the basal layer. Based on the clinical features and the histopathological findings, a diagnosis of dyschromatosis symmetrica hereditaria was made. Computed tomographic (CT) scan of the brain showed bilaterally symmetrical calcifications in the region of basal ganglia [Figure 2]. No other structural change of brain was identified. Electroencephalography (EEG) was normal. Clinical and radiological (CT scan of brain) evaluation of his parents showed no abnormality. We

could not perform any genetic analysis to confirm the mutation in the involved gene in the present case due to non-availability of required facilities and financial constraints.

Dyschromatosis symmetrica hereditaria, synonymously known as reticulate acropigmentation of Dohi, has been reported mainly in the Japanese and Chinese population. It occurs due to a mutation in the adenosine deaminase, RNA specific gene *ADAR1* which catalyzes the hydrolytic deamination of adenosine to inosine in double-stranded RNA.^[2] To date, more than 100 mutations of *ADAR1* have been reported in patients with this condition, and the catalytic domain deaminase is believed to be crucial to the activities of this gene.^[3-5] The disease is usually restricted to the skin and only a limited number of cases have been reported in association with extra-cutaneous abnormality.^[3,6] An extensive search of the English language literature in PubMed, Medline, and Google Scholar database revealed only a few cases showing an association with neurological abnormalities. Pigmentation begins in infancy or childhood and gradually increases in depth and extent. Once these hypopigmented and hyperpigmented lesions are fully established, they persist life long without any change in color or distribution. Biopsy of hyperpigmented and hypopigmented macules shows basal layer melanosis and hypomelanosis, respectively.^[11] Family history is present in 56-77.6% of patients with DSH.^[3,7] There is no definitive treatment for this condition. The disease needs to be differentiated from dyschromatosis universalis hereditaria (DUH), which is characterized by more extensive lesions including the non-acral and covered areas of the skin. Some other differential diagnoses include



Figure 1: Pigmentary changes on dorsum of feet

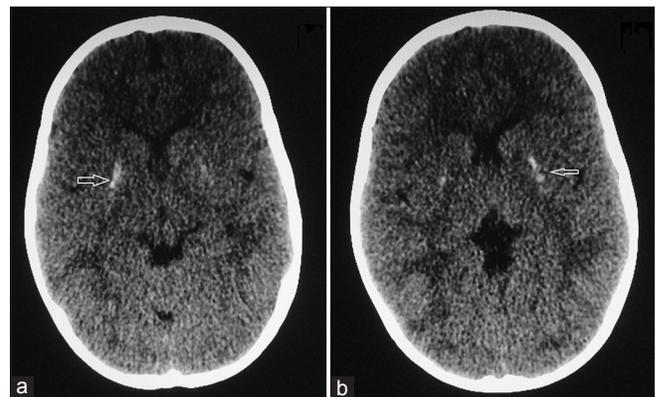


Figure 2: (a and b) Computed tomographic scan of brain showing bilateral basal ganglia calcification (marked by arrows)

reticulate acropigmentation of Kitamura, mild variants of xeroderma pigmentosum, dyschromic amyloidosis, dyskeratosis congenita, and disorders due to exposure to chemicals or radiation, amongst others.^[11] Neurological abnormalities in the form of seizure, dystonia and developmental regression, autistic disorder, and depression have been reported to be associated with dyschromatosis symmetrica hereditaria.^[3,4] In 1994, Patrizi *et al.*, reported a 9-year-old Caucasian girl who developed cutaneous changes at the age of 2 years and torsion dystonia at the age of 7 years.^[12] Kondo *et al.*, reported a case which had similar neurologic and imaging findings as in our patient.^[2] Tojo *et al.*, described a familial case of this disease with dystonia, mental deterioration, brain calcification along with aortic root sclerosis.^[13] Kaliyadan *et al.*, described a case of dyschromatosis symmetrica hereditaria in a 9-year-old Indian girl who had progressive regression of developmental milestones, feeble vocalization, difficulty in walking, and dystonic posturing.^[10] In 2013, Peng *et al.* reported a retrospective series of dyschromatosis symmetrica hereditaria, three of whom had neuro-psychiatric manifestations.^[3]

Although a few cases of this condition have been reported from India,^[7-9] we found only one previous report with associated neurological anomalies.^[10] The exact etiology of the association with neurological manifestations in general and bilateral basal ganglia calcification and dystonia in particular is not known.

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