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Case Report

Elejalde syndrome: Case presentation

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Abstract Silvery hair and severe dysfunction of the central nervous system (Neuroectodermal melanolysosomal disease or Elejalde Syndrome) characterize this rare autosomal recessive syndrome. Main clinical features include silver-leaden hair, bronze skin after sun exposure, and neurologic involvement. Large granules of melanin unevenly distributed in the hair shaft are observed. Abnormal melanocytes and melanosomes and abnormal inclusion bodies in fibroblasts may be present. We report a 10-year-old girl with a silver-leaden (silvery) hair, bronze skin color on sun-exposed areas, generalized hypopigmentation of covered body parts and congenital seizures. The child was the elder of two children born of a consanguineous marriage. The younger sibling, a female neonate, had same clinical presentation.

Key words
Elejalde syndrome, silvery hair, bronze skin color.

Introduction

Silvery hair and central nervous system dysfunction characterize Elejalde Syndrome (ES), a rare autosomal recessive syndrome. Elejalde syndrome's main features include silver-leaden (silvery) hair, intense tanning after sun exposure (bronze skin color on sun-exposed areas), severe neurological impairment either congenital or developing during childhood (seizures, severe hypotonia, mental retardation) and a wide spectrum of ophthalmologic abnormalities. ES does not involve impairment of the immune system. It appears related to or allelic to GS1, and thus associated with mutations in MYOVA, however, its gene mutation has yet to be defined.[1] Neurological manifestations are the predominant clinical features in these patients, which usually appear early, at birth or during childhood. Seizures, severe hypotonia and mental retardation are the usual clinical findings.[2] In advanced disease, flaccid or spastic hemiplegia, quadriplegia and ataxia have been reported. Differential diagnosis with Chédiak-Higashi syndrome and Griscelli syndrome GS) must be done. We report this case because of it's one of the known rare autosomal recessive syndrome.

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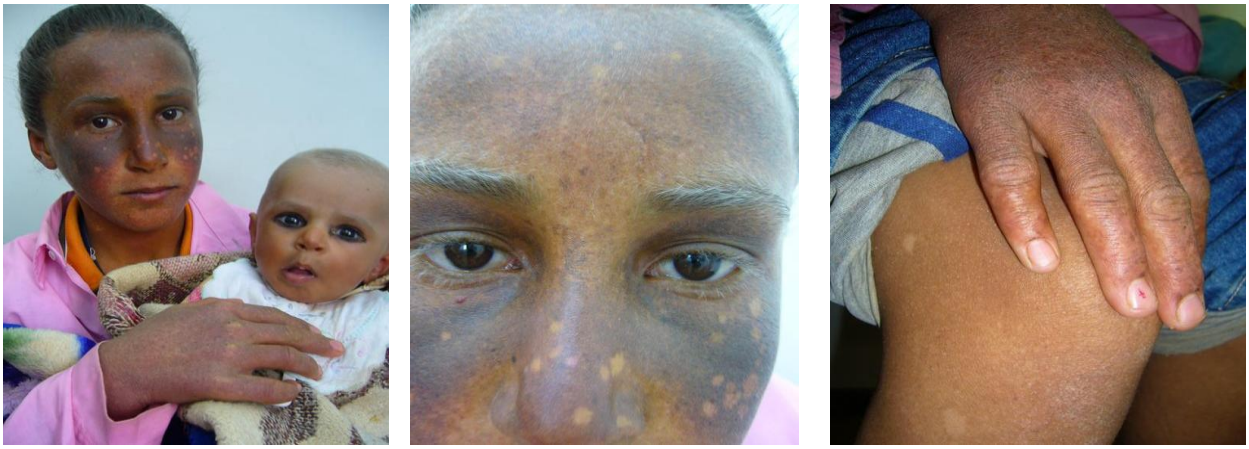
Case Report

A 10-year-old girl presented with a silver-leaden (silvery) hair, bronze skin color on sun-exposed areas, generalized hypopigmentation of covered body parts and congenital seizures. This complaint had started with a silvery gray to golden hair and congenital seizures at birth and developed the hyperpigmentation gradually over the years. The child was the elder of two children born of a consanguineous marriage. The younger sibling, a female neonate, had same



Figures 1-3. Silvery gray to golden hue of hair over the scalp, eyebrows, and eyelashes. Silvery sheen over most of the body hair. Brownish-black pigmentation of the skin over the sun-exposed sites, especially on the face, neck and extensor aspects of the upper and lower limbs. Generalized hypopigmentation of covered body parts. The younger sibling had same clinical presentation.

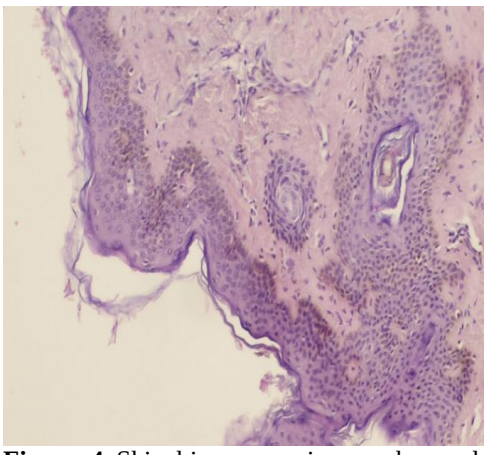


Figure 4 Skin biopsy specimens observed by light microscopical examination showed irregular distribution and irregular size of melanin granules in the basal layer.

clinical presentation. Physical examination revealed silvery gray to golden hue of hair over the scalp, eyebrows, and eyelashes (**Figures 1, 2, 3**). A silvery sheen was also present over most of the body hair. There was brownish-black pigmentation of the skin over the sun-exposed sites, especially on the face, neck and extensor aspects of the upper and lower limbs. The skin in the covered areas of the body was comparatively light colored. Ophthalmological examination revealed a visual acuity of 7/10 (both eyes). Examination of the fundus revealed mild vascular sheathing with features of papilledema. EEG was done and its result was abnormal. The magnetic resonance imaging of the brain revealed abnormalities in different areas. Immunologic studies including serum IgG, IgA, and IgM, and phagocytic function tested with nitroblue tetrazolium were within normal limits. Routine laboratory tests were within normal limits. Serological screening for connective tissue disease was negative. HIV and HBsAg serology were negative. Skin biopsy specimens observed by light microscopical examination showed irregular distribution and irregular size of melanin granules in the basal layer (**Figure 4**). Microscopic analysis of her hair showed melanin clumps irregularly distributed along the hair shafts. Chédiak-Higashi syndrome and GS were excluded in the analysis of our patient for the following reasons: there was no clinical or laboratory evidence of immunologic impairment and abnormal giant intracytoplasmic granules in neutrophils could not be found in peripheral blood smear.

Discussion

Silvery hair and severe dysfunction of the central nervous system (Neuroectodermal melanolysosomal disease or Elejalde syndrome) characterize this rare autosomal recessive syndrome. Main clinical features include silver-leaden hair, bronze skin after sun exposure, severe neurological impairment and a wide spectrum of ophthalmologic abnormalities.[3] Elejalde syndrome does not involve impairment of the immune system. It appears related to or allelic to GS1, and thus associated with mutations in MYOVA, however its gene mutation has yet to be defined.[1] Neurological manifestations are the predominant clinical features in these patients, which usually appear early, at birth or during childhood. Seizures, severe hypotonia and mental retardation are the usual clinical findings. In advanced disease, flaccid or spastic hemiplegia, quadriplegia and ataxia have been reported. Ophthalmologic abnormalities include nystagmus, diplopia, amaurosis and absence of pupillary reflex.[2] Pigmentary abnormalities are the second common clinical feature which include silvery hair, a gradual bronze-colored tan of the sun-exposed areas and generalized hypopigmentation of covered body parts. Early death due to neurological involvement is a rule and the oldest patient reported with ES was 12-year-old.[4] However, there is some degree of clinical and genetic overlap between GS, Chédiak-Higashi syndrome and ES. All three disorders manifest during childhood and central nervous system involvement is common. Inheritance pattern is autosomal recessive for these disorders. Genetically, there is a similarity between GS and ES and some authors have considered ES as an allelic variant of GS. Impaired melanosome transport, giving rise to failure of transfer of melanin to keratinocytes, results in the pigmentary abnormalities in patients with silvery hair syndrome, and the affected genes are believed to be involved in lysosomal transport of melanosomes.[5] The two closely related genes for GS are located on chromosome 15q21. These genes, RAB27A and MYO5A, function in vesicle trafficking at the cellular level. Mutations in RAB27A result in hemophagocytic abnormalities and thereby result in GS type 2, manifested as silvery hair with immunological defects.[6] Mutations in MYO5A (an actin-based motor molecule, required for pigmentation and synaptic activity in the central nervous system) result in pigmentary dilution along with neurological abnormalities, designated as GS type 1.[7,8,9] Prognosis for long-term survival of patients with GS is relatively poor, and GS2 is usually rapidly fatal within 1-4 years without treatment.[10,11] Therapeutic measures for ES patients have included the use of steroids, anticonvulsants, and antipyretics, and they have been unsuccessful in all patients. Thus, whether any medical therapy can be recommended for ES patients is unclear. To conclude, immunodeficiencies are serious problems in children, but analysis of the conglomeration of dermatological, immuno-hematological, and neurological findings can facilitate proper diagnosis in order to improve quality of life and start early therapy for these patients.

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