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Case Report

Naegli-Francesschetti-Jadassohn Syndrome: An extremely rare form of ectodermal dysplasia presenting after teenage

Huma Kamran, Najia Ahmed, Arfan ul Bari

PNS Shifa Hospital, Karachi.

Abstract Naegli-Franceschetti-Jadassohn syndrome (NFJs) is an extremely rare autosomal dominant form of ectodermal dysplasia that effects the skin, sweat glands, nails, and teeth. On exhaustive literature search, we could find less than 50 cases of this disorder reported worldwide and only one from Pakistan. To the best of our knowledge, we are reporting second case from our country with all typical clinical features but quite late onset of presentation as against all other reported cases. Majority of cases reported previously presented in childhood and subsequently improved on puberty but in our case clinical features (reticulate skin hyperpigmentation, Keratoderma, hypohydrosis, anodontia, multiple hair and nail disorders) appeared quite late, at the age of 20 years and gradually progressed during last one and half year.

Key words
Naegli-Franceschetti-Jadassohn Syndrome, Dermatopathia Pigmentosa Reticularis, Dyskeratosis Congenita, Dowling-Degos disease, autosomal dominant, ectodermal dysplasia, KRTI4 gene, dermatoglyphics, hypohydrosis, reticulate pigmentation.

Introduction

Basically Ectodermal dysplasia is an extensively varied group of inherited disorders in which primarily there is defect in development embryonic ectodermally-derived organs like hair, teeth, nails or sweat gland function. It can also involve other tissue of ectodermal origin (ears, eyes, lips, mucous membranes, and the central nervous system). More than 150 different syndromes with ectodermal abnormalities have been ascertained.[1]

Naegli-Franceschetti-Jadassohn Syndrome (NFJS) is one of the rare ectodermal dysplasia with numerous specific abnormalities.[2] It was first described by Oskar Naegeli in 1927 in a Swiss family. In 1954, Francesschetti and Jadassohn further analyzed the syndrome as did Itin and colleague in 1993.[2,3] NFJS is inherited as an autosomal dominant trait by frameshift or missense mutation of keratin 14 gene (KRT 14) located on 17q11.2-q2.[3] Keratinocytes have the gene KRT14 that helps in manufacturing the protein named as keratin 14, insufficient amount of this protein leads these cells to go through apoptosis. Lack of this protein makes these cells to go through apoptosis. If keratinocytes are lost due to any reason this will change the development of ectodermally derived tissues, including skin, nails, hair, teeth and sweat glands.[3] The clinical findings of this syndrome includes hypohidrosis with diminished sweat gland function, loss of dermatoglyphics and reticulate (lattice-like) hyperpigmentation of the neck, chest, abdomen and genitalia$_3$. Hypohidrosis is the most debilitating as it may cause collapse after exertion. Reticulate (lattice-like) hyperpigmentation (brown to gray-brown) starts in early years of life without a preceding

Address for correspondence
Dr. Huma Kamran
PNS Shifa Hospital, Karachi.
Email: kamrankidwai@hotmail.com

inflammatory stage and is localized on the trunk, axilla, proximal extremities, groins, flexures, perioral, and periocular regions.[4,9] Among dermatoglyphic abnormalities, ridge hypoplasia (growth of hypoplastic dermal ridges) and ridge dissociation (discontinuous pattern in which dermal ridges are fragmented into short segments) are routinely seen. Dermatoglyphic abnormalities may be explained as during embryologic development, dermal ridges and eccrine glands occurs in conjunction.[3] Nail findings usually seen are onycholysis, onychodystrophy, subungual hyperkeratosis, and great toe nails misaligned congenitally.[3] Other cutaneous manifestations are palmoplantar keratoderma (diffuse or punctate) that may be accentuated in palmar creases or exhibit a linear pattern. Dental anomalies include yellow discoloration of teeth ename ,defect in shape of teeth, supernumerary teeth, and early loss of teeth.[2,10] There is no specific treatment of NFJS and management is largely symptomatic and educating the patient to avoid strenuous exercises, taking good care of his teeth and nails, using emollients and keratolytics. In some cases oral retinoid may help. Reticulate pigmentation may cause significant cosmetic concern that shows a rapid increase during the first 10 years of life followed by gradual decrease and patients only have slight or no pigmentation left in later years of life.[1,2]

The aim of presenting this case is to highlight the features of this rare syndrome so that dermatologists are able to diagnose and manage this variant of ectodermal dysplasia appropriately.

Case report

A 24-year-old male, driver by occupation, presented with the complaints of hyperpigmentation over his face, trunk, groins, thighs, palms and dorsum of foot along with discoloration and thickening of nails. He also complained of loss of hairs, whitening of scalp hair, lack of sweating and loss of fingerprints for 2 years. Family history was insignificant and his parents were non-consanguineous**.** On dermatological examination the patient had reticulate (lattice-like) hyperpigmentation involving most of the body parts and getting diffused at some places **(Figure 1)**.

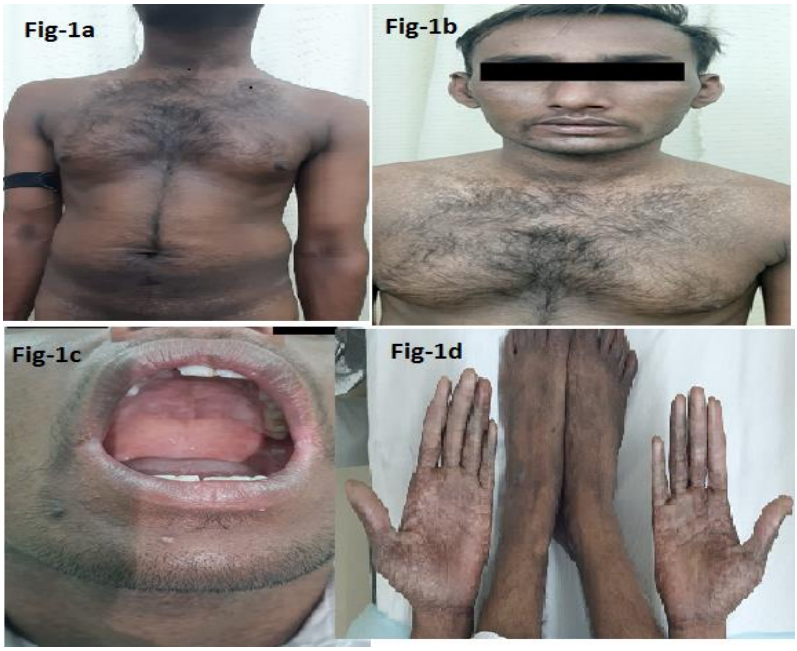

Figure 1

Figure 2

There was premature greying of hair and teeth showed yellowish discoloration along with loss of tooth and abnormal dentition (Figure 2a)**.** Hands and feet showed palmoplantar keratoderma **(Figure 2b, 2c)** with dystrophy of nails along with onycogryphosis **(Figure 2e)** and dermatoglyphics were also lost **(Figure 2d)**. Skin was dry all over his body. Systemic examination was normal. Baseline investigations were in normal range. Histopathology of skin lesion showed epidermal thinning with normal melanocytes, pigmentary incontinence along with mild lymphoplasmacytic infiltrate and fibrosis in dermis. Considering involvement of skin, hair nails, he was suspected to be a case of ectodermal dysplasia and subsequently**,** based on characteristic clinical features he was diagnosed as NFJS. Molecular level diagnosis could not be confirmed due to non-availability of laboratory support. Patient was explained about nature of his disease and possible outcome. He was advised to keep very good oral hygiene along with teeth care to prevent early carries, to avoid any kind of strenuous activity and maintain adequate hydration. He was prescribed oral antifungals for secondary onychomycosis, oral anti-oxidants, topical emollients and keratolytics for xerosis and palmoplantar keratoderma. For nail deformity, mechanical debridement was done and he was advised special footwear to limit pressure on the nail bed and definitive treatment of nail avulsion followed by matricectomy was also explained as future option.

Discussion

NFJS is one of the rare variant of ectodermal dysplasia that appears in early years of life. Main clinical presenting feature of NFJS is generalized reticulate pigmentation. Other genodermatoses associated with this kind of pigmentation include; dermatopathia pigmentosa reticularis (DPR), X-linked reticulate

pigmentary disorder, dyskeratosis congenital (DC), reticulate acropigmentation of Kitamura, dowling degos disease (pigmented reticulate anomaly of flexures) and Haber's syndrome.[3] It is difficult to differentiate NFJS from DPR as both have similar gene mutation with very few difference in clinical presentation. NFJS is believed an allelic to DPR because of dominant mutations in the non-helical E1/V1 domains of keratin 14. Both were considered as two different conditions but DPR is now often considered as a different form of NFJS and is distinguished by lifelong persistence of reticulated hyperpigmentation with truncal involvement mainly, non-scarring alopecia effects scalp and eyebrows, axillae and onychodystrophy.[6] Dyskeratosis congenita (DC) also shows reticulate hyperpigmentation, but differentiates from NFJS by oral leukoplakia, bone marrow dysfunction, cytogenetic instability and succeptibiliy to change in malignancy. In Dowling-Degos disease (DD) reticulate hyperpigmentation is mostly restricted to flexural areas while in Reticulate Acropigmentation of Kitamura (RAK) there is atrophic reticulated or lentigo-like hyperpigmentation favoring the dorsal aspects of hands and feet during childhood.[7,8]

Our patient had characteristic features of NFJS including reticulated hyperpigmentation, hypohidrosis, palmoplantar keratoderma, premature greying of hair, loss of dermatoglyphics and dental abnormalities. In addition we found onychogryphosis of his big toe nails which has not been reported earlier. Another striking difference in our patient was late onset of features. In earlier reported cases the onset of disease was described in childhood with progression of symptoms in adolescent and adult phase and improvement especially in pigmentation in adult and elderly phase but in our patient, there was no symptom at all in his childhood or adolescence and all the features started appearing at the end of his teen age. Possible explanation of this late onset could be a triggering role of environmental factor on expression of defective gene responsible for the syndrome.

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