Naegeli-Franceschetti-Jadassohn Syndrome: A Rare Reticulate Pigmentary Disorder

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Abstract

Naegeli-Franceschetti-Jadassohn syndrome is a rare autosomal dominant form of ectodermal dysplasia affecting sweat glands, nails, teeth, and skin. We report a case of 16-year-old female who had generalized reticulate pigmentation, dental changes, nail changes, and absence of dermatoglyphics and hypohydrosis.

Key Words: Dermatoglyphics, ectodermal dysplasia, KRT 14 gene, Naegeli-Franceschetti-Jadassohn syndrome, reticulate pigmentation

Introduction

Naegeli-Franceschetti-Jadassohn (NFJ) syndrome is a rare form of ectodermal dysplasia affecting skin, sweat glands, nails, and teeth. It was first described by Naegeli in 1927, and in 1954, Franceschetti and Jadassohn re-examined the original family and noted the autosomal dominant pattern of inheritance. The incidence is estimated to be one case in 2-4 million population. It is characterized by reticulate hyperpigmentation, ectodermal dysplasia (primarily dental anomalies and hypohidrosis) and hypoplastic dermatoglyphics.

Case Report

A 16-year-old girl born out of a nonconsanguineous marriage presented with complaints of generalized reticulate pigmentation, hypohidrosis, heat intolerance, and nail dystrophy since birth. There was no significant family history. The patient had normal physical, social, and mental development.

On dermatological examination, the patient had reticulate hyperpigmentation involving the whole body and hair showed mild pigmentary dilution with patchy brown discoloration. Reticulate pigmentation was especially more over the neck (Figure 1), chest, both hands and legs. The generalized xerosis of skin was noted.

Dorsal aspect of tongue exhibited diffuse pigmentation [Figure 2]. Teeth showed yellowish discoloration, abnormal dentition, and enamel defects. There was fusiform swelling at proximal interphalangeal joints and flexion at the distal interphalangeal joints. The absence of dermatoglyphics was noted over all the fingers [Figure 3]. Dystrophy of toenails was observed [Figure 4]. General and systemic examination was normal. Complete hemogram, random blood sugar, liver function test, renal function test, and urine analysis were within normal limits. A biopsy specimen taken from the left side of the neck showed basket wave pattern hyperkeratosis with diffuse pigmentation of basal layer. Upper dermis showed pigment incontinence [Figure 5].

Discussion

NFJ syndrome (MIM 161,000) is a rare autosomal dominant form of ectodermal dysplasia that affects the skin, sweat glands, nails, hair, and teeth. The syndrome is allelic to dermatopathia pigmentosa reticularis (DPR) (MIM 125595) due to dominant mutations in the KRT 14 gene.
nonhelical E1/V1 domains of keratin 14. The main symptoms and signs are hypohidrosis with diminished sweat gland function and discomfort provoked by heat, lack of dermatoglyphics (fingerprint lines); and reticulate pigmentation of the neck, chest, and abdomen. All the above findings were documented in our case with the involvement of proximal and distal interphalangeal joint which is a unique feature.

Several mutations in the KRT14 gene have been found to cause NFJS/DPR. The KRT14 gene provides instructions for making a protein called keratin 14 which is specifically produced in cells called keratinocytes. The KRT14 gene mutations that cause NFJS/DPR reduce the amount of functional keratin 14 in keratinocytes. A shortage of this protein makes these cells more likely to undergo apoptosis. Due to loss of keratinocytes, there is an alteration in normal development of ectodermal tissues including skin, hair, nails, teeth, and sweat glands.

Hypohidrosis is the most debilitating aspect of the NFJ syndrome as it can lead to collapse after exercise.

Reticulate hyperpigmentation starts around the age of 2 years without a preceding inflammatory stage. The pigmentation is brown to gray-brown and is localized on the trunk, proximal extremities, axillae, groins, flexures, periorcular, and perioral regions. The pigmentation shows a gradual increase during the first 10 years of life, and fading starts around the age of 15 years. Patients with NFJS who are older than 70 years only have minimal or no pigmentation left. Some patients develop bullae on the feet during the newborn period.

Abnormalities of dermatoglyphics are divided into four main categories: ridge aplasia, ridge hypoplasia, ridge dissociation, and ridge off the end. Embryologic development of dermal ridges occurs in conjunction with the eccrine glands, and sweat pores are found on the ridges. Ridge hypoplasia refers to poorly formed dermal ridges while ridge dissociation is characterized by a discontinuous pattern in which dermal ridges are broken into short segments. Ridge hypoplasia and dissociation
are the abnormalities that can be seen in NFJS as well as in DPR.[9]

Other cutaneous manifestations are palmoplantar keratoderma (diffuse or punctate) and onychodystrophy (onycholysis, brittle nails, subungual hyperkeratosis, and congenital malalignment of the great toenails. Dental anomalies are common and include abnormally shaped teeth, supernumerary teeth, yellow spotted tooth enamel and early loss of teeth occurs.[10] In our case, it shows all the above features except the presence of palmoplantar keratoderma.

Other genodermatoses associated with generalized reticulate pigmentation is DPR, dyskeratosis congenita (DKC), X-linked reticulate pigmentary disorder, Dowling-Degos disease, and reticulate acropigmentation of Kitamura and Haber’s syndrome[11] [Table 1].

NFJS and DPR syndrome do have overlapping phenotypic features, as both are autosomal dominant ectodermal dysplasia. Both manifest with poorly developed dermatoglyphics, reticulate hyperpigmentation of the skin, hypohidrosis, and heat intolerance. Palmoplantar keratoderma, nail dystrophy, and enamel defects are common in NFJS, whereas diffuse alopecia is only seen in DPR.[12]

Reticulate hyperpigmentation, mucosal leukoplakia, bone marrow dysfunction, cytogenetic instability, and a predisposition to malignancy are characteristic of DKC.[10]

The distribution of the reticulate pigmentation in Dowling-Degos disease, dyschromatosis symmetrica hereditaria, and reticulate acropigmentation of Kitamura makes these disorders easy to distinguish.[13]

The X-linked reticulate pigmentary disorder often presents with hypohidrosis and dental anomalies as well as reticulate hyperpigmentation, but additional systemic manifestations as well as the inheritance pattern distinguish it from NFJS.

Histologically, the hyperpigmented skin demonstrates pigment incontinence and melanophages. No specific treatment exists for NFJS, except for symptomatic management of some of the associated conditions. Genetic counseling should be offered to affected individuals planning future children.

Our case contributes to the further understanding of this rare condition. In addition, we were unable to find any previous reports of NFJ syndrome involving the proximal and distal interphalangeal joint.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not

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**Table 1: Differential diagnosis of reticulate hyperpigmentation**

| Genodermatoses                        | Features                                                                                           |
|---------------------------------------|---------------------------------------------------------------------------------------------------|
| Naegeli-Franceschetti-Jadassohn syndrome | Reticulated hyperpigmentation beginning by 2 years of age and often fading during adolescence, hypohidrosis and heat intolerance, dental anomalies, palmoplantar keratoderma, with absent or hypoplastic dermatoglyphics |
| Dermatopathia pigmentosa reticularis  | Persistent reticulated hyperpigmentation with truncal predominance, nonscarring alopecia of the scalp, eyebrows, and axillae, onychodystrophy |
| DKC                                   | Shows reticulate hyperpigmentation, mucosal leukoplakia, bone marrow dysfunction, cytogenetic instability, and a predisposition to malignancy |
| X-linked reticulate pigmentary disorder | Reticulate hyperpigmentation along the lines of Blaschko, recurrent infections and multiple systemic manifestations |
| Dowling-Degos disease                 | Reticulate hyperpigmentation in flexural sites                                                     |
| Reticulate acropigmentation of Kitamura | Atrophic reticulated or lentigo-like hyperpigmentation that favors the dorsal aspects of the hands and feet and appears during childhood |
| Haber’s syndrome                      | Photosensitive rosacea-like facial eruption followed by keratotic papules, comedone-like lesions, pitted scars, and reticulate hyperpigmentation on the trunk, proximal extremities and axillae |

DKC: Dyskeratosis congenita
be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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