**Title**
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**Journal**
Dermatology Online Journal, 22(10)

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**Publication Date**
2016

**DOI**
10.5070/D32210032896

**Volume 22 Number 10**
**October 2016**

**Case Report**

# A case and review of congenital leukonychia

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**Dermatology Online Journal 22 (10): 6**

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## Abstract

Leukonychia refers to a white discoloration of the nails. Although several conditions may cause white nails, a rare, isolated, congenital form of the disease is hypothesized to stem from disordered keratinization of the nail plate. Herein, we report a case of a 41-year-old woman with congenital leukonychia and review prior cases.

**Keywords: Leukonychia, Nail disorders, Congenital nail disease**

## Introduction

Leukonychia is defined as a white or milky discoloration of the nail plate and has traditionally been subclassified into true and apparent variants. Apparent leukonychia derives from pathological changes in the nail bed (most commonly edema) resulting in tissue pallor visible through the nail plate, whereas true leukonychia stems from structural abnormalities of the nail plate itself owing to disordered keratinization occurring in the nail matrix [1]. In the latter, the white opacity of the nail plate derives from two separate histopathologic features: retained parakeratotic cells containing enlarged keratohyaline granules and disorganized keratin fibrils [2,3]. Both of these abnormalities affect and impede light diffraction through the nail plate, ultimately contributing to the characteristic white discoloration [1]. Notably, a complete differential diagnosis for white discoloration of the nail plate should also include pseudoleukonychia, in which an external process alters the nail plate growth, most commonly onychomycosis.

True leukonychia can also be further subclassified into acquired and congenital presentations. Acquired leukonychia is more common and can be associated with a wide variety of comorbid conditions, including infections, medications, and trauma [4–6]. Conversely, congenital leukonychia is significantly rarer. Although cases are often isolated and occur in the absence of other dermatologic or systemic findings, several autosomal genodermatoses do feature leukonychia as a key clinical finding. Table 1 summarizes all reported hereditary syndromes that include leukonychia as a clinical finding.

**Table 1.** Syndromes that feature congenital leukonychia

| Syndrome | Clinical Presentation in Addition to Leukonychia |
|---|---|
| Bart Pumphrey Syndrome [7] | Knuckle pads, and sensorineural deafness |
| Bushkell Gorlin Syndrome [8] | Kidney stones, and sebaceous cysts |
| Bauer Syndrome [9] | Sebaceous cysts |
| Heimler Syndrome [10] | Sensorineural deafness, enamel hypoplasia |
| Vohwinkel Syndrome [11] | Constricting rings of fingers and toes, hyperkeratosis, congenital deafness |
| Hooft Syndrome [12] | Mental retardation, hypolipidemia, erythematosquamatous eruption |
| Basaran Yilmaz Syndrome [13] | Keratoderma, hypotrichosis |
| Lowry-Wood Syndrome [14] | Microcephaly, nystagmus, epiphyseal dysplasia, and hypoplasia of the corpus callosum |
| LEOPARD Syndrome [15] | Many defects, including lentigines, conduction abnormalities, ocular hypertelorism, pulmonary stenosis, genital abnormalities, short stature, and sensorineural deafness |
| Leukonychia with hypoparathyroidism [16] | Hypoparathyroidism, Celiac Disease, muscle cramps, acral tetany |
| Leukonychia with pili torti [17] | Pili torti |
| Leukonychia with duodenal ulcers and gallstones [18] | Duodenal ulcers and gallstones |
| Other reported syndromal presentations of leukonychia [3,15] | Leukonychia with onychorrhexis, hypoparathyroidism, cataracts<br>Leukonychia with koilonychias<br>Leukonychia with keratoderma and atrophic fibrosis<br>Leukonychia with axonal neuropathy, dilated cardiomyopathy, and conduction abnormalities |

Clinically, leukonychia has historically been classified by the extent of nail plate involvement: total, subtotal, striate, longitudinal, and punctuate presentations have all been described. However, total and subtotal leukonychia may represent variations in penetrance of disease [19]. In cases of total leukonychia, the white discoloration involves the entire nail plate, whereas the distal nail is spared in the subtotal variant. A more comprehensive classification rubric for leukonychia was previously proposed by Grossman and Scher, which further details other subvariants [15]. Herein, we report a patient with isolated congenital subtotal leukonychia.

# Case synopsis

A 41-year-old woman presented to the Nail Disorders Clinic at Stanford Univeristy Department of Dermatology for evaluation of nail discoloration. Specifically, she reported a longstanding history of white nails, likely present since birth. She denied any associated symptoms, including onychodynia, nail plate fragility or scale, onycholysis, or subungual debris. Her family history was notable for multiple relatives with similar nail changes, including her maternal grandmother and a cousin. She denied any known family history of deafness or keratoderma.

Clinical examination revealed leukonychia of all 20 nails, affecting the proximal 90% of nail plates. Thumbs showed bilateral distal erythronychia centrally. No other dermatologic or systemic clinical findings were observed. Figure 1 shows the patient's fingernails.


**Figure 1**. Appearance of fingernails

Fingernail clippings from all ten fingernails were obtained and sent for histopathologic examination. The resulting pathology revealed nail plate hyperkeratosis and parakeratosis (Figure 2), consistent with a diagnosis of true leukonychia. No fungal hyphae were observed on periodic acid–Schiff–diastase staining.

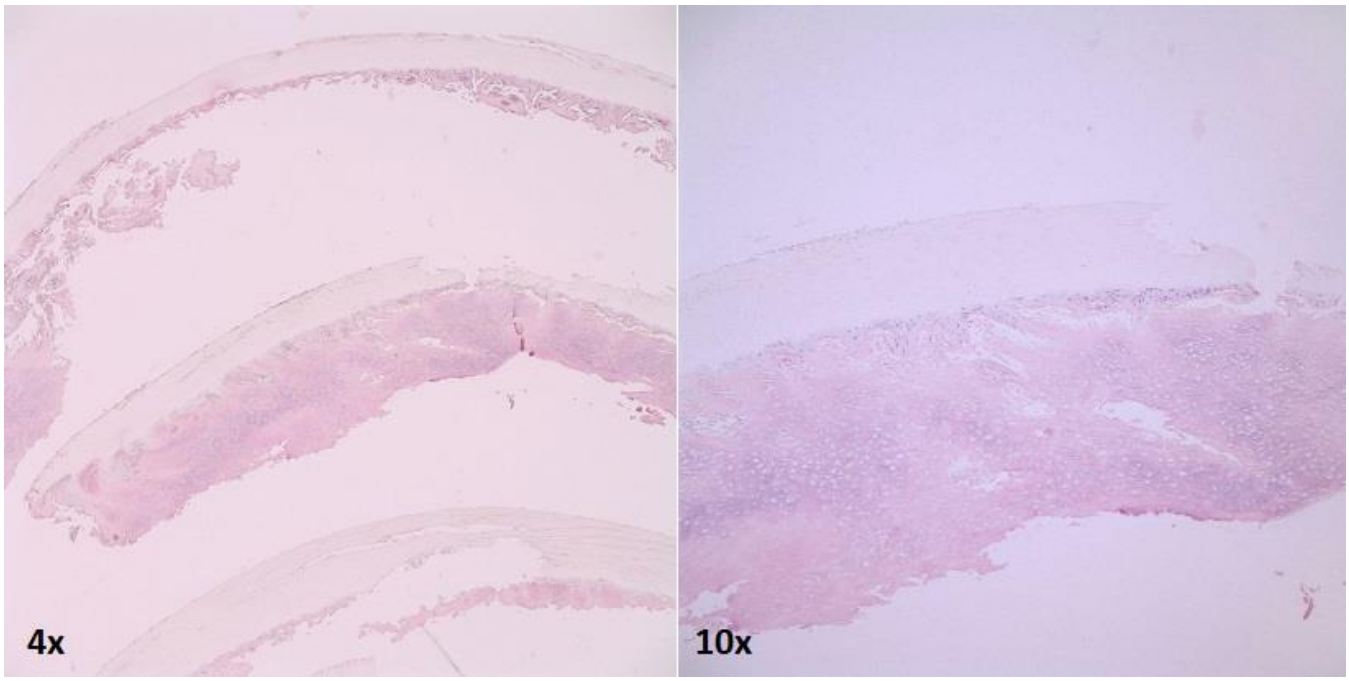


**Figure 2**. Nail histopathology.

# Discussion

Congenital leukonychia is a rare, inherited condition that manifests as white nails. A review of the literature revealed case reports of isolated congenital subtotal and total leukonychia (i.e. leukonychia that was not part of an inherited syndrome) in 23 families. Table 2 summarizes prior cases.

**Table 2.** Prior cases of isolated congenital leukonychia

| Reference | Affected Individuals | Clinical Findings | Histopathologic Findings |
|---|---|---|---|
| Gutman, 1913 [20] | Father and son | Total leukonychia | Not reported |
| Fox and Pisko, 1917 [20] | 4 individuals across 3 generations | Total leukonychia | Not reported |
| Kruse et al, 1950 [20] | 4 individuals across 2 generations | Total leukonychia in 1 individual, 3 not examined | Not reported |
| Medansky and Fox, 1960 [21] | 14 individuals across 5 generations | Total and subtotal leukonychia in 12 individuals, 2 not examined | Not reported |
| Albright and Wheeler, 1964 [22] | Mother and 2 daughters | Mother: total leukonychia of 14/20 nails<br>Daughters: subtotal leukonychia of 20/20 nails | Not reported |
| Harrington, 1964 [23] | 6 individuals across 4 generations | Total leukonychia of 18/20 nails, subtotal of 2/20 in 1 individuals 5 not examined | Not reported |
| Butterworth, 1982 [19] | Father and son | Son had waxing and waning leukonychia (sometimes total, sometimes subtotal) over a period of 5 decades, also had phenylketonuria, father not examined | Not reported |
| Bettoli and Tosti, 1986 [24] | 3 individuals across 3 generations | 2 individuals born with total leukonychia which transitioned to subtotal leukonychia over time, 1 not examined but reportedly had the same findings | Not reported |
| Frydman and Cohen, 1993 [25] | Brother and sister | Total leukonychia of 20/20 nails in both siblings | Not reported |
| Kohler et al, 1998 [26] | 2 brothers | Total leukonychia of 20/20 nails in both siblings | Not reported |
| Stevens et al, 1998 [27] | 5 individuals across 3 generations | Total leukonychia of fingernails but not toenails in 1 individual, 4 not examined but reportedly had the same findings | Not reported |
| Brown et al, 2000 [28] | 12 year old boy | Total leukonychia of 6/10 fingernails, subtotal leukonychia of 4/10 fingernails | Not reported |
| Marcilly et al, 2003 [29] | 13 individuals across 4 generations | Subtotal leukonychia of 20/20 nails in 1 individual, 12 not examined | Parakeratosis and an abnormal granular layer in the proximal and ventral womb, dissociated keratin bundles, intracytoplasmic clear vacuoles |
| Norgett et al, 2004 [2] | 13 individuals across 4 generations | Subtotal leukonychia of 20/20 nails in 1 individual, 12 not examined | Thin, poorly compacted, and scaly upper nail plate, lower part of nail shows marked parakeratosis |
| De and Handa, 2007 [30] | 6 individuals across 4 generations | Total leukonychia of 20/20 nails, diabetes, drug rash in 1 individual, 5 not examined | Not reported |
| Afifi et al, 2011 [31] | 3 brothers | Total leukonychia of 20/20 nails in all 3 cases | No ectodermal dysplasia |
| Kiuru et al, 2011 [32] | 4 families | Total or subtotal leukonychia of 20/20 nails | Abundant intracellular vacuoles and abnormal keratin |
| Lee et al, 2011 [33] | 3 individuals across 3 generations | Total leukonychia of 15/20 nails, subtotal leukonychia of 5/20 nails in 1 individual, 2 not examined | Parakeratosis with keratohyaline granules |
| Clayton et al, 2012 [34] | 2 unrelated patients | Total leukonychia of 20/20 nails in 1 individual, subtotal leukonychia of 20/20 nails in other individual | No significant alteration of nail structure |
| Ganesh and Priyanka, 2014 [35] | 16 year old male | Total leukonychia of 20/20 nails | Not reported |

On a genetic level, a linkage analysis from Norgett et al identified chromosome 12q13 as the most likely site associated with leukonychia. Specific genes were not determined, although the study identified several candidate genes that code for type II cytokeratins and hard keratins. Another linkage study mapped leukonychia in four Pakistani families to the *PLCD1* gene on chromosome 3p21.3-p22 [32]. Several additional conflicting pedigree analyses found that inheritance may be either autosomal recessive [25,25,31] or dominant [2,21,29], or may be a part of the aforementioned genodermatoses [7,8].

Butterworth [19] and Bettoli and Tosti [24] highlighted cases in which a single patient expressed subtotal and total leukonychia at different time points, whereas several other reports detail cases of subtotal and total leukonychia occurring on different nails in the same patient [23,28,33]. Such findings lend further support to the conclusion that total and subtotal leukonychia may represent variants of the same condition.

There is no treatment for any of the true leukonychia variants, though cosmetic lacquer may be recommended for patients unhappy with the appearance.

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