

Single Case

Hereditary Leukonychia Totalis: A Case Report and Review of the Literature

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Keywords

Nails · Leukonychia · Leukonychia totalis · Leukonychia partialis · White nails

Abstract

Leukonychia is defined as white discoloration of the nails caused by an abnormal keratinization of the nail matrix. Congenital leukonychia totalis is a rare nail disorder, which is typically inherited in an autosomal dominant pattern. This condition can be presented as an isolated condition or in association with systemic diseases. We report a case of a 7-year-old Thai boy who developed asymptomatic white discoloration of all the nails since birth, with an absence of any predisposing factors or associated conditions.

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Introduction

Leukonychia is defined as white discoloration of the nails. It was first described by Mees [1] in 1919 as an associated finding of arsenic intoxication. Leukonychia can be classified in several ways. Traditionally, it is classified according to the site of origin of the white discol-

oration, namely: true leukonychia, when the disorder of the nail plate originates from pathological changes in the nail matrix; apparent leukonychia, when the discoloration occurs due to pathological changes under the nail bed; and pseudoleukonychia, when external factors such as trauma lead to the whitening of the nail plates. Furthermore, leukonychia can also be clinically classified based on the extent of involvement of the discoloration such as: leukonychia totalis (complete whitening of the nails), leukonychia partialis (incomplete whitening of the nails), leukonychia punctata (white spots), and leukonychia striata (white bands). True leukonychia can either be acquired or inherited. Acquired true leukonychia is a result of alteration in the nail matrix, primarily due to other medical conditions or external exposure. Inherited true leukonychia may be considered a benign isolated finding or an associated occurrence with a range of systemic diseases [2, 3]. In this case report, we present a 7-year-old Thai boy who developed asymptomatic complete white discoloration of all the nails (congenital leukonychia totalis), with an absence of predisposing factors or associated conditions.

Case Report

A 7-year-old Thai boy presented with asymptomatic white discoloration of the entire nail plates on all fingernails and toenails. The patient's mother reported that the white discoloration on her son's nails has been present since birth. He was otherwise normal, so she did not seek medical advice. The patient was born from nonconsanguineous parents and has 1 younger sister. His family history is significant for similar nail findings in his mother only. The patient is developmentally normal and has no other medical conditions. His mother denied chemical exposure both in the antenatal period and during childhood, prescribed and nonprescribed medication use as well as prior history of serious mechanical trauma to the nails. The growth of his nails was otherwise normal. He denied pain or decreased sensation to pressure on the nails.

Physical examination revealed opaque and porcelain-white discoloration of the entire nail plate, involving all fingernails and toenails (Fig. 1). Pressure over the nail plate caused no fading of the discoloration. The nails were normal with respect to strength, shape, and texture. No other skin abnormalities were detected. Other systems were unremarkable. The patient's mother was also examined and had identical nail abnormalities (Fig. 2). Extensive diagnostic testing including complete blood count, urinalysis, liver function test, serum protein and albumin, renal function test, and thyroid function test were performed and were all found to be within normal limits. Mycological examination was also negative. Nail biopsy was not performed as the patient did not consent to the procedure.

Discussion

Leukonychia is defined as white discoloration of the nails. Its pathophysiology is not well established, although it is hypothesized to be secondary to abnormal keratinization of the nail plate. According to Newton's theory, the nail surface appears white because of the reflection of visible light into the eyes. Another theory postulated that a defect in the nail

matrix keratinization can cause persistent parakeratosis, keratohyalin granules, and the dissociation of keratin bundles, resulting in visible light reflection that is responsible for the clinically white discoloration of the nails [4].

Leukonychia exhibits two major findings histopathologically: the presence of parakeratotic cells containing abnormally large keratohyalin granules and the dissociation of the keratin bundles. Assertion by electron ultrastructural examination shows that the dissociated keratin bundles and the intracytoplasmic lipid vacuoles are the most striking ultramicroscopic features of leukonychia. These two major ultrastructural patterns may play a major role in this condition because they are insurmountable by light, which results in the subsequent loss of nail plate transparency [4, 5].

Leukonychia totalis is a relatively rare condition. It is generally classified into inherited and acquired. Acquired leukonychia is significantly more common and can be associated with several comorbid conditions. An array of previously published articles has reported that systemic diseases, malnutrition, and chemotherapeutic agents are commonly associated with the development of acquired leukonychia (Table 1). The inherited form of leukonychia, namely hereditary leukonychia totalis, however, is extremely rare. In a review article by Kruse et al. [6], the first isolated case of hereditary leukonychia totalis was reported in a 30-year-old man and his father in 1913. After an extensive review of the literature, we found a total of 43 cases of congenital leukonychia. Twenty-eight cases had complete nail involvement, whereas 15 cases had partial nail involvement. These cases were reported as far back as 1913 with the most recent cases being reported in 1998. Family history was elicited in 79% of the cases [3–10].

Although, hereditary leukonychia is predominantly inherited in an autosomal dominant pattern, there were a few case reports of autosomal recessive inheritance. Frydman et al. [7] were the first to report an autosomal recessive transmission of leukonychia totalis. Norgett et al. [4] were the first to analyze the genetic linkage of hereditary leukonychia, which presented with gene defect on chromosome 12q13 underlying the autosomal dominant familial leukonychia. Then, Kiuru et al. [8] and Farooq et al. [9] discovered the mutations in phospholipase C delta 1 (PLCD1) on chromosome 3p22.2 in both autosomal dominant and autosomal recessive hereditary leukonychia. The PLCD1 plentifully manifests in the nail matrix and encodes a phosphoinositide-specific PLCD1 subunit, which acts as a major enzyme in phosphoinositide metabolism. Recently, Nomikos et al. [11] found that PLCD1 mutations significantly alter the enzymatic properties.

In our patient, the white discoloration of the entire nail plates was present since birth. Upon applying pressure over the nail plates, there was no fading of the whiteness. Furthermore, we did not find any evidence of associated conditions. Therefore, we diagnosed the patient as having isolated hereditary true leukonychia totalis. We were able to trace the pedigree over four generations as shown in Figure 3. Using this family history, autosomal dominant inheritance is most likely. An eccentric phenotype had been expressed as a novel incidence in the third generation, with a sporadic germ line mutation of an autosomal dominant inheritance being a possible mode of transmission.

The prognosis of leukonychia remains undetermined. Although there is no specific treatment for true leukonychia, Bettoli and Tosti [10] reported that congenital leukonychia has a possibility of gradual improvement over the lifetime of an individual. Nevertheless, it is

still important to find the cause and to conduct a detailed investigation to determine underlying disorders associated with this condition.

In conclusion, we have herein presented an interesting case of isolated hereditary true leukonychia totalis. The emphasis of this report is not only the fact that leukonychia totalis is an extremely rare condition, but also that it may display itself as an important visible clinical clue to other associated systemic diseases or inherited malformations.

Statement of Ethics

According to the regulations of Mahidol University, this case report was exempted from undergoing review by the Institutional Review Board and the use of informed consent.

Disclosure Statement

No funding was utilized and all authors have no financial relationships to report.

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Fig. 1. Leukonychia totalis of all fingernails and toenails of the patient.



Fig. 2. The patient's mother revealed leukonychia totalis in all fingernails and toenails.

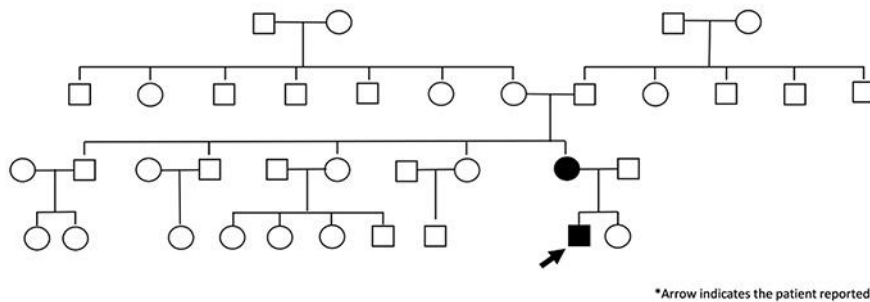


Fig. 3. Pedigree of the patient's family with leukonychia totalis indicated in black.

Table 1. Causes and classifications of leukonychia (modified from Bongiorno and Aricò [12], Yalcin and Ozge [13], Canava et al. [14], and Pathipati et al. [15])

Hereditary

Idiopathic

Associated with

LEOPARD syndrome

Bart-Pumphrey syndrome: kidney stones, sebaceous cyst, sensory-neural deafness and knuckle pads

Bauer syndrome: sebaceous cysts

Heimler syndrome: sensorineural deafness and enamel abnormalities

Vohwinkel's syndrome: palmoplantar keratoderma and marked hyperhidrosis

Lowry-Wood syndrome: microcephaly, nystagmus, epiphyseal dysplasia, and corpus callosum hypoplasia

FLOTCH syndrome: ocular hypertelorism, genital abnormalities, short stature, and sensorineural deafness

Leukonychia with pili torti

Leukonychia with severe keratosis pilaris

Leukonychia with duodenal ulcers and gallstones

Leukonychia with acanthosis nigricans-like lesions and hair dysplasia

Leukonychia with keratoderma-hypotrichosis

Acquired

Idiopathic

Associated with

Trauma

Local infection: fungal infection

Systemic infection: measles, typhoid fever, ulcerative colitis, leprosy

Drugs: chemotherapeutic drugs, cyclosporine, naproxen

Systemic disease: HIV, renal failure, liver failure, heart disease, diabetes mellitus, psoriasis, vitiligo, anemia, systemic lupus erythematosus, graft-versus-host disease

Disturbed nutrition: zinc deficiency, calcium deficiency, vitamin B₃ deficiency

External exposure: heavy metal poisoning, extreme cold exposure, chemical exposure