

# Jadassohn-Lewandowsky syndrome: A rare genodermatosis

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**Abstract** Pachyonychia congenita (PC) is a rare type of genodermatosis characterized by palmoplantar keratoderma, subungual hyperkeratosis, and oral mucosal leukokeratoses along with other features like hyperkeratotic follicular papules, hyperhidrosis of palms and soles, and hair abnormalities. It is caused by mutations in keratin genes KRT6a, KRT6b, KRT6c, KRT16, KRT17. We report a 12-year-old female patient presenting with thickened, discolored nails, palmoplantar keratoderma, and follicular papules all over the body.

**Key words**

Pachyonychia congenita, Jadassohn-Lewandowsky syndrome, palmoplantar keratoderma.

## Introduction

Pachyonychia congenita (PC) is a rare autosomal dominant genodermatosis affecting skin, nails, hair, oral mucosae, and teeth. In 1904, PC was first documented by Muller followed by further reports by Wilson in 1905 and by Jadassohn and Lewandowsky in 1906.<sup>1,2,3</sup> It is associated with mutations in five keratin genes viz. KRT6a, KRT6b, KRT6c, KRT16 and KRT17 expressed in the nail bed, palmoplantar skin, pilosebaceous unit and oral mucosa.<sup>4</sup> Two main subtypes of PC are: 1) Jadassohn-Lewandowsky PC type 1 (PC-1) and, 2) Jackson-Lawler PC type 2 (PC-2). Pachyonychia congenita tarda, another variant, characterized by a later onset ranging from late childhood to middle age has been described.<sup>5</sup>

## Case Report

A 12-year-old female born at term to

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nonconsanguineous parents presented to our outpatient clinic with thickened, brittle nails with yellow-brown discoloration and subungual hyperkeratosis involving finger- and toenails starting at the age of 8 months. Patient also had palmoplantar keratoderma associated with pain with hyperhidrosis of palms and soles. Multiple keratotic, discrete follicular papules were present all over the body noted since birth. The patient's intelligence was normal.

Examination revealed:

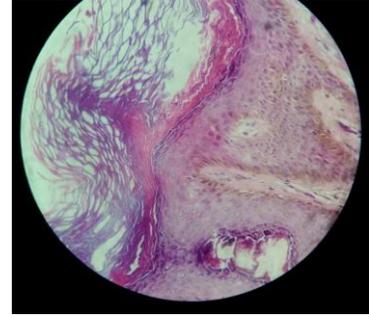
- *Nails* Hypertrophic, hoof-like nails, increased curvature with yellow brown discoloration and subungual hyperkeratosis lifting the nails from nail bed involving all the twenty nails (**Figure 1**).
- Palmoplantar keratoderma with thick, hyperkeratotic plaques with deep fissuring and oozing.
- *Skin* Multiple, discrete keratotic follicular papules present over face, neck, trunk, bilateral upper and lower limbs with flexural predominance (**Figure 2**).



**Figure 1** Hypertrophic, hoof like nails with subungual hyperkeratosis.



**Figure 2** Multiple, discrete keratotic follicular papules over neck.



**Figure 3** Hyperkeratosis and papillomatosis of epidermis with mild chronic inflammatory infiltrate in dermis.

- *Oral mucosal* leukoeratoses.
- *Teeth* within normal limits.

Hematological and biochemical investigations did not reveal any abnormality. Skin biopsy from follicular papules revealed hyperkeratosis and papillomatosis of epidermis with mild chronic inflammatory infiltrate in dermis as shown in **Figure 3**. Based on clinical and histopathological findings, diagnosis of PC type 1 or Jadassohn- Lewandowsky syndrome was confirmed. Patient was managed with topical keratolytic agents and oral acitretin and is on follow-up with mild improvement.

## Discussion

Pachyonychia congenita is a rare type of palmoplantar keratoderma characterized by a triad of subungual hyperkeratosis, keratosis palmaris et plantaris and oral mucosal leukoeratoses.<sup>6</sup> It is associated with other features like hyperkeratotic follicular papules, keratosis pilaris, hyperhidrosis of palms and soles, and hair abnormalities. Characteristic nail changes include subungual hyperkeratosis, marked thickening of distal portion of nails, and variable discoloration.<sup>7</sup> Debilitating and painful plantar keratoderma is the most striking feature of this disorder. PC is caused due to keratin gene mutations involving KRT6a, KRT6b, KRT6c,

KRT16, KRT17.<sup>8</sup> Based on these mutations, two major subtypes have been described:

- PC-1 or Jadassohn-Lewandowsky syndrome is the more common subtype characterized by hypertrophic nail dystrophy (100%), palmoplantar keratoderma (50-90%), keratotic follicular papules (37%), palmoplantar hyperhidrosis (20-75%), and oral or laryngeal leukoeratoses.<sup>9</sup>
- PC-2 or Jackson-Lawler syndrome is characterized by natal or prenatal teeth (15-50%), numerous steatocystomas and various other cystic lesions (25%), hair abnormalities (9-25%), and corneal dystrophy (8%), in addition to clinical features of PC-1 but with less severe keratodermas.<sup>9</sup>

Two other clinical variants of PC have been described:

- PC-3 or Schafer-Brunauer syndrome shows features of PC-1 along with corneal leukoeratoses and angular cheilosis.<sup>7</sup>
- PC tarda, a fourth variant, is characterized by late onset with isolated typical nail changes beginning in second or third decade.<sup>10</sup>

### Pathogenesis

The keratins are intermediate filament proteins and are important for integrity and mechanical stability of epithelial cells with the largest number of keratin genes expressed in skin. Cell fragility occurs as a result of mutations in genes encoding keratins. PC is caused due to mutations in paired keratin genes, K6a/K16 in PC-1 and K6b/K17 in PC-2. These genes are expressed in palmoplantar skin, pilosebaceous unit, nail bed, and oral mucosa thus selectively involving these sites in PC.

### Histopathology

Histological examination from hyperkeratotic papules reveals acanthosis with parakeratosis in epidermis due to rapid proliferation and differentiation of keratinocytes.<sup>6</sup> The blisters around the plantar callosities arise in the stratum malpighii due to increased intracellular edema and vacuolization. The oral lesions show epithelial thickening with extensive intracellular vacuolization.

### Treatment

For mild hyperkeratosis, emollients and keratolytics like salicylic acid, urea, benzoic acid, propylene glycol may help along with comfortable footwear to reduce callosities and blistering. The most effective and simplest therapy for thickened nail is vigorous curettage of nail bed and matrix as avulsion of nails provide only temporary relief. Oral retinoids have been reported to clear keratotic papules and mucosal leukokeratosis. Palmoplantar hyperhidrosis can be treated with aluminum chloride lotion, iontophoresis and botulinum toxin to prevent blistering and to reduce pain.

So, we made the diagnosis of pachyonychia congenita type-1 based on typical clinical and histopathological findings. PC is a rare condition with only few cases reported till now which prompted us to report this case.

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