Facial cystic lesions and onychodystrophy

María Victoria Sabogal Gómez MD1 | Victor González MD2 | José M. Martín MD, PhD2,3

1Department of Dermatology, Fundación Universitaria Sanitas, Hospital Universitario, Centro Dermatológico Federico Lleras Acosta E.S.E, Bogotá, Colombia
2Department of Dermatology, Hospital Clínico Universitario, Valencia, Spain
3Department of Medicine, University of Valencia, Valencia, Spain

Correspondence
María Victoria Sabogal Gómez, Department of Dermatology, Fundación Universitaria Sanitas, Hospital Universitario, Centro Dermatológico Federico Lleras Acosta E.S.E, Bogotá, Colombia.
Email: vickytutti@gmail.com

1 | CASE PRESENTATION

A 7-year-old Caucasian girl was referred to our dermatology department because of multiple small cystic lesions that were present since birth. They were predominantly located in the frontal region and in both armpits. Her growth and development were normal, although her parents reported a history of natal teeth and axillary bromhidrosis, without any other associated systemic symptoms.

Physical examination revealed multiple small, yellowish, cystic lesions located over the entire frontal region, lower eyelids, and bilateral axillary region (Figure 1). She had a painful nodular, erythematous lesion in her right armpit (Figure 2). Examination of the fingernails and toenails revealed thickening and deformity, distal subungual hyperkeratosis, and yellowish chromonychia (Figure 3). She had nonpainful mild keratoderma on her heels. She had straight blonde hair; findings from electron microscopy examination of the hair are shown in Figure 4. Her eyelashes and eyebrows were normal. The rest of the physical examination was normal, including mucous membranes. No other family members were affected.

2 | WHAT IS THE DIAGNOSIS?

FIGURE 1

FIGURE 2

FIGURE 3

FIGURE 4
2.1 | Diagnosis: Pachyonychia Congenita-K17

3 | ADDITIONAL STUDIES

Cutaneous biopsies from lesions on the arms and right armpit confirmed the presence of infundibular cysts. Pili torti was confirmed using electron microscopy (Figure 4). An analysis of the KRT17 gene using polymerase chain reaction showed a mutation of the gene in the sequence c.275A>G, confirming a diagnosis of pachyonychia congenita (PC)-K17 (formerly PC type 2).

4 | DISCUSSION

Pachyonychia congenita is a rare genodermatosis that is usually inherited as an autosomal-dominant trait, with variable expression and high penetrance. It is clinically characterized by nail dystrophy and focal palmoplantar keratoderma, usually painful. Other associated manifestations include follicular keratosis, mucosal leukokeratoses, hoarse voice, cystic lesions (steatocystsomas and pilosebaceous cysts), and natal teeth.1,2

Mutations in five keratin genes KRT6A, KRT6B, KRT6C, KRT16, and KRT17 that alter keratins 6a, 6b, 6c, 16, and 17, respectively, cause PC. Keratins play a key role in maintaining epidermal cell integrity and the mechanism of strength. The keratins associated with PC are predominantly expressed in basal and suprabasal layers of palmoplantar skin, epidermal appendages, and oral mucosa.2

Thickened toenails (98% of cases) and plantar keratoderma (95%) were the most frequently reported clinical finding in patients with PC.3 Historically, two major subtypes of PC were based on clinical characteristics. PC type 1 (Jadassohn-Lewandowsky) is related to oral leukokeratoses, and PC type 2 (Jackson-Lawler) is often associated with cysts and natal teeth.1,2

Phenotypic overlap of PC genotypes has made the designations of PC-1 and PC-2 obsolete. A new molecular genetic classification system has been adopted whereby the subtypes of PC refer to the specific mutated keratin gene. Thus, the new classification is based on mutations in the keratin-encoding genes KRT6A, KRT6B, KRT6C, KRT16, and KRT17 and divides PC into subtypes PC-K6a, PC-K6b, PC-K6c, PC-K16, and PC-K17, respectively.1,3 Clinical differences may distinguish between PC subtypes. The unifying feature of PC is nail dystrophy, although the clinical appearance of the nails can be variable, and it usually appears during the first year of life.3 A mutation in KRT6a or KRT16 should cause similar features, whereas a mutation in KRT6b or KRT17 will present with a different, predictable phenotype.3 Nail dystrophy at birth, especially involving all nails, predicts PC-K6a or PC-K17. Natal teeth are a manifestation almost exclusively associated with mutations in PCK17 (occurred in 13.9% of patients with PC overall and 86% with PC-K17), and there is a strong association with cysts in individuals with a KRT-17 mutation. Concurrent fingernail and toenail thickening is associated with PC-K6a and PC-K17, and follicular hyperkeratosis, hoarseness, and leukokeratosis are most often present in PC-K6a.1,3

Of the spectrum of mutations causing PC, the most frequent are KRT6A (44%) and KRT17 (24%).4

The genetic disorder that is most commonly confused with PC is hidrotic ectodermal dysplasia (Clouston syndrome), which results from mutations in connexin 30 and is associated with nail dystrophy, some palmoplantar keratoderma, and alopecia.3 Mutations on desmoglein 1, desmoplakin, keratin 9, and frizzled 6 may also mimic some features of the PC phenotype and hence should be included in the differential diagnosis.4

Despite the common signs, only 25% of children have an accurate diagnosis in their first year of life, leading in some cases to inadequate management.5 Many therapeutic modalities have been proposed to treat the clinical manifestations in PC, including topical and oral retinoids, surgical and mechanical procedures, orthotics, and keratolytics. Nevertheless, none are ideal, although they may provide some relief, with mechanical and surgical options being preferred over medical therapies.5 Recently, more targeted therapeutic strategies (including rapamycin and simvastatin) have been the focus of much attention, although they are not used routinely. Another innovative approach under investigation involves injections of small interfering RNA, which can silence gene expression.2 Given that the clinical manifestations of this girl were not limiting, she was managed with topical treatments including rapamycin, retinoids, and keratolytics.

AUTHOR CONTRIBUTION
All authors give consent for publication.

ORCID

María Victoria Sabogal Gómez http://orcid.org/0000-0001-7423-2865

Victor González http://orcid.org/0000-0002-0330-7599

José M. Martín http://orcid.org/0000-0003-2483-0482

REFERENCES


