



# Pachyonychia Congenita Project

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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.

## Pachyonychia congenita with late onset of nail dystrophy—a new clinical entity?

S. IRACI, L. BIANCHI, S. GATTI, A. M. CARROZZO, D. BETTINI AND G. NINI  
*Department of Dermatology, Tor Vergata University of Rome, Italy*

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### Summary

Pachyonychia congenita syndrome (PCS) is a genetic disease with an autosomal dominant mode of transmission in which the main sign, pachyonychia, usually arises at birth or in childhood together with other disorders of keratinization. A 28-year-old woman developed subungual hyperkeratosis of all toe-nails and thumb-nails associated with pain on pressure and walking. She had a scrotal tongue with leucokeratotic areas, blister formation, plantar hyperkeratosis, palmoplantar hyperhidrosis and dental cavities since childhood. The present case, interpreted as PCS of late onset, could be a clinical variant of the Jadassohn-Lewandowsky syndrome with the late onset of pachyonychia or else an additional form of PCS due to the expression of a new and different allele.

Pachyonychia congenita syndrome (PCS) is a rare genodermatosis characterized by hyperkeratosis of the nail-bed and other cutaneous and mucosal disorders of keratinization that affect both sexes equally.<sup>1-3</sup> PCS is transmitted as an autosomal dominant trait; an autosomal recessive inheritance has also been suggested in a few cases.<sup>4,5</sup>

Because of the wide clinical variability several classifications of the syndrome have been proposed starting with Kummer and Loos's<sup>6</sup> in 1935 to Schonfeld's<sup>7</sup> in 1980 who distinguished three types: type I (Jadassohn-Lewandowsky syndrome) characterized by symmetrical hard thickening of all fingers and toe-nails, keratosis palmo-plantaris, follicular keratosis, blister formation, leucokeratosis of the oral mucosa, hoarseness, hair abnormalities, palmar and plantar hyperhidrosis; type II (Jackson-Sertoli syndrome) having the same features as type I without leucokeratosis, but with immature teeth and multiple cysts; type III (Shafer-Brunauer syndrome) in which the clinical signs of the type I are associated with leucokeratosis of the cornea. Furthermore Feinstein *et al.*

Correspondence: S. Iraci, MD, Department of Dermatology, Tor Vergata University of Rome, Ospedale S. Eugenio, P.le dell'Umanesimo 10, 00144 Rome, Italy.

in 1988 proposed the following classification based on a survey of 168 individuals:<sup>2</sup> type I with hypertrophy of nails, palmoplantar hyperkeratosis, follicular keratosis and oral leucokeratosis (56, 20%); type II in which the clinical findings of type I are associated with bullae of palms and soles, fetal or neonatal dentition, and steatocystoma multiplex (24, 9%); type III with the clinical findings of type I and II plus angular cheilosis, corneal dyskeratosis and cataracts (11, 7%); type IV with the clinical findings of type I, II and III plus laryngeal lesions, hoarseness, mental retardation, hair anomalies and alopecia (7, 2%). Nail thickening, considered as the main clinical marker of the syndrome, usually appears at birth or within the first year of life, rarely later. In fact, only eight cases of PCS in which pachyonychia arose in the second decade of life have been reported in the literature.<sup>3,4,7,8</sup>

We describe an additional case of PCS with a late onset of the typical nail alterations in the third decade of life.

### Case report

A 29-year-old white woman first noted progressive painful thickening of all toe-nails and thumb-nails in January 1990. At the same time, she complained of palmar hyperhidrosis with mild pruritus. Topical and oral antimycotic treatment produced no clinical improvement after 9 months of therapy. On examination, in April 1991, the toe-nails were all severely affected with thickening of the distal two-thirds of the nail-bed up to 4-6 mm in depth, and mild brown-yellowish discoloration. Few splinter haemorrhages were present. Pincer and trumpet nail deformities that included subungual proliferation of soft tissues and severe pain on pressure and walking, were demonstrable either on the second and third toe-nail of the right foot (Fig. 1), and on the third toe-nail of the left foot.

The thumb-nails were only mildly affected with slight thickening and bilateral plicated overcurvature. There was no onycholysis and the remaining finger-nails were normal. A careful observation of the patient revealed a scrotal tongue present since birth which appeared



Figure 1. Marked hyperkeratosis of the nail-beds producing pincer nail deformities.

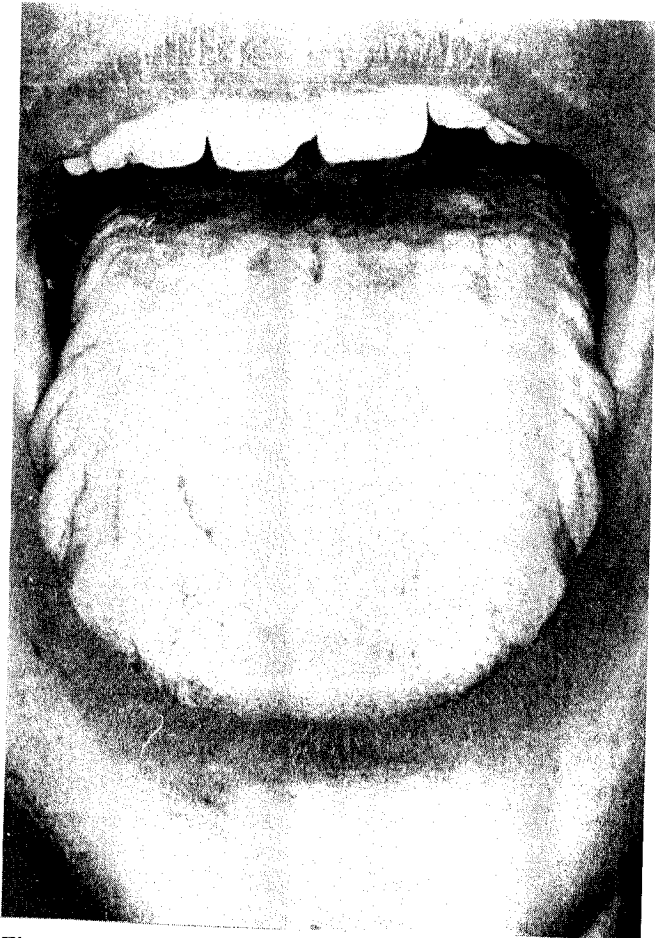


Figure 2. Scrotal tongue with leucokeratotic areas.

scallop-edged, deeply fissured with leucokeratotic areas (Fig. 2).

Since infancy the soles showed thick, yellow keratoses confined to pressure sites. The patient complained of blister formation on the feet that worsened during summer, and reported that these lesions were more severe in childhood (Fig. 3).



Figure 3. An eroded blister of the fifth toe surrounded by linear hyperkeratosis.

Hyperhidrosis with dyshidrotic eczema of the palms and dental cavities were also present. The hair was normal. No cutaneous keratoses, cysts or hyper or hypopigmented lesions were seen.

ENT and ophthalmological examination showed no tympanic, laryngeal or corneal changes, and general clinical examination was normal. Repeated microscopic and cultural examinations from oral mucosa and nail material showed no fungal infection. X-rays of hands and feet showed no anomalies. There was no history of consanguinity between the parents, and no family members were affected, except for the presence of scrotal tongue in the mother.

The patient had taken no drugs before the appearance of the onychodystrophy. She refused biopsy.

#### Discussion

Nail thickening, due to orthokeratotic hyperkeratosis of the nail-bed, is the main clinical and pathological marker of this syndrome.<sup>9</sup> Usually this sign arises at birth or in early childhood with the other anomalies. The presence of this onychodystrophy suggests the diagnosis of PCS. The development of other anomalies of keratinization such as leucokeratosis, palmoplantar hyperkeratosis, keratosis pilaris, etc. completes the clinical picture but are not diagnostic in the absence of pachyonychia; these mucocutaneous signs can sometimes arise before the appearance of nail thickening.

The protean expression of the syndrome justifies the different clinical classifications reported in the literature. Recently, an additional type of PCS, called pachyonychia congenita tarda, has been proposed because of the possible late onset of the syndrome.<sup>9</sup> Eight cases have so far been described in which nail dystrophy arose in teenagers. In Franzot's patient<sup>8</sup> and in the five cases described by Paller *et al.*<sup>9</sup> pachyonychia and other signs developed almost contemporaneously in teenagers. No chronological information about the associated signs in Su *et al.*'s case have been reported.<sup>3</sup>

Haber and Rose's patient complained of leucokeratosis and blistering since the age of 3 months, developing pachyonychia at the age of 12.<sup>4</sup>

The clinical picture of our case is that of the Jadassohn-Lewandowsky type of PCS, but is the only report so far described in the literature in which pachyonychia started in the third decade of life. We notice that the other signs such as oral leucokeratosis, frictional blister formation, plantar hyperkeratosis, plantar and palmar hyperhidrosis had been present since childhood.

We propose that our case, like the one described by Haber *et al.*,<sup>4</sup> could be interpreted as PCS of late onset rather than PCS tarda. In fact, in both our and Haber's patients not all the signs arose simultaneously in the second or third decade of life as stated by Paller *et al.*<sup>9</sup> for PCS tarda type.

Genetic studies identified two forms of PCS related to the expression of two different alleles: one with oral leucokeratosis (Jadassohn-Lewandowsky syndrome), the other without oral mucosal involvement (Jackson-Lawler syndrome).<sup>11-13</sup>

Our case could be interpreted either as a clinical variant of the Jadassohn-Lewandowsky syndrome with a late onset of pachyonychia or else as an additional form of PCS due to the expression of a new different allele. The autosomal dominant mode of inheritance is suggested by the presence of scrotal tongue in the mother, and is considered by some authors to be an essential feature of the syndrome.<sup>1</sup>

Pachyonychia in PCS must be differentiated from all other causes of subungual hyperkeratosis such as psori-

asis, onychomycosis, Darier's disease, chronic eczema, lichen planus, Norwegian scabies, pityriasis rubra pilaris, Reiter's disease or trauma.<sup>14</sup> The history, pathology and lack of other clinical associated features exclude these diseases and focuses attention on those mucocutaneous signs other than pachyonychia, often overlooked by the patient.

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