Pachyonychia Congenita Project

15 March 2005

Use of Articles in the Pachyonychia Congenita Bibliography

The articles in the PC Bibliography may be restricted by copyright laws. These have been made available to you by PC Project for the exclusive use in teaching, scholarship or research regarding Pachyonychia Congenita.

To the best of our understanding, in supplying this material to you we have followed the guidelines of Sec 107 regarding fair use of copyright materials. That section reads as follows:

> Sec. 107. - Limitations on exclusive rights: Fair use
> Notwithstanding the provisions of sections 106 and 106A, the fair use of a copyrighted work, including such use by reproduction in copies or phonorecords or by any other means specified by that section, for purposes such as criticism, comment, news reporting, **teaching (including multiple copies for classroom use), scholarship, or research**, is not an infringement of copyright. In determining whether the use made of a work in any particular case is a fair use the factors to be considered shall include - (1) the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use upon the potential market for or value of the copyrighted work. The fact that a work is unpublished shall not itself bar a finding of fair use if such finding is made upon consideration of all the above factors.

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.

2386 East Heritage Way, Suite B, Salt Lake City, Utah 84109 USA
Phone +1-877-628-7300 • Email—Info@PC-Project.org
www.PC-Project.org

Pachyonychia Congenita

Manifestations for the Otolaryngologist

Sheldon P. Hersh, MD

• When discovered, leukoplakia of the oral cavity is commonly an acquired lesion. Pachyonychia congenita is a member of a rare group of disorders in which congenital white lesions of the oral cavity are present. Additional findings of note to the otolaryngologist are described as well.

***(Arch Otolaryngol Head Neck Surg.* 1990;116:732-734)**

White lesions of the oral cavity are, for the most part, acquired by-products of the multitude of events occurring daily in the oral cavity. Less commonly, they may appear as manifestations of either local or systemic diseases such as lupus erythematosus and others. Rarely encountered is a group of congenital white lesions of the oral cavity herein referred to as oral genodermatoses. One of these disorders, pachyonychia congenita (PC), is presented along with some of its potential otolaryngologic-head and neck manifestations.

Pachyonychia congenita was first described by Jadassohn and Lewandowsky[1] in 1906 as an anomaly in which dystrophic fingernails and toenails occurred together with specific cutaneous and mucus membrane changes that may first be noted at birth or in early childhood.

The remarkable fingernails (Fig 1) in these patients are the sine qua non of this disorder. Steiglitz and Centerwall[2] have found that approximately 97% of cases reviewed have dystrophic nails with all fingernails and toenails being affected. Together with marked thickness, these nails take on a yellow-brown discoloration with pinched margins and an upward angulation of the distal tips.[3] These hyperkeratotic nails can lead to difficulties in digital dexterity, and cosmesis remains a lingering concern.

Cutaneous findings oftentimes reveal plantar and palmar hyperkeratosis in conjunction with hyperhidrosis.[4,5] Follicular keratosis of the extensor surfaces of the knees and elbows may be present. They are usually of the acneiform type.[3,5] These keratotic lesions may at times appear on the buttocks and lumbar regions as well.[6] Plantar bullae[3] secondary to hyperkeratosis and hyperhidrosis may become infected and lead to additional difficulties.

Gorlin and Chaudhry[3] described the oral lesions as white, opaque thickenings of discrete or confluent areas of the oral cavity. The entire buccal mucosa may at times be involved. An associated overgrowth of *Candida albicans* has been noted with some of these leukoplakic lesions.[4] Angular cheilosis has been described as well.[3] The tongue may often appear with scalloped edges (Fig 2), and may be partially or totally covered by a leukoplakic blanket. Aphthous ulcerations of the oral cavity have been noted to occur with PC,[5] and neonatal teeth have been described in a number of affected individuals.[2,6,7]

A number of other affected sites that occur with less frequency include the larynx, eyes, teeth, hair, and ears. The likelihood of one of these less commonly affected sites being involved will depend, for the most part, on the pedigrees under study. A rare presentation in one pedigree may stand out as a common finding in another. Gorlin and Chaudhry[3] noted the existence of white plaquelike lesions involving the interarytenoid area of the larynx. Cohn et al,[8] in a recent article, described multiple white lesions involving the ventricles, true cords, and subglottic areas of the larynx. Steiglitz and Centerwall[2] presented a pedigree in which laryngeal involvement was a common presentation. Some members of this pedigree had experienced laryngeal obstruction that ultimately necessitated tracheostomy. Dystrophic changes in the hair and cornea were described by Witkop and Gorlin,[9] Forslind et al,[4] and Steiglitz and Centerwall.[2] In addition, Forslind et al[4] made note of the possible presence

Accepted for publication January 3, 1990.

From the Department of Otolaryngology, Manhattan Eye, Ear, and Throat Hospital, New York, NY.

Reprint requests to 110-11 72nd Ave, Forest Hills, NY 11375 (Dr Hersh).

of thickened tympanic membranes with a resultant conductive hearing loss.

Pachyonychia congenita has been divided into various types based on clinical presentation. Kummer and Loos[10] proposed the following division: type 1, symmetrical keratosis of the hands and feet along with follicular keratosis of the body; type 2, oral leukoplakia in addition to those findings in type 1 (most common); and type 3, corneal dyskeratosis plus types 1 and 2 clinical findings.

Additional subdivisions have been proposed in the literature but may, in fact, be artificial in nature as the subdivisions may represent possible variations in phenotypic expression of a single disease entity.

REPORT OF A CASE

This 45-year-old man was seen in consultation for a totally unrelated problem. On routine otolaryngologic examination, a rather remarkable-appearing tongue was noted (Fig 2), which obviously led to further questioning. His fingernails were remarkable as well (Fig 1). He was aware that he had some form of genetic illness as his son had similar findings. To the best of his knowledge, no other family members were affected. Permission to obtain a biopsy specimen from the tongue and to obtain additional investigations was refused.

Pathologic Findings

There do not appear to be any microscopic features that are strictly pathognomonic of PC. A number of the genodermatoses may have histologic features that are indistinguishable from those found in PC.[9] Steiglitz and Centerwall[2] have found that all three germ layers may be involved: the ectoderm, nails, skin, hair, teeth, and oral mucosa; the endoderm, larynx; and the mesoderm, joints and laryngeal cartilage. It was thus concluded that the histologic picture of the disparate sites was essentially similar.

Witkop and Gorlin[9] performed exfoliative cytologic analyses of the oral mucosa and tongue. They noted that the epithelium was acanthotic with uniform intracellular vacuolization. Additionally, the intercellular bridges were not present in the prickle cell layer. A marked parakeratosis was in evidence, while the stratum granulosum was lacking. Gorlin and Chaudhry[3] obtained representative biopsy specimens of the tongue and oral mucosa with findings similar to those obtained by Witkop and Gorlin.[9] Cohn et al[8] found the ultrastruc-

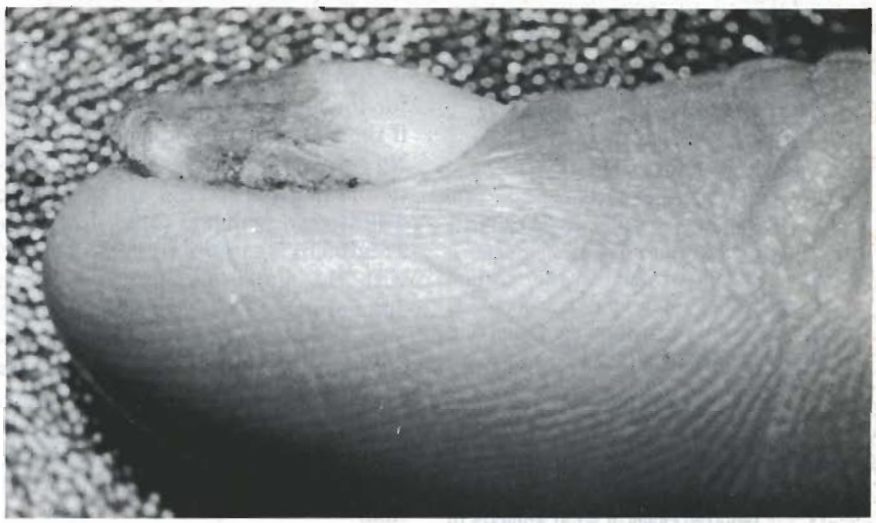

Fig 1.—Hypertrophic fingernail with characteristic upward angulation of distal tip.

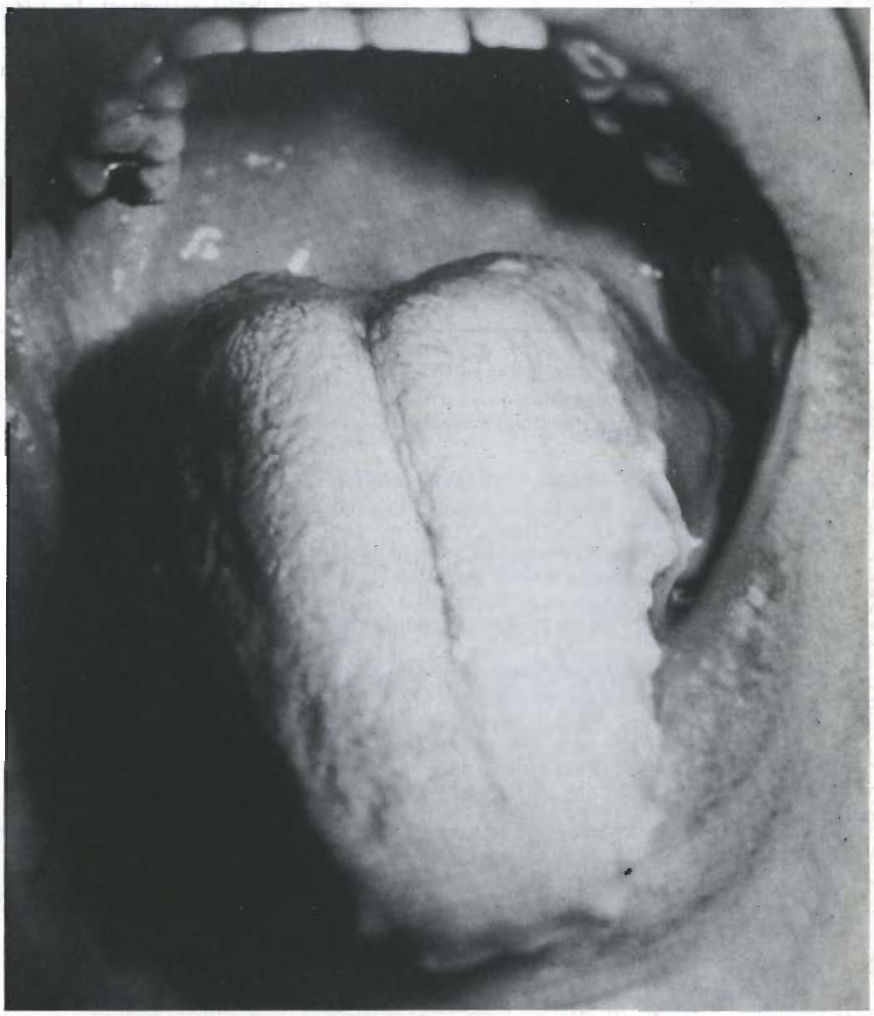

Fig 2.—Near total leukoplakic covering of tongue along with scalloped perimeter.

ture of laryngeal lesions to be identical to those found in the above studies. Nail pathology[4,11,12] seemed to be confined to the nail bed. An abnormal granular layer produces increased amounts of keratin, which, along with a deficient nail bed adhesion, gives rise to a thickened elevated nail.[12]

Electron-microscopic studies of PC[13] have revealed an increase in the tonofibrils of the basal cells. This increase in tonofibril density was more evident in the stratum spinosum, while intracellular edema was present in both the stratum spinosum and the granular layer.

Genetics

Pachyonychia congenita is transmitted as an autosomal dominant with high penetrance and variable phenotypic expressivity.[2,13,14] Isolated cases of what appears to be an autosomal recessive transmission have been reported.[15,16] A significant history of consanguinity has been revealed in these recessive cases.

COMMENT

As otolarynologists, we are accustomed to seeing various forms of leukoplakia in the oral cavity. In most cases, one can associate these white lesions with some form of local or systemic cause. A rare group of genodermatoses has been described and can, for the most part, be easily diagnosed if the appropriate history is available. No specific laboratory tests or definitive pathologic criteria are present to definitively validate the diagnosis. Treatment is essentially symptomatic, with the major emphasis placed on ameliorating the discomfort, both physical and psychological, of the hyperkeratotic skin and nail lesions. As the pathologic findings have indicated, and the literature has verified, the leukoplakic lesions of the oral cavity do not undergo malignant transformation.

References

1. Jadassohn J, Lewandowsky F. Pachyonychia congenita. *Iknograph Dermatol.* 1906;1:29.
2. Steiglitz JB, Centerwall WR. Pachyonychia congenita (Jadassohn-Lewandowsky syndrome: a 17-member, 4-generation pedigree with unusual respiratory and dental involvement. *Am J Med Genet.* 1983;14:21-28.
3. Gorlin RJ, Chaudhry DDS. Oral lesions accompanying pachyonychia congenita. *Oral Surg.* 1958;11:541-544.
4. Forslind B, Nylen B, Swanbeck G, Thyresson M, Thyresson N. Pachyonychia congenita: a histologic and microradiographic study. *Acta Dermatol.* 1973;53:211-216.
5. Brightman VJ. Red and white lesions of the oral mucosa. In: Lynch MA, Brightman VJ, Greenberg MS, eds. *Burket's Oral Medicine.* Philadelphia, Pa: JB Lippincott; 1984:241.
6. Maser ED. Oral manifestations of pachyonychia congenita. *Oral Surg.* 1977;43:373-378.
7. Clementi M, DeStefani EC, Del Rossi C, Avventi V, Tenconi R. Pachyonychia congenita Jackson Lawler type: a distinct malformation syndrome. *Br J Dermatol.* 1986;114:367-370.
8. Cohn AM, McFarlane JR, Knox J. Pachyonychia congenita with involvement of the larynx. *Arch Otolaryngol.* 1976;102:233-235.
9. Witkop CJ, Gorlin RJ. Four hereditary mucosal syndromes. *Arch Dermatol.* 1961;84:104-113.
10. Kummer L, Loos H. Uber Pachyonychia Congenita (Typus Riehl). *Wien Klin Wochenschr.* 1935;6:174.
11. Thomsen RJ, Zuehlke MD, Beckman BL. Pachyonychia congenita. *J Dermatol Surg Oncol.* 1982;8:24-28.
12. Langford JH. Pachyonychia congenita. *J Am Podiatr Med Assoc.* 1978;68:587-590.
13. Thomas DR, Jorizzo JL, Brysk MM, Tschen JA, Miller J, Tschen EH. Pachyonychia congenita. *Arch Dermatol.* 1984;120:1475-1479.
14. McKusick VA. *Mendelian Inheritance in Man.* Baltimore, Md: Johns Hopkins University Press; 1986:560-561.
15. Haber RH, Rose TH. Autosomal recessive pachyonychia congenita. *Arch Dermatol.* 1986; 122:919-923.
16. Chong-Hai T, Rajagopalan K. Pachyonychia congenita with recessive inheritance. *Arch Dermatol.* 1977;113:685-686.