



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.

Case report

Persistent hoarseness in a patient with pachyonychia congenita: an early sign of laryngeal involvement

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Case

A 13-month-old boy, born of a nonconsanguineous marriage, presented with extensor hyperkeratotic papules and subungual hyperkeratosis with yellow–brown discoloration of the nail plate affecting all 20 nails, developing within the first few months of life. Whitish plaques were also observed on the oral mucosa.

His mother reported progressive hoarseness, especially on crying. Treatment for onychomycosis and oral candidiasis for 2 months yielded no improvement. Multiple courses of antimicrobials for presumed upper respiratory tract infection did not improve the hoarseness. There were no other known medical problems, and his growth and development were within the normal range. Natal teeth, hair abnormalities, and abnormal dentition were not found. The family history regarding other ectodermal disorders was noncontributory.

On physical examination, there was subungual hyperkeratosis and yellow–brown discoloration of all the nails (Fig. 1), symmetric follicular hyperkeratotic papules on the extensor surface of the knees and elbows, and palmar blisters. Intraoral examination showed irregularly shaped whitish plaques on the dorsal tongue, palate, buccal mucosa, and both sides of the labial commissure, together with angular cheilitis (Fig. 2). Sweating was normal. A complete ophthalmologic examination (including pupil dilation) showed normal results. Potassium hydroxide (KOH) examination and fungal culture of scrapings of the nail and from the whitish mucosal plaques yielded negative findings.



Figure 1 Clinical appearance of hypertrophic nail dystrophy and discoloration of the toenails

Laryngeal examination under general anesthesia using an endoscopic video information system revealed a slightly elevated, white, hyperkeratotic plaque of 3–4 mm in diameter that extended from the posterior commissure to the anterior interarytenoid mucosa, and two small whitish clear papules, measuring 1–2 mm in diameter, on the upper part of the left vocal cord (Fig. 3). There was no history of any problems with respiratory obstruction. The boy was otherwise generally healthy with unremarkable findings on systematic examination. The results of laboratory investigation, including



Figure 2 Hyperkeratotic white plaques affecting the labial commissure and oral mucosa

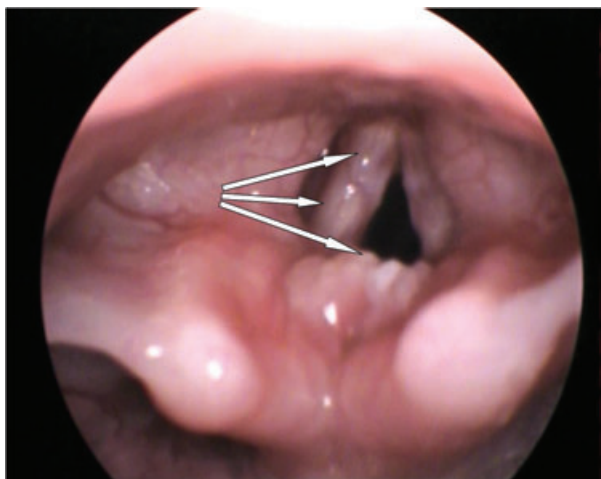


Figure 3 Endoscopic view of the larynx with whitish lesions in the posterior commissure and left vocal cord

complete blood count, erythrocyte sedimentation rate, C-reactive protein, routine serum biochemistry, and urine analyses, were all within normal limits. In view of these clinical findings, a diagnosis of pachyonychia congenita was made.

Discussion

Pachyonychia congenita (PC) represents a group of rare hereditary keratin disorders characterized by a variety of ectodermal abnormalities. The most characteristic finding of affected patients is the marked subungual hyperkeratosis with thickening of the distal part of the nails. Other findings include hyperkeratosis of the palms and soles, hyperhidrosis, leukokeratosis of the mucous membranes, follicular

hyperkeratosis, particularly on the knees and elbows, and the development of friction blisters.^{1,2} It was first documented by Jadassohn and Lewandowsky in 1906, who reported palmoplantar keratoderma and ectodermal defects.¹ It is usually inherited as an autosomal dominant trait with varying degrees of penetrance, although autosomal recessive forms and sporadic cases have also been described.^{1,3,4}

To our knowledge, few cases of laryngeal involvement in patients with PC have been described in the literature.⁴⁻⁶ Clinical laryngeal findings in PC are variable and only rarely produce a life-threatening situation requiring emergency surgery. Airway obstruction secondary to laryngeal lesions should be considered in patients with PC presenting with hoarseness and symptoms of respiratory distress.^{5,6}

Although numerous classifications of PC have been proposed, two major subtypes, PC-I (Jadassohn–Lewandowsky type) and PC-II (Jackson–Lawler type), are well recognized.⁷ Both types show hypertrophic nail changes, focal palmoplantar keratoderma, and follicular keratoses of the elbows and knees. The clinical discrimination between PC-I and PC-II usually depends on the more prominent oral leukokeratosis in PC-I or, conversely, on the finding of steatocystoma/pilosebaceous cysts, vellus hair cysts, hair abnormalities, and natal teeth in PC-II.^{8,9} Genetic mutations in keratins K6a and K16 are associated with the PC-I phenotype, whereas K6b and K17 mutations are associated with the PC-II phenotype.¹

Characteristic features of classic type I PC were present in our case. According to the classification proposed by Feinstein *et al.*,³ type III PC shows additional features of angular cheilosis (Fig. 2), corneal dyskeratosis, and cataracts, whereas type IV PC shows laryngeal lesions, hoarseness, mental retardation, hair anomalies, and alopecia. The absence of other manifestations in our patient and the discordance with the existing classification may be explained by the incomplete penetrance of these phenotypes and the inadequacy of the current classifications of this rare disease.

The actual prevalence of laryngeal involvement in PC is unclear. It seems to be uncommon. Hoarseness, the clinical sign of laryngeal involvement, was reported in less than 10% of patients with PC by Benjamin *et al.*⁴ Leachman *et al.*,¹ however, described hoarseness or laryngeal involvement in 16% of 57 patients with PC in a prospective evaluation. Although hoarseness in connection with PC was first reported as early as 1935, severe laryngeal involvement leading to obstructive symptoms has been documented only twice.^{5,6,10} The first case of laryngeal involvement in PC was reported in 1976 by Cohn *et al.*⁶ in a 3-year-old boy, who had extensive laryngeal involvement leading to severe respiratory distress. In 1983, the second case was reported in a boy with PC requiring two life-saving tracheostomies. In early infancy, the patient had been misdiagnosed with congenital tracheal stenosis and was hospitalized many times with stridor and respiratory distress.¹⁰

The clinical presentation of laryngeal involvement in patients with PC follows a variable course, ranging from an asymptomatic state to severe upper airway compromise.⁶ The posterior commissure is the most frequently affected area, but any portion of the larynx may be involved.⁴⁻⁶ The most common initial presenting feature is hoarseness in these patients. It can be the first and only manifestation of laryngeal involvement. The hoarseness associated with PC, especially following overuse, usually resolves spontaneously by relaxing the voice. It may also improve spontaneously over a period of several years.^{4,6} The rare occurrence of respiratory insufficiency can be life-threatening, however, especially in young children with laryngeal thickening, and requires emergency surgical intervention to re-establish the airway.¹ Microsurgical removal of laryngeal leukokeratosis can prevent life-threatening respiratory tract obstruction.⁵ As a result of the risk of potential injury to the laryngeal structures, aggressive surgical resection is not advised.⁴

In our patient, extensive laryngeal lesions leading to serious upper airway obstruction and obstructive respiratory symptoms did not occur, and therefore surgical intervention was not performed. Careful periodic examination, including laryngeal endoscopic evaluation, was recommended.

A complaint of hoarseness in infants and children with PC may be a sign of serious respiratory distress, and should not be ignored. With its unpredictable course, this complication remains a diagnostic and therapeutic challenge to physicians involved in the care of patients with PC. In these patients, persistent hoarseness should prompt an evaluation for laryngeal involvement by laryngoscopy to guard against an impending respiratory obstruction. Early detection and treatment may prevent the development of upper airway obstruction.

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