Recurrent hoarseness in a 12-year-old female patient with pachyonychia congenita type 1: case report and literature review

Anna Hogendorf1, Małgorzata Wojtkiewicz-Malicka1, Ewa Niebudek-Bogusz2, Agnieszka Cywińska-Bernas3, Andrzej Kaszuba4, Krzysztof Zeman4

1Department of Paediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz, Poland
Head: Prof. W. Mlynarski MD, PhD
2Department of Paediatric Otorhinolaryngology, Medical University of Lodz, Poland
Head: Prof. Anna Zakrzewska MD, PhD
3Department of Audiology and Phoniatrics, Nofer Institute of Occupational Medicine, Lodz, Poland
Head: Prof. Mariola Sliwinska-Kowalska MD, PhD
4Department of Paediatrics and Clinical Immunology with Nephrology Division, Medical University of Lodz, Poland
Head: Prof. Krzysztof Zeman MD, PhD
5Polish Mother’s Memorial Hospital Research Institute, Lodz, Poland
Head: Prof. Krzysztof Zeman MD, PhD
6Department of Dermatology and Paediatric Dermatology, Medical University of Lodz, Poland,
Head: Prof. Andrzej Kaszuba MD, PhD

Abstract

We report a phoniatric evaluation of a 12-year-old female with pachyonychia congenita type 1 (Jadassohn-Lewandowsky syndrome) and recurrent hoarseness. Pachyonychia congenita (PC) is an ultra rare genetic disorder of keratinisation that predominantly affects not only the nails, skin, hair, but also oral mucosae and larynx. Hoarseness is reported in 16% of patients with this disease and is attributed to laryngeal leukoplakia. However, assessment of this symptom in most PC cases is subjective and a detailed phoniatric assessment of patients with PC and hoarseness has not been described in the literature so far.

Key words: hoarseness, pachyonychia congenita, larynx.

Case report

A 12-year-old female diagnosed with pachyonychia congenita type 1 (PC-1) previously described in this journal [1] was referred to the Department of Pediatric Otorhinolaryngology of the Medical University of Lodz, Poland, for evaluation of recurrent hoarseness observed since early childhood, which became more intense and troublesome when she started participating in a children’s choir. Two years prior to admission she had been referred to the International Pachyonychia Congenita Research Registry and underwent genetic tests confirming diagnosis of PC type 1 due to spontaneous N172del mutation in the KRT6a gene encoding K6a type of keratin.

On physical examination, all of the patient’s fingernails and toenails were thickened, with yellowish-gray discoloration and distal elevation (Figure 1). The girl had difficulty in walking caused by painful callouses and blistering on the soles. Other typical PC symptoms such as follicular keratoses and pilosebaceous cysts were also observed.

The main complaint was recurrent hoarseness. Multiple courses of antimicrobials for presumed upper respiratory tract infection as well anti-allergic treatment did not improve the symptom. The patient complained also of the recurrence of whitish plaques on the edges of the tongue and on both sides of labial commissure. These oral lesions were reported to be intermittent and more intense in early childhood. They used to be treated by a family doctor as a yeast infection, yielding no improvement.
Phoniatric examination included the evaluation of the upper respiratory tract by laryngological examination, hearing level assessment, perceptual voice evaluation, videolaryngostroboscopy and acoustic analysis of voice.

Laryngological examination showed no pathological symptoms within the upper respiratory tract. Perceptual voice assessment showed the girl’s voice to be rather low-pitched, produced in a relaxed manner, without neck hyperkinesis. Base resonators were activated correctly. Phonation time was between 12 s and 15 s, which was fairly long for a child at that age. It might have resulted from her earlier frequent singing in a choir. Hearing level examination, i.e. pure-tone audiometry and tympanometry, was within normal limits. Otoacoustic emission was present bilaterally.

Videolaryngostroboscopy was conducted twice with a 1-year interval. In both examinations the image of larynx was similar. At the posterior glottis, erythema and hypertrophy of mucosa were observed. Epiglottis was in the correct configuration. Vestibular folds showed no pathological changes. Vocal folds were symmetrical and mobile without edema or hyperemia, but incomplete glottal closure of the posterior part of the glottis (posterior chink) was also visible. Dimensions of the phonatory function estimated in stroboscopy were correct: regular and simultaneous vocal fold vibration, proper mucosal wave and amplitude of vocal folds movements. The image of the larynx is presented in Figure 2.

The acoustic voice analysis was performed using the IRIS software, in a sound-proof room with the average level of noise of 30 decibels. A condenser microphone coupled with a computer sound card AVACS SOUNDMAN CMI 878 SX was used. The examination was conducted in a standard way: a vowel “a” with a sustained sound was recorded three times. The modules analyzed were: acoustic parameters, pitch-intensity contour of the sustained vowel “a” and formant analysis of the vowel “a”. The parameters evaluating the relative change of frequency, i.e. Jitter, RAP, PRQ and a relative change of amplitude: Shimmer and APQ were correct.

On the basis of correct mean fundamental frequency (Fo) – at 232.0, with the standard deviation (Fo stdev) of 2.7, the voice timbre was classified as an adult female voice. The parameters evaluating harmonic structure of voice: HPQ, U2H and S2H were close to exceeding normal values. However, the threshold was exceeded only for the UH2I.
Discussion

Pachyonychia congenita (PC) (Greek: thick nails since birth) is an ultra rare keratin disorder whose typical symptoms usually become apparent shortly after birth. The hallmarks of the disease are symmetrical thickening of all nails—hypertrophic nail dystrophy and variable degrees of focal hyperkeratosis of palms and soles (palmoplantar keratoderma). The other features include follicular hyperkeratoses, leukokeratosis of the mucosa of the tongue, cheeks, throat and larynx, excessive sweating, hair abnormalities, prenat al or natal teeth (teeth erupted at birth or shortly after birth) and steatocystoma and pilosebaceous cyst formation [2]. The estimated number of sufferers is about a few thousand worldwide [3]. The PC has mainly an autosomal dominant pattern of inheritance, but spontaneous mutations, like in our patient, appear to be relatively common [4, 5]. The phenotypes vary from mild with only slight nail involvement, such as nails that end prematurely, to severe, debilitating palmoplantar keratoderma with painful blisters, causing the patient to adopt a compulsory position while walking or to move with crutches or wheelchairs [6–8]. Despite characteristic dermatological symptoms, PC may manifest as oral leukoplakia, angular cheilitis, hoarseness of voice or even life-threatening airway obstruction and therefore, the patient with PC may require consultation from the orothiro-laryngologist.

Leukoplakia of the tongue, gingival and buccal surfaces and throat may be the first sign of PC soon after birth. These aphthous-like lesions can mimic oral candidiasis, white sponge nevus, or hairy tongue. Angular cheilosis is usually intermittent and frequently demonstrates secondary bacterial or yeast infection [2, 9].

Hoarseness was first reported as a PC symptom in 1935 [10]. As previously reported, this symptom is usually aggravated by overusing the voice but may improve spontaneously with age [2, 11]. According to Leachman, hoarseness or laryngeal involvement was present in 16% of 57 patients with PC. However, these results were based on questionnaires indicating that the assessment of this symptom was in most cases subjective and the real cause of hoarseness has never been confirmed by a specialist laryngologist [2]. Therefore, the actual prevalence of laryngeal involvement in PC patients is unclear but may be underestimated. To date, only a few cases of laryngeal leukokeratosis in patients with PC have been described [9, 11–14]. It presents as white-to-pink thickening or an exophytic mass on the vocal cords and posterior glottis [9, 12–14]. Clinical manifestations are variable but practitioners should be aware that in infants and young children laryngeal leukokeratosis may be progressive, leading to stridor or even life-threatening respiratory distress requiring emergent tracheotomy and tracheostomies [12–14]. Microsurgical interventions were reported to be successful in severe laryngeal obstruction in small children. However, surgical treatment in this respect may result in the recurrence of the leukoplakia and reoperations may be required [12].

Our patient with recurrent hoarseness from early childhood underwent phoniatric evaluation many years after she had been initially diagnosed with Jadassohn-Lewandowsky syndrome (PC-1). Despite the fact that at the moment of examination the assessed voice was classified as normal, with a typical female voice timbre, slight inharmonic components for the formant F2 were observed. The analysis was performed twice with a 1-year interval and the results are similar. It can be assumed to be a constant inharmonic perturbation of the voice, which was also noted in the abnormal level of U2H1 (parameter evaluating non-harmonic voice components). Nevertheless, videolaryngoscopy revealed the presence of subtle changes in the larynx, such as erythema and hypertrophy of mucosa at the posterior glottis. Although subtle, they persist over time and therefore require special attention. Location and character of this laryngeal pathology are typical of the described syndrome. All previously described laryngeal lesions in pachyonychia congenita involve the posterior glottis [11, 13]. It confirms the need of an urgent phoniatric observation and introduction of recommendations.

Taking biopsy should be considered in every case of laryngeal pathology, but in our case there was no parents’ consent. Fortunately, all previous reports with histopathological assessments of laryngeal leukoplakia confirm that the feature is benign with no signs of inflammation or cellular atypia. Squamous epithelium with focal intracellular vacuolization that spares the basal layer was described as typical of PC [11]. Although histopathologically benign, it may be potentially fatal due to airway obstruction [10, 11]. Erythema and hypertrophy of mucosa at the posterior glottis are also typical of laryngopharyngeal reflux (LPR) [15]. Therefore, after the first visit, anti-LPR empiric therapy (diet changes as well as elevation of the head of the bed and pharmacotherapy with histamine receptor 2
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References