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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 type 2

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A 22-year-old man came to our clinic and reported that he had been born with teeth in the upper and lower jaws which fell out after a few days. Later only two incisors erupted in the upper jaw and one molar in the lower jaw (Figure 1). At birth there was thickening of the fingernails and toenails, with the latter being more severe. At age 5 the patient had developed a round occipital bald spot, and during puberty he had developed multiple inflammatory skin lesions which healed with scarring. His maternal grandmother also had nail deformities and had no teeth. At the initial clinical examination there were yellow, dystrophic toenails with onychogryposis-like changes as well as concave nail bed deformities. No palmoplantar hyperkeratosis was found, nor were there signs of hyperhidrosis detected. The patient had developed multiple inflammatory skin lesions which healed with scarring. His maternal grandmother also had nail deformities and had no teeth. At the initial clinical examination there were yellow, dystrophic toenails with onychogryposis-like changes as well as concave nail bed deformities. No palmoplantar hyperkeratosis was found, nor were there signs of hyperhidrosis detected. The patient had almost no teeth in the upper or lower jaw. The mucosa appeared normal without any signs of leukokeratia. An area of occipital alopecia measuring 10 x 15 cm was identified; and there were numerous scars in axillar, cervical, inguinal and gluteal regions as well as on the elbows and behind the knees. The results of tests for internal disease were normal. Mycologic studies were negative. Based on the clinical presentation, we diagnosed type 2 pachyonychia congenita. Pachyonychia congenita (PC) refers to a group of ectodermal dysplasias that are usually inherited in an autosomal dominant pattern with high penetration and variable expressivity. The disorder was first reported in 1906 by Jadassohn and Lewandowsky [1]. Later Jackson and Lawler described a special form of disease involving formation of multiple sebaceous gland cysts [2]. The primary features of PC include transverse convex curvature of the nails, thickening of the nail plate, and subungual hyperkeratosis which are present at birth or shortly thereafter [3]. In 1988, Feinstein proposed a clinical classification that divided the disease into 4 types [3]. The de-coding of the underlying genetic defect by Munro in 1994 further advanced our understanding of the disease [4] which is now divided into type I disease, or Jadassohn-Lewandowsky syndrome, and type II, or Murray-Jackson-Lawler syndrome. The main criteria for distinguishing the two are that in type I disease there is oral leukokeratosis and severe palmoplantar hyperkeratosis, while in type II disease there is premature dentition, hair anomalies, and development of multiple cysts [5]. Although the dental anomalies are an indicator of type II PC, their absence does not preclude the presence of the disease. The same applies to oral leukokeratosis in type I PC. PC I is triggered by a mutation in the keratin genes KRT 16 or 6a and in PC II by KRT 17 or 6b which are located on chromosomes 12 and 17. The expression of keratin depends on the type of tissue and epidermal cell differentiation. Keratins 17 and 6b are expressed in the nail bed, sweat glands, hair follicles, and hair shaft, and to a lesser extent in the palmoplantar epidermis. Keratin 16 and 6a are expressed in the nail bed, the palmoplantar epidermis, and the oral mucosa [6]. As a result of keratin gene mutations, the keratin filaments clump together and can no longer be integrated into other cytoskeleton structures. This results in diminished mechanical resistance of the keratinocytes and the epithelial structure. This in turn is aggravated as the damaged keratins 6a and 16 or 6b and 17 are also more strongly expressed during wound healing, trauma, and rubbing. Due to the increased cellular fragility as a result of mutation, there is increased expression of defective keratin and thus increased cellular damage along with hyperproliferation. This could explain palmoplantar hyperkeratosis and blistering on areas of the skin that are under mechanical stress. The cause of premature dentition is still unknown. It is possible that there is a developmental disorder affecting the epithelial root sheath prior to eruption of the crown of the tooth [7]. Various differentials must be excluded before a definitive diagnosis can be made. These include congenital onychogryposis, trauma-related nail changes, twenty-nail syndrome, and steatocystoma multiplex. Differential diagnoses for leukokeratosis include lichen mucosae, oral hairy leukoplakia, dyskeratosis congenital, and nevus spongioussus albus mucosae. Dentes natales can also occur in Ellis-van-Creveld syndrome or in Hallermann-Streiff syndrome which, however, also involve other clinical characteristics.

Figure 1: Incisors in upper jaw.
There is no causal therapy for the disease. Non-invasive treatment measures include filing the nails and wearing specially-designed shoes or inlays to avoid trauma and friction. Hyperkeratosis may be cured if needed. Topical application of urea 10–20 %, salicylic acid, or propylene glycol may also be considered. Systemic retinoid therapy may be attempted. Phenytoin has been successfully used in patients with multiple blisters. In one patient, the use of L-thyroxine was successful in reducing blistering and hyperkeratosis [8]. At present, our patient is currently being fitted with a dental prosthesis; treatment for nail and skin changes was declined.

References