

A Case with Pachyonychia Congenita and B-cell Lymphoma

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Abstract- Pachyonychia congenita (PC) is a rare autosomal dominant genodermatosis characterized by hyperkeratosis affecting the nails and palmoplantar areas, oral leukokeratosis, and cystic lesions. A 39-year-old woman with PC type 1 (Jadassohn-Lewandowsky syndrome) and B-cell lymphoma is described. No similar disorders or parental consanguinity were found in her family. Typical features of PC developed since her early childhood and the diagnosis of B-cell lymphoma was established seven years ago, without a clear causal relation between these entities. Despite inherent limitations of a single case, this report may contribute to PC understanding.

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Introduction

Pachyonychia congenita, (PC) was first described by Jadassohn and Lewandowsky (1906) in a 15-year-old female with concomitant cutaneous tuberculosis (1), and 15 years later the hereditary occurrence of pachyonychia was documented by Murray in several generations of a family (2). With a base on phenotypes, PC is classified in four types: PC I to III and PC tarda (2,3). The two keratin genes that are described in association with PC1 are KRT6A and KRT16 (1-11). PC-I or Jadassohn-Lewandowsky syndrome is a rare entity characterized by onychogryposis on all the digits (100%), hyperkeratosis of the palmoplantar (50-90%) and of extensor areas, follicular keratosis (37%), oral (50-75%) or laryngeal (6-15%) leukokeratosis, acral hyperhidrosis (20-75%) and blisters (36%) (1-5,8-10). Onychogryposis due to subungual hyperkeratosis is the hallmark of this condition, which typically appears at birth or early childhood, but may have a late onset as occurs in PC-IV or tarda (2,3,5,7,8,11). In patients with PC-II (Jackson-Lawler syndrome) main changes are natal or neonatal teeth (15-50%), cutaneous cystic lesions (25%), disorders in scalp and eyebrow hairs (9-25%), in addition to corneal dystrophy (8%); moreover, the nail hyperkeratosis is less accentuated in PC-II than in PC-I

(2,4,5,8-10). PC-III (Schafer-Brunauer syndrome) shows clinical features of PC-I, in addition to corneal leukokeratosis (3). Despite recent advances in genetic analysis, an understanding about PC remains incomplete, and some clinical features are probably associated with PC by mistake (6). Misdiagnosis can occur because same mutations may show diverse features (11). The objective of this case study is to describe the concomitance of PC-I with B-cell lymphoma. Although with inherent limitations of a single case study, this report may contribute to better understanding about this rare condition.

Case Report

A 39-year-old woman was admitted with dry cough and respiratory pain on the right posterior chest wall for three days. She has antecedent of allergic bronchitis since childhood, polycystic ovary syndrome, and adult-onset hypothyroidism treated with levothyroxine 100 mcg once daily. Diagnosis of pachyonychia congenita was established at the age of six months, and her nail changes evolved associated with recurrent episodes of plantar blisters, follicular hyperkeratosis over the dorsum, and angular cheilitis. She was nulliparous, with no antecedent of immunodeficiency. Seven years before actual

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admission, she underwent sessions of chemotherapy and chest radiation therapy to control a high-grade B-cell lymphoma, with success. Physical examination disclosed body temperature: 36.5o C, BMI: 37 kg/m², blood pressure: 160/80 mm/mmHg, heart frequency: 128 bpm, and SpO₂: 87%. The most remarkable changes on physical examination were observed in the skin of soles, nails, and oral mucosa, in addition to obesity. Discoloration of the nail plates, excessive curvature on the transverse axis, accentuated hyperkeratosis and upward slant feature of all fingernails (“wedge-shaped,” “pincer nails”), in addition to sparse hyperkeratotic plaques on the palmar surfaces (Figure 1); dystrophy of all toe nails, with massive thickening and positioned at an angle of approximately 45o to the distal phalanx axis (“leaning tower nails”). There was associated severe plantar keratoderma, which was more conspicuous over pressure areas. Although less noticeable following local treatment, there were angular cheilitis and white oral patches (leukokeratosis) along the right bite line (Figure 2).



Figure 1. Discoloration of the nail plates, hypercurvature on the transverse axis, accentuated hyperkeratosis and upward slant feature of all fingernails (“wedge-shaped, pincer nails”), in addition to sparse hyperkeratotic plaques on the palmar surfaces (arrows)

Physical signs indicative of parenchyma consolidation were elicited by percussion and auscultation of the right hemithorax, and there was bilateral pitting edema in lower extremities. Chest radiography showed suggestive images of collapsed tissue and fibrous bands in the right lung. Further images of CT and angio MRI of the thorax confirmed partial right lung atelectasis (Figure 3) corresponding to compressive sequels of the mediastinal lymphoma previously treated. Laboratory serum determinations showed urea nitrogen 38.5 mg/dL, creatinine 0.6 mg/dL, albumin 5.3 g/dL, globulins 4.6 g/dL, calcium 1.25

mmol/L, phosphate 3.7 mg/dL, sodium 140 mEq/L, potassium 4.4 mEq/L, magnesium 1.8 mEq/L, uric acid 6.2 mg/dL, glucose 142 mg/dL, glicate hemoglobin (HbA1c) 6%, ALT 36.2 U/L, AST 26.3 U/L, alkaline phosphatase 85.7 U/L, Gamma-GT 280 U/L, C-reactive protein 2.5 mg/dL, TSH 3.73 μU/mL, and free T4 1.72 ng/dL, triglycerides 178 mg/dL, total cholesterol 282 mg/dL, HDL 82 mg/dL, LDL 164.4 mg/dL, and VLDL 35.6 mg/dL. Hematology tests revealed leukocytes 10.65 x 10⁹/mm³, red cells 4.54 x 10¹²/mm³, hematocrit 43.5%, hemoglobin 13.1 g/dL, and platelets 387 x 10⁹/mm³. Respiratory symptoms gradually improved with clinical management, and after the hospital discharge the patient was referred to Pneumology and Dermatology outpatient surveillance.



Figure 2. Discoloration and conspicuous dystrophy of all toe nails, characterized by intense thickening and positioned at an angle of approximately 45o to the phalanx angle (“leaning tower nails”), associated with severe plantar keratoderma, which is more evident at pressure areas. Moderate grade of edema is evident on the dorsum of both feet

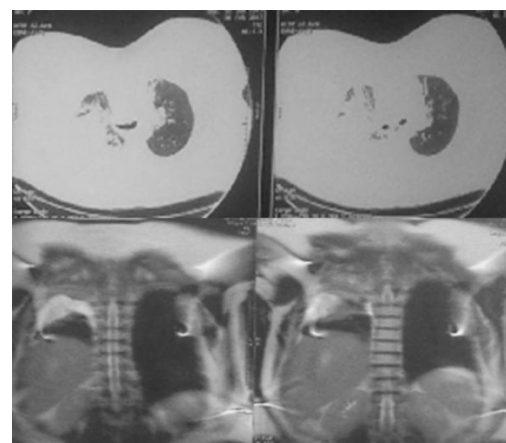


Figure 3. Images of CT and angio MRI of the thorax revealing collapsed tissue and fibrous bands, which are related to longstanding partial right lung atelectasis

Discussion

Diagnosis of PC-I was herein established with a base on classical clinical features (1-4,5,7,8,10). Histological, immunohistochemical and ultrastructural data can be contributory, but not essential (10). Actually, molecular genetic testing is considered the gold-standard method to confirm clinical classifications of PC (10), and sequence analysis of KRT6A, KRT6B, KRT16, and KRT17 can identify mutations in approximately 90% of patients with previous clinical diagnoses of PC (10). Notwithstanding, this sophisticated resource is not disposable for daily practice in the majority of developing countries. In patients presenting with less typical features of PC, differential diagnoses should be ruled out, including Clouston syndrome, dyskeratosis congenital manifestations, epidermolysis bullosa simplex, familial onychogryphosis, focal non-epidermolytic palmoplantar keratoderma, onychomycosis, palmoplantar keratoderma striata, pityriasis rubra pilaris, psoriasis, traumatic thickening, and twenty nail dystrophy without keratoderma (10,11).

Management of pain and discomfort due to palmoplantar keratoderma includes reduction of local pressure and trauma, limitation of walking or standing, control of body weight and use of adequate socks and shoes. Special care with removal of dystrophic nails and hyperkeratotic areas, and use of keratolytics are frequently needed; emollients containing petrolatum or lanolin, and creams or lotions with urea, lactic acid, salicylic acid, or propylene glycol are often utilized (8,10,11). The patient herein described had a mediastinal lymphoma at the age of 32 years. The immunohistochemistry study of tumor specimens (Figure 4) showed expression of B-cell markers (CD-20 and CD-79), high index of proliferation (reactivity of nuclear pattern to Ki-67 protein), absence of T-cell markers, as well as of markers for Hodgkin and anaplastic lymphomas (CD-15 and CD-30).

Therefore, an interesting aspect in this case study is about the triad of discolored and dystrophic nails, pulmonary disorders, and bilateral edema of lower limbs, which could mimic the classical hallmark of the yellow-nail-syndrome. Moreover, association with cancer or lymphoma has been described in patients with yellow-nail-syndrome (12,13). However, the course of the disease, the aspect of the nails and massive hyperkeratosis ruled this syndrome out. Although squamous cell carcinomas may occur in the course of the plantar lesions of PC, there is a unique report of coexistent acute lymphoblastic leukemia and PC, in a

20-month-old boy (14). With a base in rare data, the association between PC1 and lymphoma seems to occur for chance.

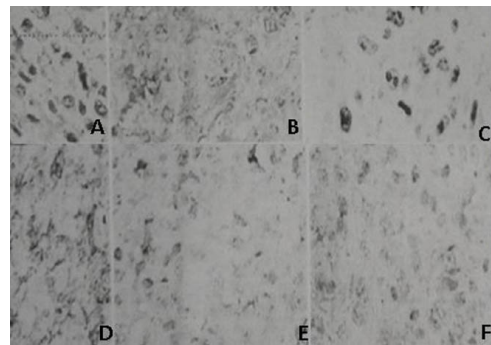


Figure 4. (Immunohistochemical study/ Phenotypic characterization of lymphoma). A and B: Neoplasm features, with absence of epithelial markers; C: High proliferation index (nuclear reactivity to Ki-67 protein); D: Presence of B phenotype (CD-20); E: Absence of T phenotype (CD-3); F: Absence of CD-30 marker (Avidin-biotin-peroxidase complex method x400)

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