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Original Article

Keratoderma of palms and soles is an umbrella for the first manifestation of different skin diseases

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Abstract

Backgound Keratoderma is a manifestation of different skin diseases whether inherited or acquired, systemic or cutaneous diseases, and is demonstrated as the thickening of the epidermis of palms and soles singly or in combination.

Objective To record all cases of keratoderma those are seen in daily clinical practice over a specified period.

Methods This is a case series descriptive study where all patients with keratoderma of palms and or soles were recorded during years between 2014-2022years.Full history and clinical examination were carried out aiming to establish the right clinical diagnosis and all demographic features were recorded. Biopsies for histopathological assessment were carried out in suspected cases and a scrape for fungus was done in patients with tinea as a confirmatory test.

Results Forty-two patients with keratoderma were seen during this specified period, their ages ranged from 6 months-30years with a median of 6 years, with 32 (94%) males and 2 (5.88%) females. Regarding the diagnosis of keratoderma, 13(30.95%) with congenital, 11 (26%) with pityriasis rubra pilaris, 7 (16.66%) with lichen planus, 6 (14.7%) with dermatophytes and 5 (11.9%) with psoriasis.

Conclusion Kertatoderma is a disease of male patients which has different etiological factors commonly congenital, followed by pityriasis rubra pilaris, then lichen planus, dermatophytes, and Psoriasis. Keratoderma could be the only manifestation of these diseases where the diagnosis could be very difficult, especially in the acquired variants.

Key words
Keratoderma; Lichen planus; Ppityriasis rubra pilaris; Dermatophyte; Psoriasis; Hhyperkeratosis.

Introduction

Palmoplantar keratoderma (PPK) refers to a skin thickening of the palms and soles caused by excessive production of keratin.[1] Most reported studies demonstrate PPK a heterogeneous group of disorders that are classified as congenital or acquired.[2,3] Congenital PPK usually occurs earlier in life, can be traced in family members, and may be accompanied by well-described syndromes. Acquired PPK occurs later in life, without a positive family history, and tends to be attributable to an underlying etiology as reported by Bolognia and Patel carried out studies.[4,5]

Congenital PPK has been reviewed in the

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literature, in a study performed by Stevens *et al*. in1996[6] suggested a new classification for these disorders. Itin and Fistrol in 2005 classified congenital PPK according to inheritance and molecular basis.[7] The main features that distinguish congenital PPK from acquired PPK are the presence of a positive family history, early age of onset of disease, associated syndromes, and relative treatment resistance as reported by the Schiller *et al*. carried out study.[8] The clinical examination can usually differentiate congenital PPK into 3 categories: diffuse, focal, or punctate as a study carried out by Thomas *et al*.[9] Diffuse hereditary palmoplantar keratodermas: with no associated features.[10] Diffuse non- epidermolytic palmoplantar keratodermas.[11] Diffuse Hereditary Palmoplantar Keratodermas: with associated Features.[12] Focal hereditary palmoplantar keratodermas: with no associated features.[13] Focal hereditary palmoplantar keratodermas: with associated Features.[14] Papular hereditary palmoplantar keratodermas: with no associated Features.[15] Papular hereditary palmoplantar keratodermas: with associated Features.[16]

Acquired PPK have different epidermal patterns of involvement: diffuse, focal, and punctate. Diffuse PPK refers to uniform involvement of the palms and plantar surfaces, including the central palmer area and the instep. Focal PPK describes localized areas of hyperkeratosis, mainly over pressure points that may be oval (nummular) or linear (striate). Punctate PPK (papular or disseminated) consists of multiple scattered, discrete round lesions of tiny keratotic papules on the palms and soles. A similar study was carried out by Champion and Bolognia.[3,4]

Histopathological examination of keratodermas are in general nonspecific, with marked hyperkeratosis of the stratum corneum being the most prominent finding, along with the presence of the following characteristics: epidermal acanthosis, parakeratosis, hyperplasia of the stratum spinosum and granular layer, and perivascular infiltrate of chronic inflammatory cells as reported by Farmer *et al*. study.[17] Acquired PPK can be classified as studied carried out by Patel et. al.[5] into: Keratoderma climectericum,[18] drug-associated (e.g. glucan, fluorouracil, lithium),[19] malnutrition-associated,[20] chemically-associated (e.g. Arsenic, chloracnegens),[21] systemic disease-associated (e.g. hypothyroidism, myxedema),[22] malignancy-associated (e.g. acrokeratosis paraneoplastic, tripe palms, mycosis fungoides),[23] dermatosis-associated (e.g. psoriasis, lichen planus, pityriasis rubra pilaris, lichen nitidus, and lupus erythematosus, atopic dermatitis),[24-27] infectious (e.g. syphilis, trichophytosis, leprosy, tuberculosis)[28] and idiopathic cause.[29]

Palmoplantar lichen planus are rare and challenging to diagnose. Different clinical forms of lichen planus of the palms and soles have been documented by most of the reported studies: Hypertrophic, diffuse scaly, psoriasiform, a plaque with collarette scale, keratotic plaque with pits, punctate keratosis, vesicular, macular, and diffuse keratoderma.[30,31] The carried out study demonstrated by Sharquie *et al*. considered the percentage of hypertrophic type of lichen planus on lower legs was 9.4%.[31]

Palmoplantar psoriasis involvement alone is rare approximately 3-4% of all psoriasis presentations as reported by most of the carried-out studies.[32] Hyperkeratosis of palms and soles can be both central and diffuse. Nail pitting, depressed keratotic plaques on the sides of the fingers, involvement of the knuckles, presentation of psoriatic plaques, and histopathology results, may aid in the correct diagnosis of palmoplantar psoriasis as considered by Kumar *et al*. studies.[24] Pityriasis rubra pilaris can present as thickening of the

palms and soles with red-orange waxy or yellowish PPK so-called "sandal-like" PPK which may occur with, before, or after the development of other clinical findings as reported by Eastham et. al. study.[33] Tinea pedis or dermatophytosis is called "athlete's foot". It is caused by a fungus that grows predominantly in warm moist environments and causes this infection that usually involves feet and toes as demonstrated by the Kumar et. al. study[34] Hyperkeratotic or Moccasin type Tinea pedis: consists of dry, scaling and hyperkeratosis involving the plantar and lateral aspect of the foot. This infection is commonly bilateral and is usually accompanied by subungual onychomycosis. This type of infection is commonly to be due to Trichophyton rubrum infection as described in the literature.[35]

Patients and Methods

Forty-two patients complaining of keratoderma of palms and/ or soles gathered during the period from 2014-2022 years were involved in this descriptive, observational, case-series clinical-histopathological study. Patients primarily presented with keratoderma of hands and/ or feet included in the study while others presented as part of generalized body involvement were excluded. The study followed the principles of the Declaration of Helsinki. Informed Consent forms were reported from all patients after discussing the nature of the study. The close-up photo was taken at the same place with a fixed distance and illumination. In addition, all included patients accepted the idea to share their photos in this present work. A thorough full history including family history, history of malignancy, blistering, sweating, and associated features including hearing loss, abnormal hair, nail, teeth, and mucosal problem aiming to establish the right clinical diagnosis with a well-established examination was done. Name, age, gender, residence, occupation, and past medical and drug history were taken from all patients. The type of lesions, duration of the disease, site, size, and number of lesions were also evaluated. All demographic features were recorded. Biopsies for histopathological assessment were carried out in suspected cases and a scrape for fungus for potassium hydroxide (KOH) and culture exam was done in patients with tinea as a confirmatory test.

Results

Forty-two patients with different variants of keratoderma were considered in the present work, their ages ranged from 6 months-30years with a median of 6 years, with 32 (94%) males and 2 (5.88%) females. The Types of keratoderma of palms and soles in the studied patients were illustrated in **Table 1**.

Regarding the diagnosis of keratoderma, 13 (30.95%) with congenital mostly ectodermal dysplasia cases, 11 (26%) with pityriasis rubra pilaris, 7 (16.66%) with lichen planus, 6 (14.7%) with dermatophytes and 5 (11.9%) with psoriasis. **(Figures 1-6).** In the present study, keratoderma of both palms and soles were documented in 11 (26%) patients, while palms only in 17 (40.47%) patients and soles only in 14 (33.33%) patients making the hands were dominant presentations with keratodermas.

Discussion

PPK has been considering challenging conditions whether congenital or acquired and

Table 1 Clinical diagnosis of Keratoderma of palms and soles in the present study.

Clinical type of Keratoderma	*Numbers of Patients*	*Percentage of Total*
Congenital mostly ectodermal dysplasia	13	30.95
Pityriasis rubra pilaris	11	26
Lichen planus	7	16.66
Dermatophytes	6	14.7
Psoriasis	5	11.9

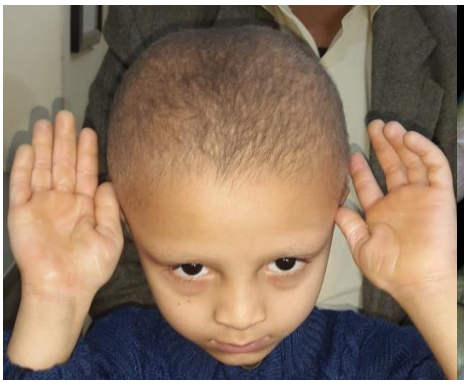

Figure 1 Showing keratoderma of palms in a child with ectodermal dysplasia.

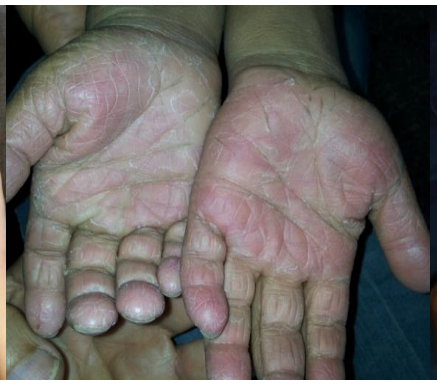

Figure 2 Showing keratoderma in a patient with ectodermal dysplasia.

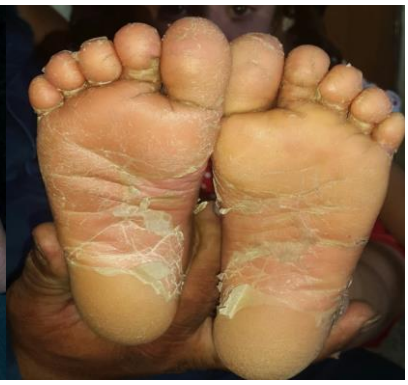

Figure 3 showing keratoderma of soles in a patient with pityriasis rubra pilaris.

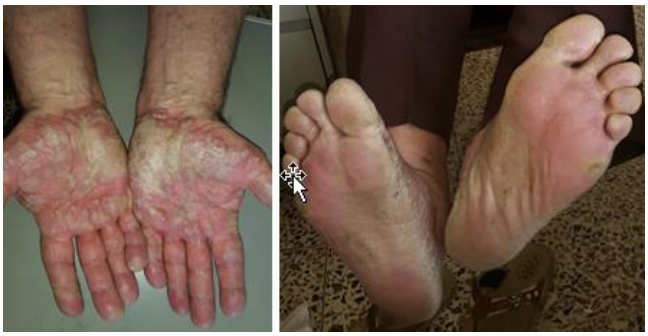

Figure 4 Showing keratoderma of palms and soles in a patient with lichen planus.

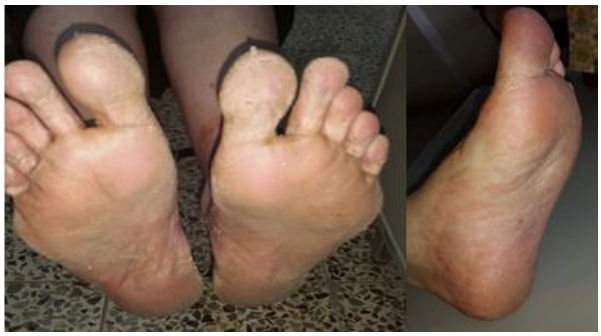

Figure 5 Showing keratoderma of soles in a patient with chronic dermatophyte infection.

Figure 6 Showing keratoderma of soles in a patient with psoriasis.

associated with a wide range of etiologies making the diagnosis of this category important as may predict the underlying systemic involvement.

It's highly significant to distinguish congenital from acquired PPK as reported.[8] Congenital keratoderma presented early onset of life, with positive family history and without identified cause, diagnose genetically, and sometimes difficult to differentiate from other causes of keratoderma. Treatment is usually symptomatic because of little improvement on conventional therapy. Periodic follow-up of patients with congenital keratoderma is required as other systemic features might appear later in life. In acquired PPK the cause can be identified and treated accordingly. Histopathology is less significant in the diagnosis of congenital PPK but can establish the diagnosis in some other types of acquired PPK like psoriasis, and lichen planus.

In the present study, keratoderma of both palms and soles were documented in 26% of patients, while palms only in 40.47% of patients, and soles only in 33.33% of patients making the

hands were dominant presentation with keratodermas. Congenital keratoderma of hands and feet was large in number because those patients are mostly children and have purely hands and feet problems identified. Palms and soles are uncommon sites of lichen planus involvement.[36] The studies carried out by Landis and Sinha demonstrated only 12.9% of all lichen planus patients have palmoplantar lesions and only a quarter of them present with exceptional lesions on palms and soles.[37,38] In the present study 16.66% of palmoplantar lichen planus patients were demonstrated. It's not surprising the high number of lichen planus on hands and feet in the present study because it's a common problem and there is an upsurge of cases of lichen planus in the Iraqi population.[31] In cases of lichen planus palmoplantar keratoderma, it's important to look for lichen planus in missing or hidden areas like nails and inside the mouth, for whitish Wickham striae discoloration to help in establishing the right diagnosis.

In Psoriasis, keratoderma of hands and feet mostly occurs as part of generalized skin involvement and does not commonly involve just hands and feet alone and this explains the low number of cases of psoriasis in the present study. During diagnosis of palmoplantar psoriasis, examination of other parts of the body especially nails for pitting, scalp for thick scales, and post-auricular erythema are required as these areas are commonly involved and could be helpful to reach the right diagnosis in difficult cases. Also, positive family history of psoriasis can aid in the correct diagnosis. Palmoplantar psoriasis although with lower surface area involvement can impact the quality of life of the patients and could be the warning sign for the early manifestation of psoriatic arthritis, therefore early diagnosis and treatment prevent the progression of the disease.

Pityriasis rubra pilaris affect different age groups and is mostly presented in infancy and children, this explains the high reported numbers in the present study. Keratoderma of palms and soles are yellowish in discoloration and over time other manifestations appear like perifollicular keratotic papules and plaques over elbows, knees, and trunk and these manifestations can lead to correct diagnosis, especially in doubtful cases. Also, it could be confused with many other causes of congenital and acquired PPK but Proper history, physical examination, and histology aid in diagnosis.

Dermatophytosis is now running an epidemic state in the Iraqi population with diverse clinical manifestations thus mimicking many skin diseases and often resistant to treatment.[39,40] This explains the high frequency of dermatophyte infection as a cause of keratoderma but surprisingly no associated nail infection was observed. Examination of the groin as a hidden site for tinea cruris identification sometimes gives clues to the diagnosis of dermatophyte keratodermas as these cases were often misdiagnosed and treated as psoriasis. So this is the first reported study that demonstrated fungal infection as one of the main causes of acquired PPK.

Conclusion

Keratoderma is a disease of male patients which has different etiological factors commonly congenital, followed by pityriasis rubra pilaris, then lichen planus, dermatophytes, and Psoriasis. Keratoderma could be the only manifestation of these diseases where the diagnosis could very difficult. This present study will be very helpful for dermatologists to delineate the correct diagnosis of keratoderma.

References

1. Arnold Jr HL, Odom RB, James WD. Andrews' diseases of the skin: clinical

dermatology. 8th ed. Philadelphia (PA): WB Saunders, 1990.
2. Freedberg IM, Eisen AK, Wolff K, *et al*. Fitzpatrick's dermatology in general medicine. 6th ed. New York: McGraw-Hill, 2003.
3. Champion RH, Burton JL, Burns DA, *et al*. Rook, Wilkinson, Ebling textbook of dermatology. 7th ed. Malden (MA): Blackwell Science Ltd, 2004: 34, 79-107.
4. Bolognia JL, Jorizzo JL, Rapini RP. Dermatology. New York: Mosby, 2003: 809-10.
5. Patel, S., Zirwas, M. & English, J.C. Acquired Palmoplantar Keratoderma. *Am J Clin Dermatol*. 2007;**8**:1–11. https://doi.org/10.2165/00128071-200708010-00001.
6. Stevens HP, Kelsell DP, Bryant SP, *et al*. Linkage of an American pedigree with palmoplantar keratoderma and malignancy (palmoplantar ectodermal dysplasia type III) to 17q24: literature survey and proposed updated classification of the keratodermas. *Arch Dermatol*. 1996;**132**:640-51.
7. Itin PH, Fistrol SK. Palmoplanter keratodermas. *Clin Dermatol*. 2005;**23**:15-22.
8. Schiller S, Seebode C, Hennies HC, Giehl K, Emmert S. Palmoplantar keratoderma (PPK): acquired and genetic causes of a not so rare disease. *J Dtsch Dermatol Ges*. 2014;**12**:781–8.
9. Thomas BR, O'Toole EA. Diagnosis and Management of Inherited Palmoplantar Keratodermas. *Acta Derm Venereol*. 2020; **100(7)**:adv00094. doi: 10.2340/00015555-3430. PMID: 32147745; PMCID: PMC9128927.
10. Navsaria HA, Swensson O, Ratnavel RC, Shamsher M, McLean WH, Lane EB, *et al*. Ultrastructural changes resulting from keratin-9 gene mutations in two families with epidermolytic palmoplantar keratoderma. *J Invest Dermatol*. 1995;**104**: 425–9.
11. Blaydon DC, Lind LK, Plagnol V, Linton KJ, Smith FJ, Wilson NJ, *et al*. Mutations in AQP5, encoding a water-channel protein, cause autosomal-dominant diffuse nonepidermolytic palmoplantar keratoderma. *Am J Hum Gen*. 2013;**93**:330–5.
12. Maestrini E, Monaco AP, McGrath JA, Ishida-Yamamoto A, Camisa C, Hovnanian A, *et al*. A molecular defect in loricrin, the major component of the cornified cell envelope, underlies Vohwinkel's syndrome. *Nat Genet*. 1996;**13**:70–7.
13. Rickman L, Simrak D, Stevens HP, Hunt DM, King IA, Bryant SP, *et al*. N-terminal deletion in a desmosomal cadherin causes the autosomal dominant skin disease striate palmoplantar keratoderma. *Hum Mol Genet*. 1999;**8**:971–6.
14. Blaydon DC, Etheridge SL, Risk JM, Hennies HC, Gay LJ, Carroll R, *et al*. RHBDF2 mutations are associated with tylosis, a familial esophageal cancer syndrome. *Am J Hum Genet*. 2012;**90**:340–6.
15. Pohler E, Mamai O, Hirst J, Zamiri M, Horn H, Nomura T, *et al*. Haploinsufficiency for AAGAB causes clinically heterogeneous forms of punctate palmoplantar keratoderma. *Nature Genet*. 2012;**44**:1272–6.
16. Chourabi M, Liew MS, Lim S, H'Mida-Ben Brahim D, Boussofara L, Dai L, *et al*. ENPP1 Mutation Causes Recessive Cole Disease by Altering Melanogenesis. *J Invest Dermatol*. 2018;**138**:291–300.
17. Farmer ER, Hood AF. Pathology of the skin. 2 nd ed. New York: McGraw-Hill, 1990: 143, 653-4.
18. Haxthausen H. Keratoderma Climactericum. *Br J Dermatol*. 1934;**46**:161-7.
19. Duvic M, Reisman M, Finley V, *et al*. Glucan-induced keratoderma in acquired immunodeficiency syndrome. *Arch Dermatol*. 1987;**123**:751-6.
20. Lee BY, Hogan DJ, Ursine S, *et al*. Personal observation of skin disorders in malnutrition. *Clin Dermatol*. 2006;**24**:222-7.
21. Poskitt LB, Duffill MB, Rademaker MR. Chloracne, palmoplantar keratoderma, and localized scleroderma in a weed sprayer. *Clin Exp Dermatol*. 1994;**19**:264-7.
22. Miller JJ, Rolling D, Spiers E, *et al*. Palmoplantar Keratoderma associated with hypothyroidism. *Br J Dermatol*. 1998; **139**:741-2.
23. Kerdel FA, MacDonald DM. Palmo-plantar keratoderma associated with carcinoma of the bronchus. *Acta Dermato Venereol*. 1982; **62(2)**:178-80.
24. Kumar B, Saraswat A, Inderjeet K. Palmoplantar lesions in Psoriasis: A study of 3065 patients. *Acta Derm Venereol*. 2002; **82**:192-5.
25. Munro CS, Cox NH, Marks JM, *et al*. Lichen nitidus presenting as palmoplantar

hyperkeratosis and nail dystrophy. *Clin Exp Dermatol*. 1993;**18**:381-3.
26. Ashinoff R, Werth VP, Franks AG. Resistant discoid lupus erythematosus of palms and soles: successful treatment with azathioprine. *J Am Acad Dermatol*. 1988; **19**:961-5.
27. English JC, McCollough ML. Transient reactive papulotranslucent acroker atoderma. *J Am Acad Dermatol*. 1996;**34**:686-7.
28. Premalatha S, Augustine SM, Yesudian P, *et al*. Punctate palmoplantar keratosis acuminate: an unusual form of tuberculid. *Int J Dermatol*. 1982;**21**:470-1.
29. Herman PS. Punctate porokeratotic keratoderma. *Dermatologica*. 1973;**147**: 206-13.
30. Landis M, Bohyer C, Bahrami S, Brogan B. Palmoplantar lichen planus: A rare presentation of a common disease. *J Dermatol Case Rep*. 2008;**2(1)**:8-10.
31. Sharquie KE, Noaimi AA, Shararah ZAA "Upsurge of cases of lichen Planus in Iraqi Population in Baghdad City with Frequency of Hepatitis Viruses." *IOSR J Dental Med Sci*. 2015:78-81.
32. Farber EM, Nall ML. Natural history of psoriasis in 5600 patients. *Dermatologica*. 1974;**148**:1-18.
33. Eastham AB. Pityriasis Rubra Pilaris. *JAMA Dermatol*. 2019;**155(3)**:404.
34. Kumar, Vikas & Tilak, Ragini & Prakash, Pradyot & Nigam, Chaitanya & Gupta, Richa.. Tinea Pedis– an Update. *Asian J Med Sci*. 2011;**2**:134-8.
35. Masri-fridling GD. Dermatophytosis of the feet. *Dermatologic Clinics*.1996;**14**:33-40. http:// dx.doi.org/10.1016/S0733-8635 (05)70322-3.
36. Gutte R, Khopkar U. Predominant palmoplantar lichen planus: A diagnostic challenge. *Indian J Dermatol*. 2014; **59(4)**:343-7.
37. Landis M, Bohyer C, Bahrami S, Brogan B. Palmoplantar lichen planus: A rare presentation of a common disease. *J Dermatol Case Rep*. 2008;**2(1)**:8-10.
38. Sinha S, Sarkar R, Kumar V. Palmoplantar lesions of lichen planus. *Indian J Dermatol*. 2018;**63(1)**:57-61.
39. Sharquie KE, Jabbar RI. Major outbreak of dermatophyte infections leading into imitation of different skin diseases: Trichophyton Mentagrophytes is the Main Criminal Fungus. *J Turk Acad Dermatol*. 2021;**15(4)**:91-100.
40. Sharquie KE, Jabbar RI. New multiple therapy of resistant and relapsing dermatophyte infections during epidemic status. *J Pak Assoc Dermatol*. 2022; **32(3)**:464-71.