Triangular Lunulae in Papillon-Lefèvre Syndrome_ A Case Report

Zarak Shiraz[1], Fahad Faizullah[2], Qaisar Ali Khan[3], Irfan Ullah[1], Mehran Khan[1], Bader Semakieh[4], Zain Islam[5], and Ravina Verma[6]

[1]Khyber Teaching Hospital MTI KTH
[2]Hayatabad Medical Complex
[3]Khyber Teaching Hospital MTI KTH, Peshawar
[4]Arkansas College of Osteopathic Medicine
[5]KMU Institute of Dental Sciences
[6]St.Georges University School of Medicine

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Abstract

Background: Papillon-Lefèvre Syndrome is a rare autosomal recessive disorder characterized by the presence of palmoplantar hyperkeratosis and severe periodontitis leading to premature loss of dentition. Triangular lunulae is a feature considered pathognomonic for an entirely unrelated condition, the Nail and Patella Syndrome, and has not been previously reported together with Papillon-Lefèvre Syndrome.

Case Summary: A 16-year-old girl presenting with a long-term history of palmoplantar hyperkeratosis extensive loss of dentition and a short-term history of pyogenic infection of the right big toe. The examination of the patient revealed a rare finding of triangular lunulae on all fingernails. The patient was diagnosed clinically as a case of Papillon-Lefèvre Syndrome. Evaluation of other family members allowed early diagnosis of the syndrome in another sibling and the timely initiation of treatment to prevent similar morbidity as in the primary patient.

Conclusion: Triangular lunulae, considered pathognomonic for Nail-Patella Syndrome, may also be a feature of other syndromes, such as the case here.

Keywords: triangular lunulae, Papillon-Lefèvre syndrome, case report

Key Clinical Message: Triangular lunulae, considered pathognomonic for Nail-Patella Syndrome, may also be a feature of other syndromes, such as the case here. Papillon-Lefèvre syndrome is a rare genodermatosis associated with significant morbidity. Consanguinity is an established high-risk factor. Early diagnosis and treatment can mitigate the morbidity in affected individuals and societal awareness around consanguinity can help reduce the burden of the disease in populations where the practice is common.

Introduction: First described by Papillon and Lefèvre in 1924 [1], Papillon-Lefèvre Syndrome (PLS) is a rare, autosomal recessive disorder [2] characterized by the presence of palmoplantar hyperkeratosis and frequent bacterial infections, particularly severe periodontitis resulting in early loss of deciduous and, eventually, permanent teeth [2-3]. The prevalence of the PLS is reported to be 1-4 cases per million individuals [4]. Skin changes are the earliest to appear, usually within the first year of life, with diffuse, erythematous, palmoplantar hyperkeratosis being the most commonly noted presentation [3]. Additional features may inclu-

de dural and choroid plexus calcifications, hyperkeratotic plaques on the elbows and knees, pseudo-ainhums around digits, and infrequently, mental retardation [3, 4]. PLS is caused by a mutation in the CTSC gene encoding a lysosomal protease, cathepsin C [5]. The gene is widely and strongly expressed in immune cells, such as neutrophils and macrophages, and also at sites mainly affected in PLS, including the palms, soles, knees, and keratinized gingiva in the oral cavity, elucidating the mechanisms underlying the symptomatology that is observed [5]. Aberrations in the normal functioning of cathepsin C in neutrophils in PLS have been noted to result in their excessive recruitment to periodontal tissue which, paired with their reduced antimicrobial ability due to the protease deficiency, leads to the classical, severe periodontitis that is noted in the disorder and which is the main reason for the premature exfoliation of primary and secondary teeth [6]. Besides periodontitis, infections of other sites are also common in patients with PLS, including pyogenic skin infections, abscesses in internal organs such as the kidneys and liver, and recurrent respiratory and urinary tract infections [7]. An allelic variant of PLS, Haim-Munk syndrome is also characterized by the cardinal features of PLS, namely, palmoplantar hyperkeratosis and premature periodontal destruction but with the addition of onychogryphosis, acro-osteolysis, and arachnodactyly [8].

Nail and Patella Syndrome is a distinct clinical entity, a rare autosomal dominant condition comprising variable nail, skeletal, and systemic anomalies, including patellar hypoplasia and agenesis, elbow dysplasia, radial head dislocation, characteristic iliac horns, nail abnormalities, nephropathy and glaucoma [9]. Though nail abnormalities are variable, triangular lunulae in the fingernails are considered pathognomonic for the condition [10]. So far, the presentation of triangular lunulae has not been reported with other conditions. Identifying the feature in our patient with PLS is the first report of its nature.

Case History and Clinical Examination: A 16-year-old girl, the second eldest of four daughters to parents who were first-degree cousins, was referred to the dermatology clinic at Khyber Teaching Hospital, Peshawar, Pakistan with a 3-months-long complaint of a small, soft outgrowth from the lateral periungual skin fold of the right big-toe that appeared spontaneously as an erythematous papule and grew slowly in size with time, eroding the adjacent nail plate and ultimately exuding purulent discharge. On further inquiry, the patient's mother reported a history of persistent and progressively worsening thickening, scaling, and fissuring of the palms and soles that was first noticed when the patient started walking at the age of one. Initially, the complaint was restricted to the palms and soles but later progressed to involve the dorsal surfaces of the hands and feet. The skin complaints were accompanied by frequent swelling and friability of the gums which became more noticeable and pronounced when the patient began to prematurely lose her primary dentition by the age of two, which had sprouted normally. The gum complaints subsided once all deciduous teeth were lost, only to reappear with the eruption of secondary dentition. Consequently, the patient also lost most of her secondary dentition by the age of 11. The patient also had a history of recurrent, focal skin infections over the years, primarily on the scalp, that were slow to resolve and would frequently lead to ulceration. However, these lesions were responsive to topical and oral antibiotics. There was also a history of progressively worsening dystrophy of the nails of the fingers and toes and thickened, scaly plaques on the elbows and knees that had resolved a few years back to leave behind atrophic, hypopigmented skin. According to the mother, there were no ante- or postnatal complications, and the patient was otherwise healthy and achieved her developmental milestones on time. Over the years, the patient had had numerous outpatient visits to dental and dermatological clinics, however, a firm diagnosis was not made, resulting in interrupted and mostly symptomatic medical management. The youngest sister of the patient, age 9 years, was also found to be following an almost identical sequence of symptoms as the patient, including palmoplantar thickening, loss of secondary dentition, and frequent slow-healing, scalp infections.

On examination, the patient had diffuse palmoplantar erythema, thickening, and scaling that extended confluently onto the dorsal aspects of the hands and feet. Multiple areas of fissuring were noted on the palms and soles (Figures 1 & 2).

Concentric band-like thickening of the skin of the fingers was also observed (Figure 3A) resulting in accentuation of the pulp of the soft tissue between the interphalangeal joints. The fingernails showed an exaggerated longitudinal curvature, an enlarged triangular lunula (Figures 2A & 3B), multiple pits and horizontal grooves,

and slight distal discoloration (Figure 3B).

The right big toenail had a 1x1cm soft, fluctuant, exophytic growth with purulent exudate and crusting arising from the left, lateral periungal skin fold and involving the lateral nail bed (Figure 4A). Both big-toe nails showed yellow discoloration and multiple horizontal and longitudinal grooves. The second and fifth toenails of the left foot showed onychogryphosis while the remainder of the toenails of the left foot showed mild dystrophy (Figure 4B). The second to fifth toenails of the right foot were normal (Figure 4A). Triangular lunulae were not noted in the toenails.

Oral cavity examination revealed signs of mild gingival inflammation of the right, lower side. Two upper molars, a single left lower molar, and a loose right upper incisor were the only teeth noted (Figure 5). The elbows had bilaterally symmetrical hypopigmented, atrophic plaques (Figure 6A) whereas the knees showed similar plaques without atrophy (Figure 6B). No abnormality of the hair was noted. A systemic examination was also unremarkable.

Examination of the younger sister of the patient revealed plantar thickening and scaling, increased dental spacing with signs of gingival inflammation, and an ulcerated plaque on the scalp with alopecia (Figure 7).

Methods: Biochemical and radiological workup was unremarkable. This included an ultrasound of the abdomen and pelvis, a skull X-ray, and an X-ray of the hands and feet to rule out liver and renal abscesses, intracranial calcifications, and acro-osteolysis, respectively. A genetic analysis could not be done given the nonavailability of the facility in Pakistan. Work-up did not identify features consistent with Nail and Patella syndrome.

Results and Conclusion: Based on the history and examination, a clinical diagnosis of Papillon-Lefèvre Syndrome was made. The patient and family were counseled regarding the diagnosis in both the patient and her sister and its implications and prognosis. The patient was started on oral Isotretinoin, antibiotics, a topical combination of a Vitamin D analog and steroids, and emollients. Surgery and Dentistry departments were involved in the management of the right big toe granulation tissue and dental rehabilitation, respectively. Papillon-Lefèvre syndrome is a rare genodermatosis associated with significant morbidity. Consanguinity is an established high-risk factor. Early diagnosis and treatment can mitigate the morbidity in affected individuals and societal awareness around consanguinity can help reduce the burden of the disease in populations where the practice is common.

Discussion: Despite the inability to pursue genetic testing for a confirmed diagnosis, the abundant clinical evidence in the patient, supported by the consanguinity of the parents and similar clinical findings in another sibling helped in establishing the diagnosis of Papillon-Lefèvre Syndrome. Papillon-Lefèvre Syndrome is a rare autosomal recessive disorder whose prevalence is estimated at 1-4 cases per million individuals using statistical analysis [2]. The results of such estimations depend on the accuracy of the data on consanguinity in the study population, indicating that the mentioned prevalence may be an underestimation for populations with higher rates of consanguinity, such as Pakistan [11]. Higher numbers of PLS in countries with similarly high rates of consanguinity, for example, Saudi Arabia and India [12,13], may serve as an indication of the prevalence of the disease in Pakistan. Early diagnosis and treatment may control the periodontitis observed in PLS and significantly delay or even stop the loss of teeth. Rigorous dental care under the supervision of a dentist, stringent oral hygiene, prophylactic antibiotic cover, and the use of oral retinoids have all been indicated in the preservation of teeth in PLS [14]. Dental prostheses can significantly reduce morbidity in patients with extensive teeth loss. Unfortunately, a timely diagnosis was missed in our patient resulting in loss of almost all teeth. Establishing the diagnosis in our patient helped us diagnose the younger sibling with PLS as well, allowing her to seek early treatment. The allelic variant of PLS, Haim-Munk syndrome, is extremely rare, however, cases have been reported in Pakistan and in Pakistani origin families [15]. Our patient had onychogryphosis of her toenails, a feature found in Haim-Munk syndrome [8] but lacked acro-osteolysis and arachnodactyly. The remarkable finding noted in our patient was the presence of a triangular lunula, which is one of the pathognomonic features of Nail-Patella syndrome [16]. To the best of our knowledge, literature on PLS has not mentioned the presence of triangular lunula of nails, which in our patient indicates an extremely

rare finding. The underlying mechanisms behind the development of the triangular lunulae remain an enigma though its association with median nail dystrophy has been reported [17]. Identification of the triangular lunulae in our case opens the possibility of the feature occurring in other conditions as well.

Author's Contribution: ZKS, MK, and IU conceived the idea, collected the patient information, and critically reviewed the manuscript. ZI was responsible for graphics, and ZI, QAK, BS, and RV wrote the initial manuscript. All authors reviewed and approved the final manuscript before submission.

Consent: Written informed consent was taken from the parents of the patients for publishing this case report and its accompanying images.

Conflicts of Interest

The authors report no conflicts of interest.

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Figure 1. Diffuse plantar erythema, thickening, and scaling**(B & C)** extend onto the dorsum of the feet **(A).**

Figure 2. Diffuse palmar thickening, with erythema and scaling on the wrist and thenar eminence of the right hand **(B)** extending onto the dorsum of the hand **(A).** Similar changes were noted on the left hand.

Figure 3. **(A)** Early pseudo-ainhum formation over the interphalangeal joints. **(B)** Exaggerated longitudinal curvature of the fingernails along with pits and horizontal grooves. A triangular lunula is also noted.

Figure 4. (**A)** An exophytic outgrowth from the right toe, likely indicating granulation tissue post-pyogenic site infection.**(B)** Onychodystrophy with prominent onychogryphosis of the 2nd toenail of the left foot.

Figure 5. Loss of multiple secondary dentition with some inflammation of right lower gingival tissue noted.

Figure 6. **(A)** Hypopigmented, atrophic plaque on right elbow.**(B)** Hypopigmented patch on the right knee.

Figure 7. **(A)** Increased spacing of secondary dentition with signs of gingival inflammation. **(B)** Well-demarcated ulcerated plaque with alopecia on the scalp. **(C)** Plantar erythema, hyperkeratosis, and scaling.

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