Olmsted Syndrome in a 12-year-old Filipino Male: A Case Report and Future Directions

Aznaida T. Pandapatan, MD, Cindy J. Tan, MD and Joyce Anne S. Tan, MD

Department of Dermatology, Philippine General Hospital, University of the Philippines Manila

ABSTRACT

We report a case of a Filipino child who presented with yellowish hyperkeratotic plaques on the palms and soles with palmar transgredient extension to the wrists, a yellowish hyperkeratotic plaque over the coccygeal area, and brownish-black hyperkeratotic perianal plaques. Patient had delayed physical development and short stature, but no intellectual disability. Histopathologic examination showed palmoplantar keratoderma. These clinical findings of symmetrical palmoplantar keratoderma with periorificial keratotic plaques were consistent with Olmsted Syndrome.

Oral retinoids with topical keratolytics afforded significant improvement with increased hand mobility. Although there is no curative management for these patients, current experimental therapies like epidermal growth factor receptor (EGFR) inhibitors and Transient Receptor Potential Vanilloid-3 (TRPV3) antagonists are promising.

Olmsted Syndrome is a rare genodermatosis with 73 cases officially reported as of this writing. This is the first case to be reported from the Philippines.

Keywords: Olmsted Syndrome, case report, palmoplantar keratoderma, Acitretin, hyperkeratosis

INTRODUCTION

Olmsted syndrome (OS) is a rare keratinizing disease characterized by classic bilateral mutilating transgredient palmoplantar keratoderma (PPK) and periorificial keratotic plaques and other variable features. First described by HC Olmsted in 1927, the hallmark findings were usually evident during childhood with marked clinical heterogeneity. There have been 73 cases officially reported as of this writing, and this is the first Olmsted case to be reported from the Philippines.

The debilitating and progressive keratoderma as well as auto-amputation of digits can significantly limit fine movements like grasping and writing and gross motor movements like walking. An association between malignant epithelial tumors and Olmsted syndrome has also been reported. Improving the quality of life of these patients entailing the use of keratolytics, systemic retinoids, and occupational rehabilitative therapy is of utmost importance in the light of lacking definitive medical intervention.

To our knowledge, this is the first reported case of Olmsted syndrome and we briefly review the potential management strategies for patients with this rare genodermatosis.

CASE DESCRIPTION

A 12-year-old Filipino male presented with extensive yellowish hyperkeratotic plaques on the palms and soles

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Corresponding author: Aznaida T. Pandapatan, MD
Department of Dermatology
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila 1000, Philippines
Email: aznaidapandapatan2014@gmail.com
ORCiD: https://orcid.org/0000-0002-6714-8769

with areas of fissuring and extension to the wrists (Figure 1A) which were noticed at around two years of age. The hyperkeratotic areas were noted to be anhidrotic and foul smelling. Patchy hyperkeratosis on the knuckles and distal digits of the feet with concomitant toenail dystrophy with autoamputation of the 5th toe of the left foot were also observed (Figures 1B-D). Over time, there was growth of a hyperkeratotic plaque on the skin overlying the coccygeal area and brownish-black hyperkeratotic perianal plaques (Figure 1E). There were no noted changes in his hair, nails, and teeth. Patient had delayed physical development and short stature but no intellectual disability. Patient was able to write comfortably and independently eat, change clothes, and bathe but required assistance in tying his shoelaces. He has no known family member with similar findings. He was born via NSD, at home, attended by a midwife, and there were no complications at birth and infancy. Mother had regular prenatal checks at a nearby barangay health center, with no noted prenatal complications. There is no familial consanguinity between his parents.

Histopathology of the hyperkeratotic plaques showed findings consistent with palmoplantar keratoderma (Figure 2).

Genetic testing was not done due to financial constraints. Differentials considered and ruled out were palmoplantar psoriasis which was not supported by the histopathologic findings; Vohwinkel Syndrome which usually presents with a honeycomb pattern of keratoderma; and Pachonychia congenita which presents with nail dystrophy and plantar pain. With the presence of mutilating palmoplantar keratoderma and periorificial keratotic plaques, a diagnosis of Olmsted Syndrome was made.

Treatment was initiated with topical urea 40% paste once daily for a month which yielded minimal improvement in the thickness of the plaques. Mechanical debridement and paring were advised but there was no parental consent. Baseline blood tests were all within normal limits thus patient was then started with acitretin at 0.5 mg/kg/day with concomitant application of a combination of urea 20% + salicylic acid 10% lotion twice daily. After one month, the palmoplantar plaques became less thick (palms > soles) (Figure 3) enabling the patient to extend his fingers considerably, tie his shoelaces by himself, and do other daily activities with less difficulty. No new lesions were observed, and the erythematous borders also lessened. Liver function tests, blood counts, and lipid profiles stayed within normal limits on first and third months of follow-up. Patient was able to take the acitretin for three months without adverse effects but had to discontinue due to financial constraints.

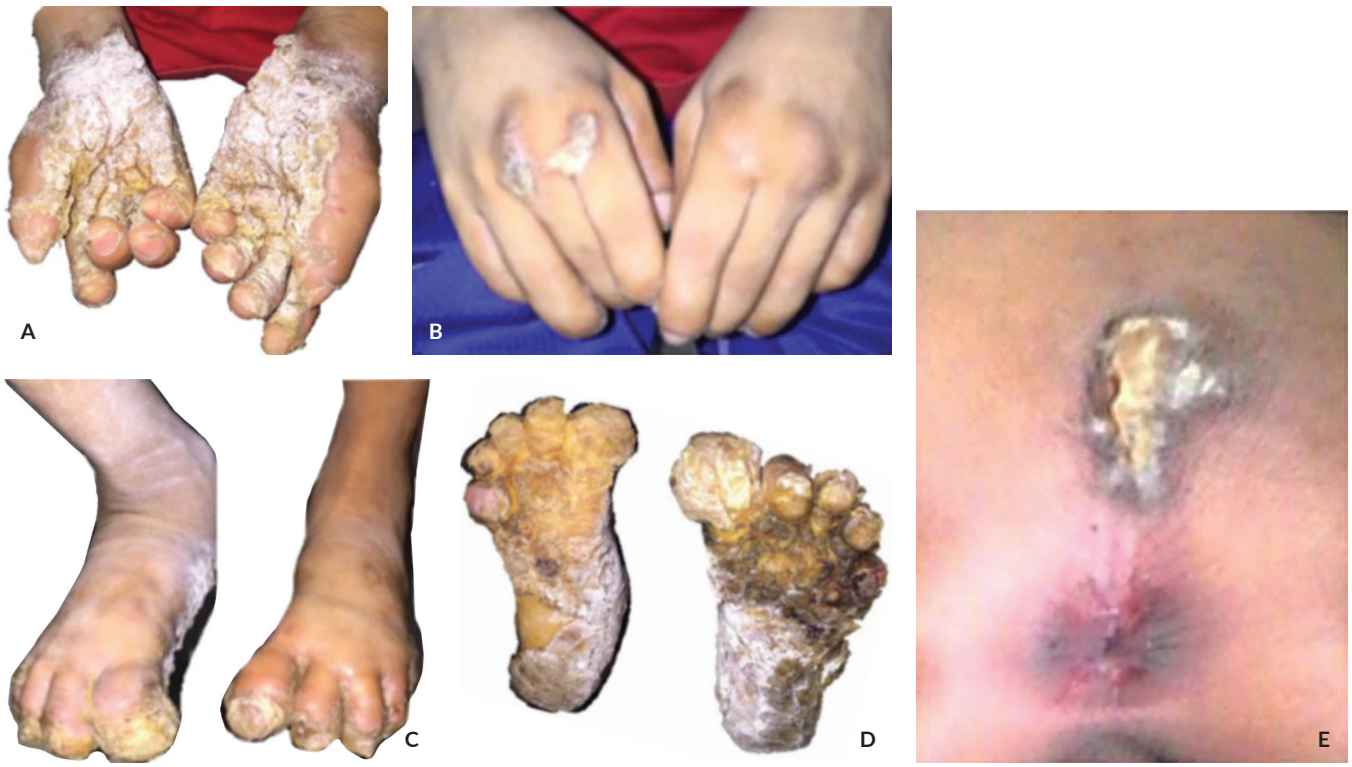

Figure 1. Multiple yellowish thick plaques covering the palms and palmar fingers, up to the wrist with erythema of the borders of the plaques over the wrist **(A)**; thick yellow plaques over the 2nd and 3rd knuckles of the right hand **(B)**; absent 5th toe on the left foot, thick plaques over the toes and toe webs **(C)**; yellowish thick scaly plaques on both soles, with hemorrhagic crusts **(D)**; hyperkeratotic plaque on the coccygeal area and brownish-black hyperkeratotic perianal plaques **(E)**.

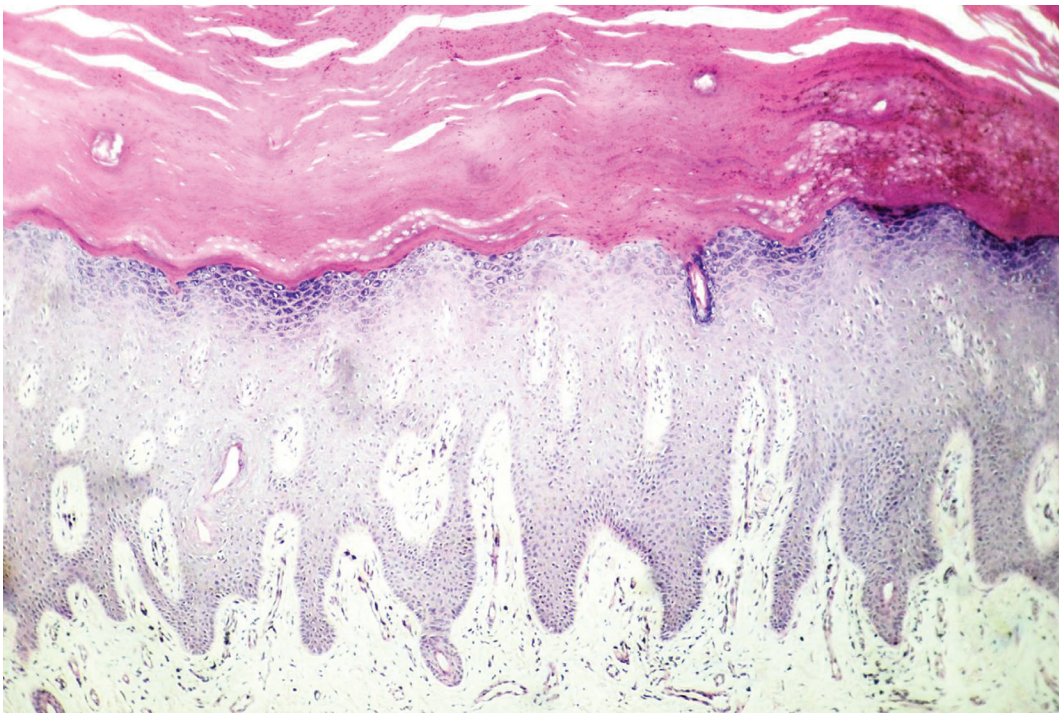

Figure 2. Biopsy on scanning view (H&E stain; 40x) showed hyperkeratosis with parakeratosis, hypergranulosis, psoriasiform hyperplasia, spongiosis, numerous dilated blood vessels, superficial perivascular lymphohistiocytic infiltrates and neutrophils in the stratum corneum, consistent with keratoderma.

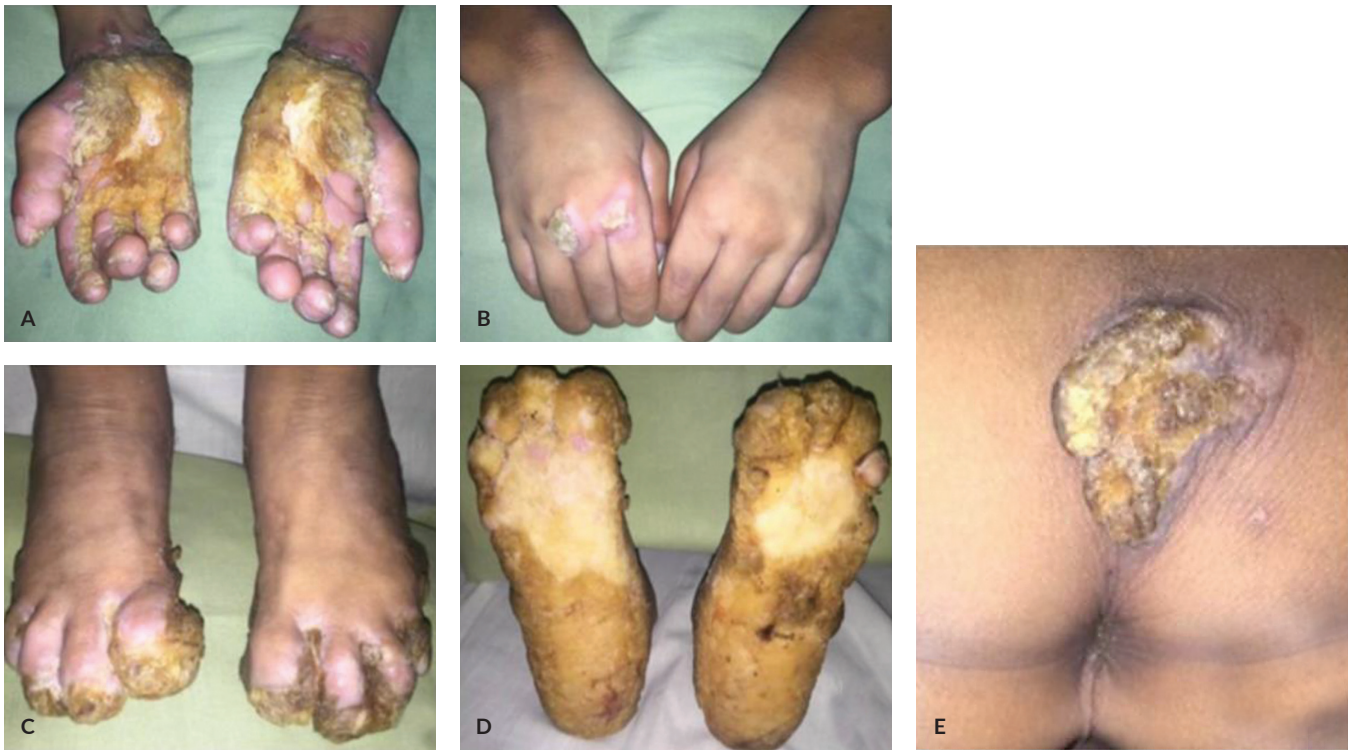

Figure 3. Three months after acitretin and urea+salicylic acid lotion showing significantly thinner plaques, less marginal erythema on palms **(A)**, knuckles **(B)**, toes **(C)**, soles **(D)**, and perianal skin **(E)**.

Family was advised regular follow-up and long term plans involve balancing patient functionality and avoiding possible adverse effects with long term use of oral retinoids.

DISCUSSION

Olmsted Syndrome is a diagnosis that relies mainly on classic hallmark clinical findings of severe palmoplantar keratoderma and periorificial keratotic plaques, albeit with marked clinical heterogeneity.[1] Diagnosis may be challenging when there are incomplete phenotypic features. Histopathologic findings are not specific and less contributory. Genetic screening is more definitive but only indicated in unusual clinical presentation (i.e., lack of periorificial keratinization).

OS commonly becomes apparent at birth or during early childhood and is more frequently reported among males. Most reported cases are sporadic, but there are familial cases reported (X-linked, and dominant or recessive autosomal). The genetic basis has been elucidated by findings of mutations in Transient Receptor Potential Vanilloid-3 (TRPV3) in 14 patients with different genetic backgrounds (Caucasian, Iranian, Indian, Chinese).[1] The pathogenesis of OS is unclear. There have been reports on the role of the following in its pathogenesis: defect in the expression of mature epidermal keratins 1 & 10, and persistence of basal keratins 5 & 14; as well as increased expression of Ki-67 (a mitotic activity marker in basal and suprabasal epidermal layers.[2-5] Mutations in MBTPS2 (membrane-bound transcription factor protease, site 2) gene were identified in a recessive X-linked form and may explain overlapping features with IFAP (ichthyosis follicularis, atrichia, and photosensitivity) and keratosis follicularis spinulosa decalvans.[6] Recently, mutations in the PERP gene encoding the p53/p63 tetraspan membrane protein have been defined in patients with OS which can lead to abnormal desmosome structure and adhesion defects of keratinocytes. These patients have hair phenotypes ranging from curly blonde hair to alopecia universalis.[7]

Other associated findings reported in some patients are hyperkeratotic linear streaks, follicular keratosis, pachyderma, cheilitis, ichthyotic lesions, chronic blepharitis, pain (50%), and pruritus (16%).[1] Progression of the keratoderma may lead to flexion deformities and joint restrictions. Complications such as autoamputations may worsen the disability and affect functional mobility as well. Severe pruritus and pain increase the discomfort and may result in insomnia. There are reported cases of high tendency to develop tumors in the keratotic areas such as squamous cell carcinoma and epithelioma cuniculatum.[8-10] Corneal dystrophy, if present, can cause blindness.[11]

Supportive therapy remains to be the norm in PPK management with goals of improving the quality of life and delaying the progression of the disease. Topical keratolytic agents such as urea 10-40% and salicylic acid 2-10% may be used singly or in conjunction to reduce hyperkeratotic plaques. Other options are tretinoin, lactic acid 10-20%, saltwater soaks, and paring. For inflammatory lesions, topical corticosteroids may be helpful.

Systemic retinoids such as acitretin may be employed for severe refractory cases after careful evaluation of renal and hepatic functions and lipid profiles. Combination therapy of topical and systemic keratolytics in our patient has led to a significant improvement in fine and gross motor skills as early as one month of therapy with note of walking, wearing shoes with ease and considerable extension of fingers. Surgery and CO_2 laser have also been reported to improve PPK in OS.

Recent advancements in the understanding of pathophysiology have uncovered the possible role of epidermal growth factor receptor (EGFR) inhibitors such as erlotinib, which may block the transactivation of TRPV3. Three patients aged 13-17 diagnosed to have progressive pain-associated severe OS were noted to improve within three months of initiating erlotinib therapy vastly improving symptoms such as anorexia, insomnia, depression as well as ability to resume social activities.[12] Targeted therapy with the EGFR inhibitor has profoundly life-altering effects on the overall quality of life in patients with OS and expands the therapeutic highway for these patients.

There is no cure for OS and the goal of management is to improve patient quality of life. However, recent targeted therapeutic options have reported improvement in the overall clinical profile and quality of life. Close monitoring and follow-up are advised due to high incidence of recurrence as well as potential association with malignant epithelial tumors.

This case report aims to add to the limited information available on Olmsted syndrome. The authors believe that this case will be able to contribute significant information for those who want to gain insight on OS management with Acitretin and keratolytics. Limitations of this case include the lack of genetic testing and short duration of treatment with acitretin.

CONCLUSION

Olmsted Syndrome is a rare genodermatosis requiring astute clinical recognition and prompt management. For the past years, less than satisfactory treatment options were utilized leading to poor treatment response and high recurrence rates. Treatment efforts can be focused on the careful use of oral retinoids and topical keratolytics, as was done with this patient. However, the debilitating nature of this illness and profound effect on quality of life warrant further studies on more definitive therapies. With better understanding of the disease mechanisms, EGFR inhibitors or TRPV3 antagonists would represent a targeted treatment strategy for genetically acquired OS.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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