Olmsted Syndrome in an Iranian Family: Report of Two New Cases

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Olmsted syndrome is a rare congenital entity characterized by combination of symmetrical, sharply-defined palmoplantar keratoderma with flexion deformities of the digits, periorificial keratosis, perianal involvement, onychodystrophy, and variable leukokeratosis. Herein, we report two new related male patients—the third familial cases of Olmsted syndrome—one with the full-blown spectrum of the syndrome, and the other with early signs and symptoms of the disorder.

Keywords: Family • Iran • Olmsted syndrome

Introduction

Olmsted syndrome (OS) is a rare keratinization disorder characterized by combination of periorificial keratotic plaques and bilateral palmoplantar transgredient keratoderma.1, 2 These hallmarks represent an exceptional combination of findings, and allow the exclusion of other syndromes of keratoderma.1 Other clinical manifestations include diffuse alopecia, leukokeratosis of the oral mucosa, onychodystrophy, hyperkeratotic linear streaks, follicular keratosis, and constriction of the digits.1, 2 OS is a very rare condition, and almost 20 cases have so far been reported.3 Herein, we report on two new patients and the third familial cases of OS.

Case Reports

Case 1

A 20-year-old male was visited because of his alopecia universalis and hyperkeratotic lesions, especially around his body orifices and palmoplantar areas. He was born at term from a nonconsanguineous parents in Khuzestan Province, South-West of Iran. At six months of age, he had developed small hyperkeratotic lesions on his neck, elbows, buttocks, palms, and soles. The lesions gradually turned into massive hyperkeratosis with painful deep fissures, especially on the palms and soles. His general condition was good and his physical, mental, and hearing developments were normal. Family history was positive for similar skin disease in his nephew (his sister’s child) (case 2). His parents and other siblings were free of verrucous lesions.

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Physical examination showed universalis alopecia and thick hyperkeratotic plaques around all of the body orifices and on the palms and soles (Figure 1). Sharply marginated, thick, verrucous, and erythematous hyperkeratotic plaques were seen around the mouth, nostrils, on the posterior aspect of his neck, outer parts of his forearms, in his groin, genitalia, intergluteal area, and both extensor surfaces of his knees and legs. The lesions of the prepuce, perianal areas, genitalia, and inguinal folds were severely hyperkeratotic and malodorous. There were diffuse yellowish-brown hyperkeratosis with deep fissures extending to wrists and external borders of hands and feet. The patient’s palmoplantar keratoderma caused flexion contracture so that he was unable to walk or grasp (Figures 2 and 3). All lesions were pruritic and
The keratoderma of the right foot had been complicated by development of an infected and exophytic mass on the base of toes, causing the patient not be able to wear his shoes and had a disturbed gait (Figure 3). The clinical feature of the exophytic mass was similar to epithelioma cuniculatum. All the nails were hyperkeratotic, fork-like, yellow, and severely dystrophic with subungual hyperkeratosis. Examination of oral cavity, except for the absence of lower premolar teeth on both sides, was normal. An ophthalmologic consultation revealed bilateral chronic blepharitis with lid erythema, small scales, fine telangiectasia in lid skin, madarosis, and meibomian glands dysfunction. Slit-lamp examination of the eyes showed subepithelial and anterior stromal opacities with corneal vascularization which extended to central cornea. General examination was unremarkable. There was no associated cutaneous or systemic diseases. The routine laboratory tests and serum zinc level were within normal limits. X-ray findings were consistent with osteoporosis of the bones of extremities. Histopathological examination of a skin biopsy specimen from forearm lesions revealed hyperkeratosis, parakeratosis, mild acanthosis, and papillomatosis. The dermis showed mild perivascular lymphocytic infiltration. Biopsy specimen from the mass on the right sole of the foot showed massive hyperkeratosis, parakeratosis, acanthosis, and prominent papillo-matosis. The dermis showed moderate acute and chronic inflammation. The last histopathological findings were not enough for making the clinical diagnosis of epithelioma cuniculatum, and therefore, the diagnosis of epithelioma cuniculatum was not confirmed.

The patient was treated with topical urea 15%, 20%, and 40% for skin lesions, keratoderma, and painful. Good improvement of the lesions was obtained with keratolytic treatment. Therapy with oral retinoid, acitretin (0.5 mg/kg/day) was proposed to prevent development of new hyperkertotic lesions. The results of this treatment was also good after six months of follow-up.

Case 2

A seven-year-old male presented with alopecia universalis. He was born at term from healthy and nonconsanguineous parents in Khuzestan Province, South-West of Iran. At the age of five months, he developed bilateral palmoplantar thickening and scaly erythema around his mouth, and on his elbows and knees. In his second year of life, hyperkeratotic lesions appeared on the palmoplantar regions, elbows, knees, buttocks, natal cleft, and outer surface of his thighs. Family history was positive and his uncle (case 1) had similar skin manifestations.

Physical examination at the age of seven years showed alopecia of the scalp and eyebrows. Well-defined and mild hyperkeratotic plaques were noted around his mouth and nares (Figure 4).
Symmetrical, thick, sharply-marginated, red to yellowish areas of hyperkeratosis affected the extensor surfaces of his elbows, knees, hands, and feet (Figure 5). The finger tips showed mild scaly erythema without nail dystrophy. There were also keratoderma, especially on the weight bearing areas of his soles.

No abnormality in teeth and mucous membranes was detected. The mental, physical, and hearing developments were also normal. Radiological and laboratory findings, including serum zinc level, were normal. The patient was treated with topical urea 15% at night and topical steroid at day which produced improvement of skin lesions.

Discussion

OS is a rare congenital condition characterized by combination of periorificial keratotic plaques and bilateral palmoplantar transgredient keratoderma.1, 2 These two main signs constitute the characteristic composition of findings, and allow the distinction of this syndrome from other syndromes of keratoderma.1 OS was first described by Olmsted in 1927.1, 2 To date, almost 20 cases of OS have been reported in literature.3 Although some patients had other affected family members, most reports describe sporadic cases.1, 2, 4 Herein, we reported the third familial cases showing a progressive course with relative response to conventional treatments. Hereditary transmission from mother to son has been described earlier which suggests an autosomal dominant mode of inheritance.5

Cambiaghi et al reported transmission in two monozygotic male twins. They suggest that this condition is inherited as an X-linked dominant trait with reduced expression in female subjects.4 Our report also confirms the genetic nature of this syndrome. The pathogenesis of this disorder is still poorly understood, but it is believed that OS is a disorder of keratinization; Kress et al found a defect in the expression of mature epidermal keratins (types 1 and 10) and persistence of acidic keratins (types 5 and 14) in the involved epidermis. They suggested that the alteration in keratin expression seen is specific to the epidermis and that these keratins are expressed normally in other sites. These findings have not been reported in the other disease states, which show acidic keratins 5 and 14 in suprabasilar layer.6

Onset of OS usually occurs in early childhood when the child starts to walk and grasp.1, 2 Although the first manifestation is the palmoplantar keratoderma in the first six months of life, like our cases, hyperkeratotic periorificial plaques are the main manifestation.1 The periorificial plaques are symmetrical, yellowish-brown, and sharply demarcated from the normal skin. The plaques usually appear on the body folds.
such as axillae, neck, and groins, and show a progressive course characterized by skin thickening.\(^1\) Lesions around perianal area, mouth, and axillary region may regress spontaneously.\(^7\)

The disease has a slow and progressive course over many weeks or months. The keratoderma which is initially soft, hardens and an erythematous halo develops around them. Finally, after many months and years, progression of keratoderma to the dorsal aspect of hands and feet may lead to flexion contracture of the fingers and Ainhum deformity.\(^1,\)\(^7\) The keratotic lesions are pruritic and mildly painful with pressure.\(^4\) Patients with OS may show a higher susceptibility to develop epidermal tumors such as squamous cell carcinoma and epithelioma cuniculatum.\(^8\) Some improvement of the lesions during the summer months and a clear improvement of the keratoderma during febrile diseases may occur.\(^4\)

Other findings are chronic paronychia, onychodystrophy, universalis congenital alopecia, oral leukokeratosis, hyperkeratotic follicular lesions, linear hyperkeratotic streaks, and hyperhidrosis of the palms and soles. Other associations include large joint laxity, absent premolar teeth, hearing loss for high frequencies, chronic blepharitis, corneal epithelial dysplasia, corneal opacities, and primary sclerosing cholangitis.\(^1,\)\(^2,\)\(^7,\)\(^9,\)\(^10\)

In the differential diagnosis of OS, one should consider acrodermatitis enteropathica, congenital pachyonychia, Mal de Meleda, Papillon Lefèvre syndrome, keratoderma hereditarium mutilans of Vohwinkel, hidrotic ectodermal dysplasia of the Clouston type, and other forms of palmoplantar keratodermas.\(^1,\)\(^2,\)\(^10\) – \(^12\)

There is no satisfactory treatment for this condition.\(^1,\)\(^2\) Topical treatments include solution of potassium permanganate, wet dressing, salicylic acid in various concentrations, boric acid, urea, tar, retinoic acid, corticosteroids, and prolonged soaking of the affected parts in warm water. Application of a hydrocolloid dressing can decrease pain in patients with deep fissure.\(^1,\)\(^2,\)\(^7\) Oral retinoids have proved effective in some cases.\(^1,\)\(^2,\)\(^4,\)\(^7,\)\(^9,\)\(^12\) For nonresponsive patients, full-thickness excision of hyperkeratotic plaques followed by skin grafting is another therapeutic option to alleviate the pain.\(^1,\)\(^2,\)\(^5,\)\(^9,\)\(^12\) This treatment may improve flexion contracture of the fingers, but the risk of recurrence persists.\(^1,\)\(^5\)

References


