Case report:

Olmsted Syndrome a Rare Type of Mutilating Palmoplantar Keratoderma: A Case Report

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Abstract

Olmsted syndrome is a rare genetic disease characterized by mutilating transgradient palmoplantar keratoderma (PPK) associated with periorificial keratotic plaques. Its starts in the neonatal period or in childhood. The disease has a slow but progressive and extremely disabling course. We present a case with clinically and pathologically confirmed Olmsted syndrome. This case report is an important one for its rarity and disability.

Key words: JAK inhibitors, Alopecia Areata

Introduction

Olmsted syndrome is a rare type of palmoplantar keratoderma that shows marked clinical and genetic heterogencity. Mutilating palmoplantar keratoderma and periorificial keratotic plaque define this disease. The keratotic plaques observed on the skin appear as a result of overexpression of keratin 5 & 14.[1] The finding of Ki -67 immunostaining of suprabasal keratinocyte supports the notion that Olmsted syndrome is a hyperproliferative disorder[2]. Genetic linkage analysis added this disease to the list of skin channelopathies. Gain of function mutation in TRPV[3] gene give rise to AD, AR variants of Olmsted syndrome[3]. Stimulation of TRPV3 in keratinocytes causes keratotic plaques that characterized Olmsted syndrome. Sporadic cases by denovo mutation in TRPV3 thermosensitive cation channel may occur. On contrary XR variant of Olmsted syndrome is a result of specific mutation in MBTPS2 associated with alopecia universalis & nail dystrophy. Very rarely XD cases are also reported[4]. This report documents a further case of this syndrome.

Case report

A 3 year 10 months old boy was presented with painful pruritic palmoplantar keratoderma associated with periorificial and intertriginous keratotic erythematous scaly plaques. There were limitation of movement of fingers of the hands. He was born at term . There was no history of consanguineous marriage. The patient has one elder sister,she was at 9 years old & healthy. According to the statement of parent, the disease was started when the baby was about 10 days old. Initially the patient developed some papules & vesicles in the groin, axilla, and antecubital area. Soon after a few days vesicles become ruptured leaving a moist eroded surface. At this time, after consultation with a local physician, his mother applied some topical medications but the result was unsatisfactory. In course of time, papules became larger and coalesce

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to form erythematous keratotic scaly plaques. Gradually keratotic lesions developed around the nose, mouth, eye, ear, front and back of the neck, and perianal areas. He developed thick horny plaques in the palm & soles associated with erythema & scales at the age of 3 months. At the age of 1 year, the mother noticed scaly crusted plaques with non-scarring alopecia in the center of the scalp. The nails became thickened and discoloured at the age of 3 years.

Examination of skin revealed bilateral symmetrical diffuse palmoplantar keratoderma. The lesions were yellowish-brown in color and extended to the dorsum of both hands & feet. There were fixed flexion contracture on the distal phalanges. But, there were no constriction bands or pseudo ainhum around the digits. No evidence of auto-amputation was found. The nails were thickened, rough, dystrophic, discoloured with subungual hyperkeratosis. Both palmar & plantar lesions were hyperhydrotic & malodorous. Well-defined erythematous scaly hyperkeratotic plaques were seen around the mouth, ear, nose, anus. There were also hyperkeratotic areas noted in intertriginous areas like groin, axilla, antecubital area, popliteal fossa, front and back side of neck & flank. Scaly and crusty lesions were found in the scalp associated with central non scarring alopecia. Hairs in other areas were normal.

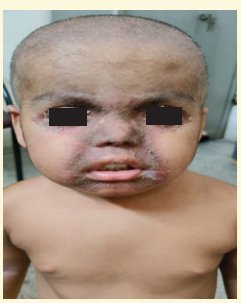

Fig 1. Well-defined erythematous scaly hyperkeratotic plaques were seen around the mouth, ear, nose

Fig 2. Hyperkeratotic fissured plaques on palms

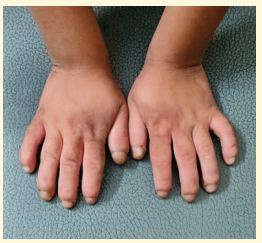

Fig 3. Keratoderma extending over dorsal aspect of hands

Odontological examination revealed leukokeratosis of buccal mucosa. Teeth were normal. Ophthalmological and Otological examination revealed no abnormality. On general examination, the child was undernourished, other findings were non-contributory.

Laboratory findings including Complete Blood Picture, Serum Albumin, Serum Zinc, Serum Alkaline Phosphatase,Total Protein, FT4,TSH,Urine routine Examination were normal. Skin scrapping & Nail shaving for fungal microscopic examination & culture was negative for fungi. Histopathological study showed psoriasiform hyperplasia, thick granular layer, alternating parakeratosis and hyperkeratosis, and acanthosis in the epidermis. Dermis reveals moderate infiltration of chronic inflammatory cells (Mast cells mixed with lymphocytes). No fungus or granuloma was seen.

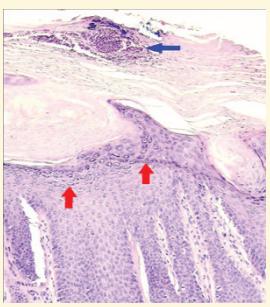

Fig 4. Red arrow-Thick granular layer,
Blue arrow-Polymorphs in thick stratum corneum H&E

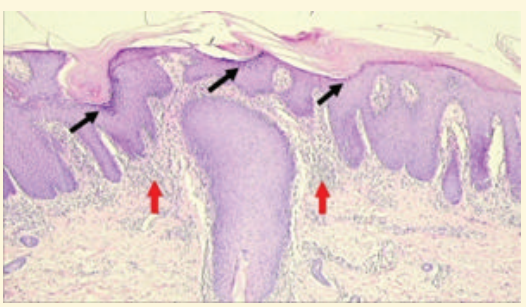

Fig 5. Black arrow- Thick granular layer ,
Red arrow -Chronic inflammatory cells in dermis H&E

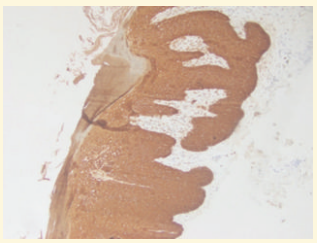

Fig 6. Pancytokeratin AE1/AE3 positive in all layers of epidermis including basal layer

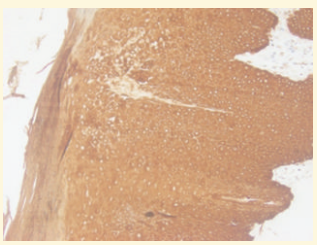

Fig 7. Pancytokeratin AE1/AE3 positive in all layers of epidermis including basal layer

Discussion

In 1927, H.C. Olmsted reported the first case of Olmsted syndrome, a 5-year-old Italian American boy with congenital PPK with periorificial hyperkeratosis. There was no such type of lesion seen previously[5]. To date, there have been 106 cases of Olmsted syndrome reported (up to June 2019)[6].

This is another case of Olmsted syndrome where lesions start in the neonatal period. The disease has a slow but progressive and extremely disabling course.

Major clinical manifestations include palmoplantar keratoderma and periorificial hyperkeratosis.

Clinical manifestations include other than two major ones are.

Hair: Diffuse, universal or patchy alopecia. In our context, there was patchy alopecia of scalp hair.Hypotrichosis, sparse, thinning, curly, wooly, coarse, dry, or easily broken hair also noted.[7]

Nail: Nail abnormalities including dystrophic, lusterless, onychogryphosis, leukonychia, irregular curvatures, subungual hyperkeratosis.[8]

Oral cavity: Leukokeratosis of tongue, palate, buccal mucosa.[9]

Teeth: Edentulous maxilla, premature loss of teeth, absence of premoler teeth, reduced masticatory ability.

Growth (Physical &mental): Delayed physical development ,Short stature, Mental retardation.

Malignancy: SCC, Malignant melanoma ,Adenocarcinoma of lung in one case.

Hearing: High tone loss hearing,Congenital deaf-mutism.

Recurrent infections: Bacterial /candidial infection in keratotic areas.[10]

Eye: Corneal opacity, dystrophy, epithetial dystrophy.[11]

Bone: Osteoporosis, Osteolysis of hand and feet.[12]

Others: Joint laxity, Primary sclerosing cholangitis, Erythromelalgia, Thrombocytosis, Non-Mutilating PPK.[13]

The summary of the clinical manifestations of Olmsted syndrome and similarities in the present case is as follows

1 Early age of onset	+
2 Short Stature	+
3 Delayed social age	+/-
4 Delayed bone age	+/-
5 Alopecia	+
6 Joint laxity	-
7 Auditory disturbance	-
8 Leukokeratosis of tongue	+
9 Hyperkeratosis of	+
Palm	+
Soles	+
Periorificial	+
Intertriginous area	+
10 Contracture of fingers	+
11 Dystrophic nail	+
12 Corneal opacity	-
13 Hyperhidrosis	+
14 Teeth abnormalities	-
15 Malignant potential	Negative until now
16 Infection in keratotie areas	+

Histopathological features of keratoderma of palms & soles are not diagnostic. They consist of psoriasiform hyperplasia, thick granular layer, hyperkeratosis,and parakeratosis. The involved epidermis shows acanthosis and papillomatosis. Dermis shows infiltration of chronic inflammatory cells with an increased number of mast cells.[14] Similar non-specific features have been found in biopsies taken from keratoderma of palm & souls in our case.

Cytokeratins have been identified as abnormal in the skin affected by keratoderma. Keratoderma in Olmsted syndrome remains in an immature, proliferative state.[15] The failure to differentiate to mature keratinocytes is responsible for the excessive deposition of acidic keratin 5 & 14, which is detected

by monoclonal antikeratin Ab AE1.[16] Cytokeratin AE1 immunostaining is noted through the entire thickness of the epidermis (normally this cytokine only stains the basal layer of the epidermis). Cytokeratin 10 is stained in the upper layer of the epidermis. Further immunohistochemical studies with Ki 67 marker demonstrated hyperproliferative activity involving basal & suprabasal keratinocytes in Olmsted syndrome.

The ultrastructural study was not informative, where electron microscopy of palmar keratoderma showed nonspecific defective keratinization, and KHG was decreased or absent.

Olmsted syndrome has to be differentiated from other severe forms of PPK such as Vohwinkel syndrome, Mal de Maleda syndrome, tyrosinemia type II, Pachyonychia congenita, Clouston syndrome, Haim-Munk syndrome in addition to inverse psoriasis, chronic mucocutaneous candidiasis, acrodermatitis enteropathica. Nutritional deficiencies that mimic Olmsted syndrome are essential fatty acid deficiency, multiple carboxylase deficiency, and PEM, but these are not keratrodematous disorders. Acrodermatitis enteropathica was excluded by measurement by zinc level which shows improvement with zinc therapy. Candida organisms are invariably confined to statum corneum and are demonstrable in scrappings, nall shaving & culture. Thus, the full-blown Olmsted syndrome with its typical association of mutilating bilateral PPK and periorificial keratotic plaque is distinctive enough to lead to the correct diagnosis.

Conclusion

Olmsted syndrome is a rare disease. As because histopathological, Immunohistochemical and Electron microscopy findings are not specific and molecular genetics are not readily available and yet to be explored we believe that, the diagnosis of Olmsted syndrome remains essentially clinical and must include the two major ones.

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