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Case report

Mal de Meleda: a case successfully treated with acitretin

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Abstract

Mal de Meleda (MdM) is an autosomal recessive form of palmoplantar keratoderma that is characterized by transgradient keratoderma with associated scleroatrophy, nail changes, pseudoainhum around digits and perioral erythema, without a tendency for spontaneous resolution. Mal de Meleda can lead to severe flexion contractures in some patients as well as mycotic over-infections with significant impact on quality of life and daily activity. Mal de Meleda is a rare genetic disorder but no standardized treatment has been established. Treatment options for this disease include topical keratolytic agents, propylene glycol, topical 5-fluorouracil and surgical treatment. In addition, it has been reported that etretinate and acitretin, usually produce improvement. Herein, we present a case of Mal de Meleda with lips involvement which showed significant clinical improvement with acitritin.

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Introduction

Palmoplantar keratoderma (PPK) is a genetically heterogeneous group of skin diseases characterized by erythema and hyperkeratosis. Mal de Meleda, also known as keratoderma palmoplantaris, transgrediens is a rare type of PPK, associated with mutations in the autonomously replicating sequence (ARS) gene, encoding SLURP1 (secreted Ly-6/uPAR-related protein 1), whose prevalence is estimated in the general population of 1 in 100,000. We present a case of MdM which showed significant clinical improvement with acitritin.

Patient and observation

We report the case of a 20-year-old woman, born from a consanguineous second-degree marriage of parents without antecedents; her younger sister had similar condition. She has a palmar-plantar keratoderma, made of a thickening involving the palms and the plants bilaterally with loss of dermatoglyph, straw-yellow in appearance from early childhood with extension to the palmar-plantar dorsal surfaces and wrists of limited appearance, associated with hypersudation, gradually increased to a thickened hands and sclerotic appearance giving painful contractures in flexion of the fingers and a pseudo ainhum at the level of the fingers (Figure 1, Figure 2, Figure 3), associated with a foul odor as well as a sensation of burning of the hands and feet hindering its daily activity and its social integration. This plantar keratoderma is surmounted by several small cupuliform depressions punctuated appearance in favor of a punctate keratolysis (Figure 3). It also showed an intertrigo macerated in inter-digital and diffuse inter-toe mycotic. Diffuse xanthopachyonichia associated with koilonychia in places. The lips were erythematous, dry with mild hyperkeratosis, with lingual keratosis (Figure 4). As well as finely scaly erythematous patches well limited and pigmented at the periphery with the lumen of wood a coral red color in favor of corynebacterium uptake Figure 5. The diagnosis of Mal de Meleda was selected based on the above mentioned clinical criteria. The patient was treated with topical tretinoin for 2 months without success and then with acitretin orally at a dose of 1mg/kg/day with treatment of bacterial and mycotic surinfection. The evolution was marked by the disappearance of the pain, the sensation of burns and the nauseating odor as well as the improvement of retraction of the fingers, the recovery of their mobility and their daily activity. However, there was the persistence of the PPK. The patient is still on treatment for 6 months.

Discussion

Mal de Meleda is also known as keratosis palmoplantaris transgrediens of Siemens, is an autosomal recessive palmoplantar keratoderma with transgrediens and progrediens and the estimated disease frequency is 1/100,000 [1], it was first observed by Luca Stulli in 1826 on the island of Meleda (Mljet) in Dalmatia, which was on a Mediterranean trade route in the middle ages. For more than 50 years it was thought to be a form of Hansen's disease. However, Hovorka and Ehlers noticed that it was not an infectious disease and used the term "Mal de Meleda" [2]. It is caused by a mutation in the SLURP-1 gene 2 that is a secreted protein of the three-finger neurotoxin family and modulates nicotinic acetylcholine receptors [3]. It is a late marker of epidermal differentiation, and there is a correlation between its location in the stratum granulosum and the a-7 acetylcholine nicotinic receptor. In addition, this receptor is present in eccrine sweat glands and ducts, whose secretions are regulated by the cholinergic system. Interestingly, patients with Mal de Meleda generally suffer from hyperhydrosis and have hypertrophic sweat glands [2]. Mutations in SLURP1 would therefore appear to lead to alterations in the sweating process.

The main clinical features are the result of abnormal keratinization, characterized by differentiation of the keratinocytes in the stratum granulosum, leading to the formation of a palmoplantar hyperkeratotic covering. The obligatory clinical features of Mal de Meleda are [1]: 1) autosomal recessive inheritance; 2) onset of diffuse keratoderma palmoplantaris soon after birth (or up to 3 years of life); 3) transgressive and progressive nature of the keratoderma which tends to involve the dorsa of hands and fingers, feet and toes, flexor aspect of the wrist (glove and stocking keratoderma) with sharp margin. Hyperkeratotic plaques resembling knuckle pads may be seen on the interphalangeal joints [1].

The facultative clinical features are [1, 3] : 1) palmoplantar hyperhidrosis; 2) pitting in the keratoderma palmoplantaris; 3) lichenoid polycyclic plaques on the elbows, knees and groins; 4) subungual keratosis, koilonychia, dystrophy of the great toenail ; 5) progressive conical tapering of the fingertips which may lead to contractures of the fingers; 6) perioral erythema; 7) high arched palate; 8) corneal lesions. Digital constrictions (pseudoainhum) and angular cheilitis are also common [1]. Other rare features include lingua plicata, syndactyly, left handedness and hair on palms and soles [1].

Mal de Meleda must be differentiated from other syndromes that present with diffuse palmoplantar keratoderma. This can be difficult because of the broad spectrum of clinical manifestations. Observation of any associated lesions and the inheritance pattern can help in the differential diagnosis. Transgrediens and progrediens palmoplantar keratoderma (Greither's syndrome) can present with similar manifestations to those of Mal de Meleda, but it has an autosomal dominant inheritance pattern and progressive evolution and presents with epidermolysis [4]. Papillon-Lefèvre syndrome, an autosomal recessive condition, characterized by diffuse keratodermia together with gingivitis, early loss of teeth, periosteal changes and intracranial calcifications [5]. Vohwinkel's syndrome, an autosomal dominant condition characterized by mutilating palmoplantar keratodermia, which can progress to spontaneous amputation, alopecia, ichthyosis and deafness [6]. Huriez syndrome (also referred to as "sclerotylosis") is characterized by the triad of congenital diffuse scleroatrophy of the distal extremities, mild or lamellar keratoderma of the palms and to a lesser extent the soles, presence from birth and ridging or hypoplastic nail changes. There is also an absence of dermatoglyphics. Atrophic parchment-like skin is present on the dorsal surface of the hands. Dense hyperkeratosis gives a pseudosclerodermatous appearance with nail atrophy. Nail changes include hypercurvature, longitudinal ridging, onychorrhexis and koilonychia. Another prominent feature of Huriez's syndrome is almost invariable family history [7, 8].,Unna-Thost syndrome is a hereditary disease with an autosomaln dominant inheritance. It is characterized by a well-defined and symmetrical diffuse keratoderma affecting the palmoplantar region which stops suddenly at wrist level. It has no other associated clinical manifestations [9]. Other types and variations are described in the literature and should be considered in a differential diagnosis.

Since Mal de Meleda is a rare genetic disorder, no standardized treatment has been established. Treatment options for this disease include topical keratolytic agents, propylene glycol, topical 5- fluorouracil and surgical treatment. In addition, it has been reported that etretinate and acitretin, which are aromatic retinoids, usually produce improvement. This is the case of our patient who responded favorably to acitritine. However, early and long-term use of these retinoids associate with several well-known adverse effects such as a long period of contraception and liver toxicity [10].

Conclusion

Mal de Meleda is a rare subtype of palmoplantar keratoderma which can cause severe flexion contractures as well as mycotic over-infections with significant repercussions on quality of life and daily activity. Acitretin can improve these patients and avoid complications. We reported another case that responded well to acitritin.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors contributed in writing this article and all read and agreed to the final manuscript.

Figures

Figure 1: palmoplantar keratoderma (PPK) with extension to the dorsal sides of the hands and feet

Figure 2 : A) straw-yellow palmar keratoderma with pseuainhum and loss of dermatoglyph and extension to the dorsal sides of the hands; B) thickened hands and sclerotic appearance giving painful contractures in flexion of the fingers

Figure 3: straw-yellow plantar keratoderma, which tends to involve the dorsa of hands and fingers with sharp margin and loss of dermatoglyph with punctate keratolysis, and koilonychia of the big toes

Figure 4: A) scaly erythématous patches well limited and pimented at the periphery; B) wood lamp showed a coral contrast

Figure 5 : A) erythematous lips, dry with mild heperkeratosis ; B) lingual keratosis

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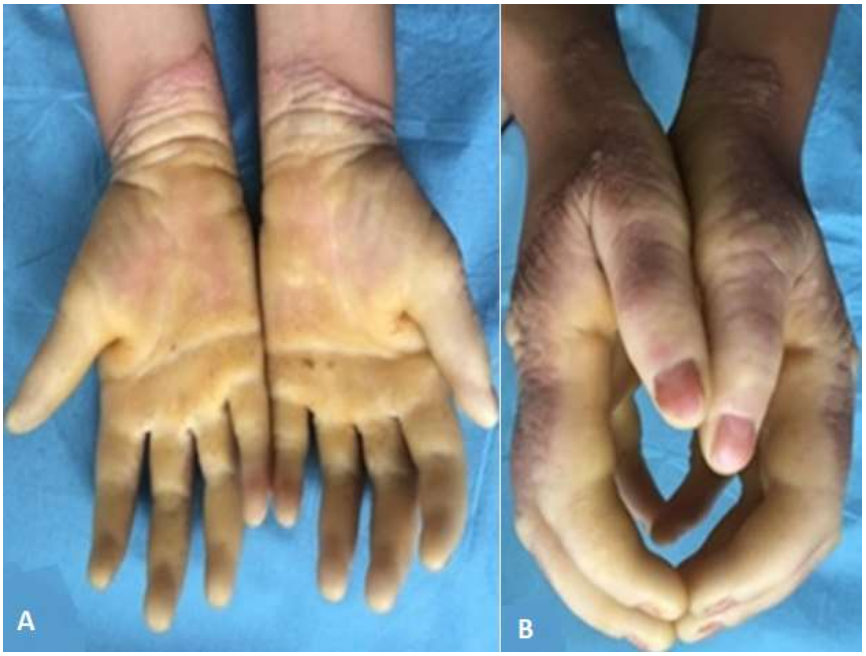


Figure 2: A) straw-yellow palmar keratoderma with pseuainhum and loss of dermatoglyph and extension to the dorsal sides of the hands; B) thickened hands and sclerotic appearance giving painful contractures in flexion of the fingers

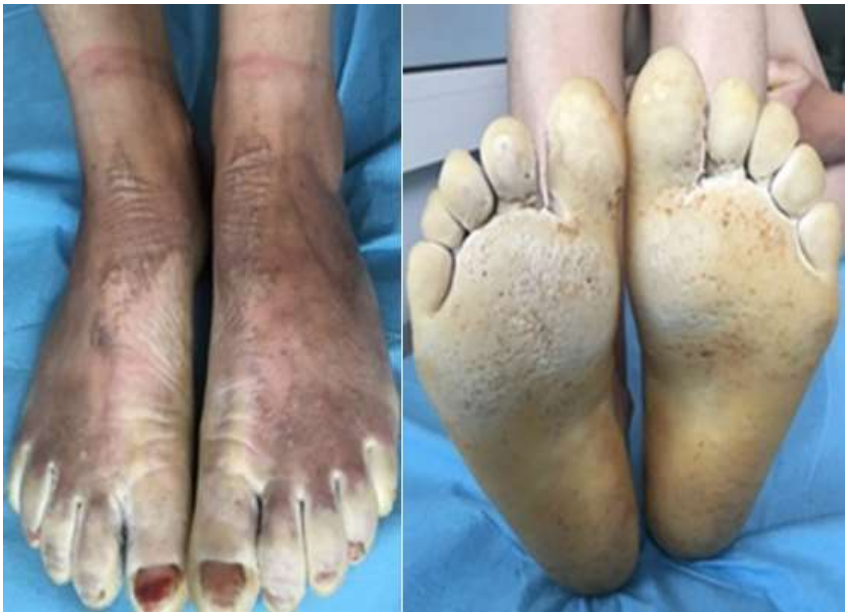
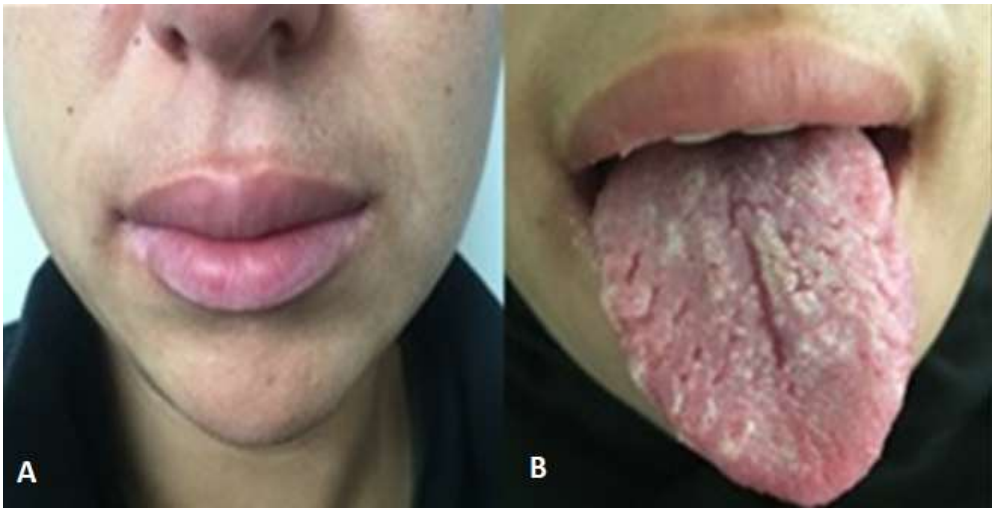


Figure 3: straw-yellow plantar keratoderma, which tends to involve the dorsa of hands and fingers with sharp margin and loss of dermatoglyph with punctate keratolysis, and koilonychia of the big toes



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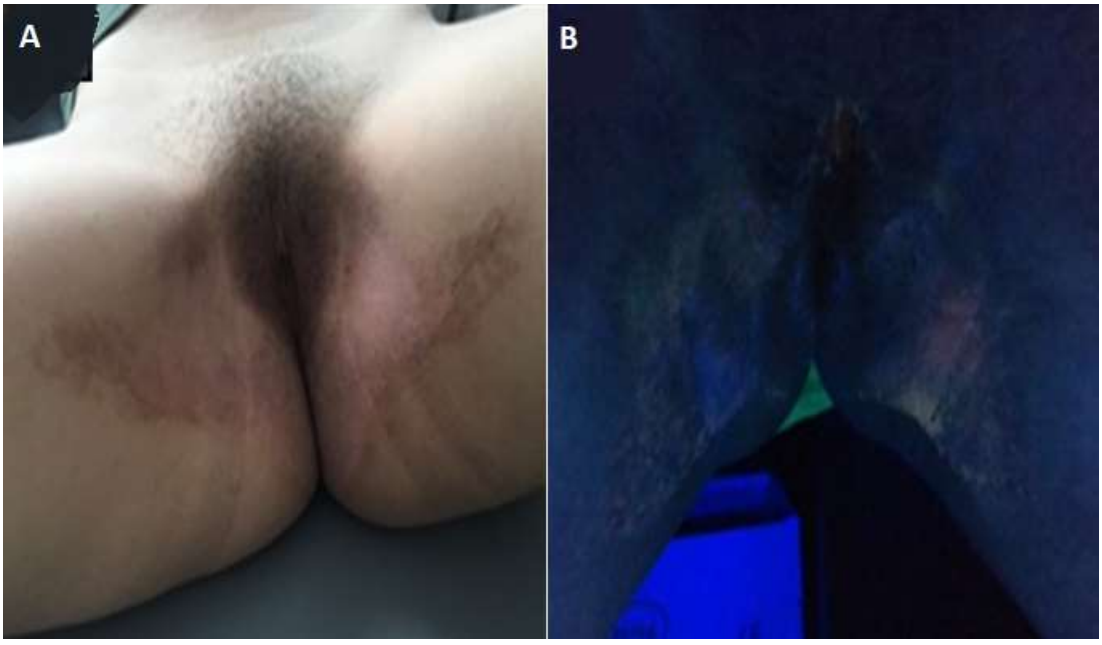

Figure 5: A) erythematous lips, dry with mild heperkeratosis; B) lingual keratosis