A Mal De Meleda patient with severe flexion contractures of hands and feet
A case report in West China
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Abstract

Rationale: Palmoplantar keratoderma (PPK) is a genetically heterogeneous group of skin diseases, which is characterized by erythema and hyperkeratosis. Mal de Meleda (MDM) is a rare type of PPK with an estimated prevalence in the general population of 1 in 100,000.

Patient concerns: In this study, we report a MDM patient with severe lesion in skin and flexion contractures of fingers and toes.

Diagnoses: MDM was diagnosed based on clinical manifestations and gene test.

Interventions: This patient was treated with oral acitretin and topical tazarotene.

Outcomes: Physical examinations indicated that the hyperkeratosis was in remission, but the erythema was expanding to her elbows progressively. Due to the adverse events (e.g., dry eyes and lips), the patient stopped taking the oral drug.

Lessons: MDM is a rare subtype of PPK, which is inherited in an autosomal recessive pattern and has characteristics that skin lesions on hands and feet appear soon after birth and develop progressively. MDM can lead to severe flexion contractures in some cases. The reliable method for the diagnosis of MDM is gene test.

Abbreviations: MDM = Mal de Meleda, PPK = palmoplantar keratoderma, SLURP-1 = secreted LY6/urokinase-type plasminogen activator receptor (uPAR)-related protein-1.

Keywords: flexion contractures, Mal de Meleda, palmoplantar keratoderma

1. Introduction

Mal de Meleda (MDM) is a rare autosomal recessive disease with an estimated prevalence in the general population of 1 in 100,000. It is a subtype of palmoplantar keratoderma (PPK), which characterized by erythema with a clear boundary and hyperkeratosis of palms and soles, appearing soon after birth and progressively expanding to other areas, such as elbows, knees, backs of hands, and insteps of feet. Moreover, MDM can lead to serious flexion contractures. Individuals with MDM are at an obvious disadvantage regarding long-term disability, and this disadvantage significantly limits patient’s daily activity, and increases the burden of this illness on patients and their own family members. Although this disease has been reported in several countries or regions around the world, few such cases have been reported in China. MDM with a Chinese background remains unclear. Therefore, in this case report, we represent a MDM patient from West China to strengthen and extend the understanding of MDM.

2. Case report

A 48-year-old woman, who complained about symmetrical and diffuse erythema and hyperkeratosis in her palms and soles from infancy, was admitted to our hospital. She also complained about flexion contractures of her hands and feet, which bring a significant inconvenience to her daily life. Unfortunately, these conditions were slowly progressive and got worse and worse. Physical examinations presented that both her hands and feet are covered with yellowish, waxy, and thick hyperkeratosis with an obvious erythematous border (Figs. 1 and 2). Moreover, her skin lesions were atrophic and sclerotic, due mostly to the long-term flexion contractures in some cases. The patient was admitted to our hospital. She also complained about flexion contractures of her hands and feet, which bring a significant inconvenience to her daily life. Unfortunately, these conditions were slowly progressive and got worse and worse. Physical examinations presented that both her hands and feet are covered with yellowish, waxy, and thick hyperkeratosis with an obvious erythematous border (Figs. 1 and 2). Moreover, her skin lesions were atrophic and sclerotic, due mostly to the long-term flexion contractures of the fingers and toes caused by hyperkeratosis (Figs. 1 and 2). After we got informed consent of this patient and her parents, we took her and her parents’ peripheral blood samples for gene test. This gene test was supported and conducted by the Department of Dermatology, The Peking University First Hospital, China. Primers flanking containing all exons and intron–exon boundaries of secreted LY6/urokinase-type plasminogen activator receptor (uPAR)-related protein-1 (SLURP 1) was designed in this gene test, and Sanger sequencing was performed and finally presented.
that this patient is an identical homozygous missense mutation c.256 G>A (p.G86R) and her parents are heterozygous carriers (Fig. 3).

2.1. Family pedigree

There is no consanguineous relationship between her parents. The patient has a brother and a daughter, but neither of them has been affected by PPK.

2.2. Treatment

Oral acitretin and topical tazarotene have been given to this patient. After she took these treatments for nearly one month, physical examinations indicated that the hyperkeratosis was in remission, but the erythema was expanding to her elbows progressively. Due to intolerable dry eyes and lips caused by oral acitretin, the patient stopped taking it.

3. Discussion

PPK, characterized by erythema and hyperkeratosis, is a genetically heterogeneous group of skin diseases. MDM is a rare form of PPK, which is inherited in an autosomal recessive pattern and has characteristics that skin lesions on hands and feet appear soon after birth and are slowly progressive. In some cases, MDM can lead to severe flexion contractures that may cause physical problem for patients. The patients with MDM are characterized by high degree of consanguinity and inbreeding. The genetic etiology of MDM is the mutations in SLURP-1 gene which is involved in keratinocyte apoptosis regulation. In MDM, the property of mutant SLURP-1 proteins is heterogeneity. It is reported that missense mutation of SLURP-1 in MDM may result in changes of protein’s 3D structure and eventually cause nonfunctional protein, which can cause severe hyperkeratosis in patients with MDM. Recently, previous published studies have investigated the underlying molecular mechanism of MDM, but the mechanism of it still remains unclear and worthy of further research.

MDM has rarely been documented in China, and only patients with MDM from Taiwan and Shanghai have been reported by previous published case reports. Moreover, some of their clinical presentations were milder than that in the original MDM and some of the usual signs are not obvious. To our best knowledge, our report is the first MDM report in West China. In our report, the patient shows a typical glove-and-stocking distribution and obvious flexion contractures. It is worth noting that the missense mutation of SLURP-1 in this case was similar with the missense mutation reported by the previous published case report from Shanghai, which may help us know more information about MDM in China. To some extent, our case can enrich the understanding of MDM and the gene phenotype in China and East Asia. The patients with MDM may need a long-term oral acitretin to alleviate MDM. The main adverse effect of oral acitretin is dryness of eyes and lips, which may reduce the medication adherence. Therefore, to improve adherence to oral acitretin in patients with MDM, we should give more health education and appropriate moisturizing treatment to them. Moreover, several published cases reports indicated a hereditary association between autosomal dominant PPK and malignancies, such as esophageal carcinoma and dermatoma; as a subtype of PPK, patients with MDM have a high risk of developing epithelial malignancies, particularly malignant melanoma. However, to date, any evidence of malignancies has not been
found in this patient, and she still needs a long-term follow-up observation.

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Figure 3. Gene test of this patient and her parents. (A) An identical missense mutation c.256G>A (p.G86R) was detected in SLURP1 of this patient. Arrow indicates the site and pattern of mutation in SLURP1. (B) Her parents are heterozygous carriers. Arrow indicates the site and pattern of mutation in SLURP1.