Mal de Meleda

Alternative Names
MDM
Meleda Disease
Keratosis Palmoplantaris Transgradiens of Siemens
Keratoderma Palmoplantaris Transgradiens

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
248300

Mode of Inheritance
Autosomal Recessive

Gene Map Locus
8qter

Description
Mal de Meleda derives its name from its relatively high frequency among inhabitants of the Dalmatian Island of Mljet, Croatia, called Meleda in Italian, with 1 in 200 individuals affected. However, the condition has also been observed in countries distant from Mljet. In world populations, the disease has an average prevalence of 1 in 100,000. The disease was first described in 1826 and diagnostic criteria were presented in 1969. Mal de Meleda is a rare autosomal recessive disorder characterized by diffuse transgressive palmoplantar keratoderma, keratotic skin lesions, perioral erythema, brachydactyly, and nail abnormalities. Hyperkeratosis soon appears after birth and progresses with age and extends from the palms and soles onto the dorsal surface of the hands and feet, elbows and knees without involvement of other organs. A broad spectrum of clinical presentations has been described in patients with a diagnosis of Mal de Meleda. Histopathologically, hyperorthokeratosis and acanthosis, and foci of parakeratosis are also seen.

Molecular Genetics
Mal de Meleda can be caused by mutations in the secreted leukocyte antigen-6 (Ly6)/urokinase-type plasminogen activator (uPAR)-related protein gene, also known as SLURP1. The Ly6/uPAR protein family can be divided into two subfamilies. One comprises glycosylphosphatidylinositol (GPI)-anchored glycoprotein receptors with 10 cysteines and no GPI-anchoring signal sequence.

Epidemiology in the Arab World

Algeria
Fischer et al. (1998) performed linkage analysis of two large consanguineous families from Algeria, including 10 affected individuals. Three of the patients presented a phenotype with unusual presence of lesions in inguinal area of the body.

Palestine
Eckl et al. (2003) analyzed 13 affected and 29 unaffected members of a large Palestinian family with multiple consanguineous marriages. The family originated from a town in the region of Vadi Aara. Affected individuals had clinical features similar to those in patients from the island of Meleda and had the characteristic 'glove-and-stocking' keratosis. However, they did not show any extension onto the knees or elbows as seen in a Bedouin Emirati family [See also: United Arab Emirates > Eckl et al. (2003)].

Tunisia
Charfeddine et al. (2003) investigated 17 patients and 22 unaffected members from eight large consanguineous Mal de Meleda families.
originating from cities in northern Tunisia. All the clinical features of Mal de Meleda were constantly present and variable severity was noted among patients.

**United Arab Emirates**

Lestringant et al. (1992) reported the case of a United Arab Emirates national patient with Mal de Meleda with three unusual facultative features. These were: prominent knuckle pads, peculiar finger-nail anomalies and pseudo-ainhum on both fifth fingers. Four other members of the patient’s family were also affected by Mal de Meleda. Five years later, Lestringant and colleagues re-examined the four young Mal de Meleda patients (Lestringant et al., 1997). Patients were members of a consanguineous Bedouin family and were the result of first cousin marriage. They were 7 months to 12 years old and presented with keratoderma palmoplantaris and transgressive pachyderma that had both been present before the first year of age. Keratoderma palmoplantaris and transgressive pachyderma were more pronounced in the two oldest patients. When the oldest patient was aged 23, keratoderma palmoplantaris was grayish, diffuse and waxy, and smooth (Eckl et al., 2003). Transgressive pachyderma was present in a triangular pattern on the flexor aspects of the wrists and over the Achilles tendons. The sides of the feet and hands were covered by circumscribed pachyderma, which also tightly encased the fingers and toes. The relatively mild features in the patient were in sharp contrast to the clinical picture two years earlier, after six months of hard manual labor in the fields. At that time, keratoderma palmoplantaris was thicker, irregular, rough, and scaly, with deep cracks, abraded patches, and keratotic nodules. Transgressive pachyderma was also thicker and larger, rough and scaly with patchy abrasions, and knuckle pads were prominent (Eckl et al., 2003). Family histories were consistent with autosomal recessive inheritance.

Lestringant et al. (1997) concluded that the development of Mal de Meleda lesions appears to be age-related and that environment and individual factors may also play a role in the development and persistence of the lesions. Eckl et al. (2003) further analyzed the patients in the family of Lestringant et al. (1997) and said that they showed an extension of keratoses onto the knees or elbows.

**References**


**Contributors**

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