Darier disease (DD) is a rare skin condition with autosomal dominant inheritance that manifests in childhood or adolescence (1, 2). It is characterized by keratotic papules that may coalesce into large warty plaques, predominantly affecting seborrhoeic areas, such as the forehead, central chest, back and scalp borders, usually accompanied by palmoplantar pits and characteristic nail changes (i.e. longitudinal leukonychia and V-shaped notches at the distal end of the nail plate) (1, 3). Involvement of intertriginous areas and psychiatric symptoms may also be present (1, 3). Heat or humidity, excessive sweating, exposure to ultraviolet (UV) light, friction, medications and infections, as well as pregnancy or delivery, aggravate the disorder (3).

Histologically, DD is characterized by loss of adhesion between epidermal cells, termed acantholysis, leading to suprabasal cleavage and abnormal keratinization, which manifests as corps ronds and grains (4).

DD is caused by mutations in the ATP2A2 gene, which encodes isoforms of the sarcoplasmic reticulum ATPase type 2 (SERCA2) in keratinocytes and cells from other tissues (5). SERCA2 is a calcium pump incorporated in the endoplasmic reticulum (ER) membrane that regulates Ca\(^{2+}\) transport from the cytoplasm into the ER lumen. It is organized in 10 transmembrane helices (M1–M10) intercalated by 5 stalk sectors (S1–S5), and in a cytosol-exposed region comprising the phosphorylation and ATP-binding domains (5). In 2000, genetic mosaicism for mutations in ATP2A2 was demonstrated to cause the segmental form of the disease (6), which is quite rare. Segmental DD can manifest in a mosaic pattern distinctive of 2 disease subtypes: segmental DD type 1, which is characterized by warty papules distributed in a linear pattern on a background of clinically normal skin, and segmental DD type 2, in which linear DD lesions are usually more severe and may manifest early after birth, superimposed on a background of generalized DD (7, 8). Segmental DD type 1 was hypothesized to result from a de novo postzygotic ATP2A2 mutation that occurs during embryogenesis, and a few studies have provided genetic proof for this aetiology (4, 9), whereas a loss-of heterozygosity (LOH) in a heterozygous individual was hypothesized for segmental DD type 2 (10).

Although there is no direct evidence for LOH as a causal event for DD type 2, molecular genetic support has been provided (8). We report here on the molecular basis of the mosaicism in an Italian woman with segmental DD type 1.

**CASE REPORT**

A 47-year-old woman presented with keratotic papules on the right side of her trunk, and right arm and leg. The lesions appeared on...
her chest when she was 27-year-old and spread to the right arm and leg 8 years later, during her first pregnancy. She reported worsening symptoms during summer and spontaneous improvement in winter. None of her family members had similar cutaneous manifestations. Examination showed a linear grouping of papules following Blaschko’s lines on the right arm, thigh and leg, and on the right side of the dorsum, abdomen and chest, where lesions also extended beyond the midline (Fig. 1a-c). No oral, nail or hair abnormalities were found. A skin biopsy taken from a lesion of the posterior aspect of the right leg showed suprabasal acantholytic dyskeratosis with corps ronds and grains (Fig. 1d). Based on the clinical presentation and histopathological findings a segmental DD type 1 was suspected. Treatment included topical steroids, antibiotics and emollients, followed by tazarotene 0.05% and, finally, isotretinoin 0.05%, with only temporary symptom relief.

In conclusion, this report demonstrates that the spontaneous somatic p.Tyr753del mutation is the cause of the segmental phenotype in our patient. She was informed about the possibility that the mosaic condition could also involve the gonads, with a risk of transmitting the full-blown disease to her children. Absence of the mutation in the blood DNA of the patient’s son allowed us to exclude clinical onset of DD in this individual.

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REFERENCES