

Debilitating Darier's disease

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ABSTRACT

Darier's disease is an inherited dermatitis that is due to a mutation in the ATP2A2 gene. This mutation causes disrupted signaling within cells and leads to a skin condition that is resistant to many dermatologic treatments. Though serious complications are rare, Darier's disease can result in bacterial sepsis and Kaposi's varicelliform eruption. In some families seizure disorders are linked to Darier's disease. There is also a paraneoplastic variant that could be considered in patients without a family history of Darier's disease. This article reports a case with typical verrucous masses and waxy papules which, over twenty years, became disabling. Symptoms included pruritus and foul odor and were relieved, along with the keratotic rash, utilizing systemic treatment with acitretin though the condition recurred rapidly when treatment was interrupted. Darier's disease must be considered when patients present with hyperkeratotic lesions that are resistant to usual forms of therapy for inflammatory dermatoses.

Key words: Darier's Disease, acitretin, inherited dermatoses.

Case Report

A 52-year-old man presented with a life-long history of a progressively more severe, tender, keratotic, mildly pruritic dermatosis most notable on his mid-chest, back, lower legs and feet. A foul odor was also present. The rash had previously failed to clear with topical corticosteroids, emollients, and oral antibiotics. The patient's father and grandfather were afflicted in a similar way. Physical examination revealed keratotic lesions, 1 to 8 mm in diameter, resulting in curled cutaneous horns which were focally confluent on the dorsal feet

and legs forming fungating, verrucous masses (Figure 1). Lesions on the chest and back showed less grotesque dirty-brown, waxy papules. Histopathology demonstrated acantholytic dyskeratosis characteristic of Darier's disease. Treatment with oral amoxicillin and topical metronidazole gel relieved his immediate discomfort and diminished the associated odor. Acitretin 25 mg twice daily for 12 months led to an 80% improvement in the plaques. Drug holidays as short as three months led to marked flaring of this condition.

Discussion

Darier's disease is an autosomal dominant genodermatosis caused by dysfunction

of the sarco/endoplasmic reticulum Ca²⁺ ATPase leading to abnormal intracellular Ca²⁺ signaling (1). This results in disadhesion of suprabasilar cells (acantholysis) and apoptosis (dyskeratosis). A mutation in the ATP2A2 gene on chromosome 12q23-24 is responsible for this defect (1).

The onset of Darier's disease is often in childhood (2, 3), and most cases begin before the age of 20. While the full development of the skin disorder may be delayed until late adolescence or middle adult years, some of the potential complications may occur in younger persons.

The present case demonstrates that Darier's disease can be difficult to treat

and can require intermittent courses of acetretin, initially as high as one mg/kg and sometimes prolonged treatment with low-dose systemic retinoids. In milder



Figure 1: Keratotic lesions with grotesque appearing horns form in several plaques on the left foot of this patient with Darier's Disease. Focal impetiginization is of more recent onset.

cases, treatment with 12% ammonium lactate cream or topical retinoids during periods of worsening (such as summer months) may be all that is required. Even in severe cases, the disease is not frequently life-threatening and is compatible with a normal lifespan.

Several complications can result in severe sequelae that lead to emergency room visits. Sepsis, due to a portal entry through skin, has been reported and may become a more serious problem for persons with Darier's disease with the emergence of community-acquired methicillin resistant staphylococcus aureus (4). The foul odor associated with these patients is caused by chronic bacterial colonization of their diseased skin and can be treated with hexachlorophene liquid soap in the shower, mupirocin ointment, metronidazole gel, and intermittent courses of systemic antibiotics. Timely

and appropriate therapy prevents more serious complications such as sepsis. Widespread herpes simplex infection (Kaposi's varicelliform eruption) may also occur when local recurrences spread over the surface of the body due to abnormal barrier function (5). This can be life-threatening if not promptly diagnosed and treated with systemic antiviral medications such as acyclovir, valcyclovir, and famciclovir.

While Darier's disease occurs primarily as a genetic disorder, there do appear to be paraneoplastic variants as well (6). Patients with neoplasm may have a variety of other conditions which may require intensive care interventions, and their skin disorder may be one of many problems which need to be addressed in hospital. Finally, seizure disorders have been associated with Darier's disease in some families (7).

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