

# A Peculiar Case of Darier's Disease in a Patient with HIV Infection

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## INTRODUCTION

Darier's disease also known as Darier-White disease or Keratosis follicularis is a rare genodermatosis with autosomal dominant inheritance first described in 1886 by Marrow and later in 1889 by Darier and White.<sup>1</sup> It has a high penetrance and variable expression although many cases also occur sporadically.<sup>1,2</sup> The disease occurs due to a mutation in the gene ATP2A2 which encodes the sarcoplasmic/endoplasmic reticulum Ca<sup>2+</sup>ATPase type 2 protein (SERCA2) at chromosome 12q23–24.1<sup>1,3</sup>

Novel mutations in the ATP2A2 gene have been reported.<sup>4-6</sup> The disease has a worldwide and equal sex distribution.<sup>1</sup> It typically presents in most cases in the first and second decades of life<sup>1</sup> with males more severely affected than females.<sup>7-9</sup> Prevalence rates vary widely with reported rates of 1 in 30,000-35,000 in Northern England and Scotland<sup>2,10</sup> to 1 in 100,000 in Denmark<sup>11</sup>

It is characterised clinically by hyperkeratotic papules especially in the seborrheic areas, oral mucosa changes, nail changes such as short and wide nails, subungual hyperkeratosis, V-shaped notching, scalloping of the distal nail plate<sup>1</sup>, and histologically by suprabasal acantholysis with a distinctive overlying dyskeratosis.<sup>12,13</sup> Most patients present with the classical seborrheic distribution but there may be variation in severity from localized nail and palmar changes to generalized skin involvement.<sup>1</sup> The disease tends to run a chronic relapsing course without affectation of general wellbeing although spontaneous remission may occur.<sup>1</sup> A positive family history is usually associated with the classical presentation<sup>14</sup> although this was absent in 47% of patients in a larger case series<sup>15</sup>. Only one case report of Darier's disease associated with HIV has been documented in literature and it was from West Africa.<sup>16</sup>

We report a case of Darier's disease in a treatment naïve newly diagnosed HIV positive patient whose lesions improved markedly after commencement of Anti-Retroviral Therapy (ART).

## CASE REPORT

A 41 year old man who works as a fuel pump operator at a petrol station presented with a two month history of worsening slightly itchy and foul-smelling lesions in the armpit, neck and groin areas. Symptoms were exacerbated by sun exposure, heat and sweat. There was no history of similar lesions in the past or in any of his family members. Patient also noted some changes in his nails. He had used some local herbal remedies and antifungal drugs prior to presentation with no improvement of symptoms.

Examination revealed a young man, anxious looking with vegetative malodorous hyperkeratotic lesions at the back of the neck, axilla and groin, and some erosion within the lesions. He also had dystrophic nail changes in the right thumb and both halluces. The oral mucosa was not involved. A clinical assessment of Darier's disease to rule out Hailey-Hailey disease, Pemphigus vegetans and Inverse psoriasis was made. Patient was counselled on the need for a skin biopsy for histology to make a definitive diagnosis. He was commenced on antibacterial wash and ointment with vitamin supplements pending the time when definitive diagnosis was made.

HIV screening was positive and a confirmatory test was done which confirmed the result. Routine hemogram showed an elevated Erythrocyte Sedimentation Rate (ESR) of 52mm in the first hour with other parameters normal. Serum biochemistry was essentially normal. Skin biopsy for histology was done which showed suprabasal acantholysis with the acantholytic keratinocytes disposed in a dilapidated brick appearance.

Hyperkeratosis, moderate acanthosis and lymphocytic infiltrates within the upper dermis were also seen. The histologic features were in keeping with Darier's disease. Patient was referred to the Aids Prevention Initiative of Nigeria (APIN) clinic where he was counselled on his diagnosis of HIV infection and was subsequently commenced on ART. The lesions improved significantly leaving just post inflammatory hyperpigmentation in previously affected areas four weeks after commencement of ART. No new lesions were noted on his follow up visit. The patient is also moisturising daily with pH balanced emollients and is being followed up every three months at the Dermatology outpatient clinic.

## **DISCUSSION**

Darier's disease usually begins in the first to second decade of life and tends to run a chronic course.<sup>1,17</sup> There may be affectation of the nails and mucosal involvement.<sup>1,7,13,18</sup> Nail involvement may range from white and red longitudinal bands which may give a pathognomonic notch at the free margin of the nails, short and wide nails and subungual hyperkeratosis<sup>1</sup>. Mucosal involvement may be in the mouth, tongue, epiglottis, larynx, vulva and the rectum.<sup>1,18,19</sup> Lesions in the mouth may resemble leukoplakia.<sup>17</sup> Darier's disease may initially be localized to the nails and hands but may later become generalised<sup>1</sup>. There may be a malodorous smell especially when intertriginous areas are affected as seen in our patient.<sup>17</sup> Several reports of unilateral segmental cases of Darier's disease have also been documented.<sup>17, 20-22</sup> The first congenital case of Darier's disease was reported in a child who had family members affected in three preceding generations.<sup>23</sup> The first reported case of Darier's disease in Nigeria was in a 70 year old Nigerian woman about twenty years ago.<sup>24</sup>

Darier's disease may be exacerbated by heat, sunburn, humidity and drugs such as lithium and steroids as seen in the patient described.<sup>1,13</sup> There is also an increased incidence of bacterial and viral infections such as staphylococcus and herpes simplex infections which may worsen the condition.<sup>1, 25-28</sup> Treatment of Darier's disease includes the use of emollients, personal hygiene,

sun protection and avoidance of precipitating factors to prevent exacerbation and relapse.<sup>1</sup> Several topical medications such as retinoids<sup>29, 30</sup> vitamin D analogues,<sup>31</sup> and 5 fluorouracil<sup>32,33</sup> are also used in treatment of the condition. Systemic medications such as oral retinoids<sup>34-36</sup> and Ciclosporin<sup>37</sup> have been used in extensive disease with varying degrees of success. Other medications that have also been used include oral magnesium<sup>38</sup> and topical 1 diclofenac sodium.<sup>39</sup> Counselling is also very important as the disease has a lot of psychological impact and adversely affects the quality of life.<sup>40-43</sup> The lesions on the patient presented cleared with ART, topical antimicrobials and pH balanced skin emollients

Human Immunodeficiency Virus (HIV) is caused by either HIV-1 or 2 that belong to the family Retroviridae<sup>44</sup>. These viruses specifically attack CD4+ T cells with consequent immune dysregulation and predisposition to several opportunistic infections, dermatoses and malignancies.<sup>44,45</sup> Only one case of Darier's disease has been previously reported in an HIV positive patient.<sup>16</sup> The patient had late onset Darier's disease with no family history of similar disease suggesting sporadic occurrence, widespread skin involvement and sparing of the nails and mucous membranes.<sup>16</sup> Similarly, the index patient had late onset disease, no family history, nail and skin involvement in the typical sites affected in Darier's disease with mucosal sparing. Interestingly, the patient's skin lesions resolved completely with post inflammatory hyperpigmentation four weeks after commencement of ART as he was treatment naïve at presentation. He has not had a relapse of skin lesions since initial lesions resolved. This brings to question whether the immune dysregulation that occurs in HIV can predispose to Darier's disease in a genetically susceptible individual as his lesions cleared with commencement of antiretroviral therapy.

In conclusion, although immune dysregulation has not been documented in Darier's disease, the immunological abnormalities that occur in HIV infection may predispose a susceptible individual to develop the disease. The natural course of the disease may also be different in HIV positive

individuals. More studies need to be done to determine the association between Darier's disease and HIV.



Figure 1 – Initial presentation



Figure 2 – Four weeks after commencement of antiretroviral therapy

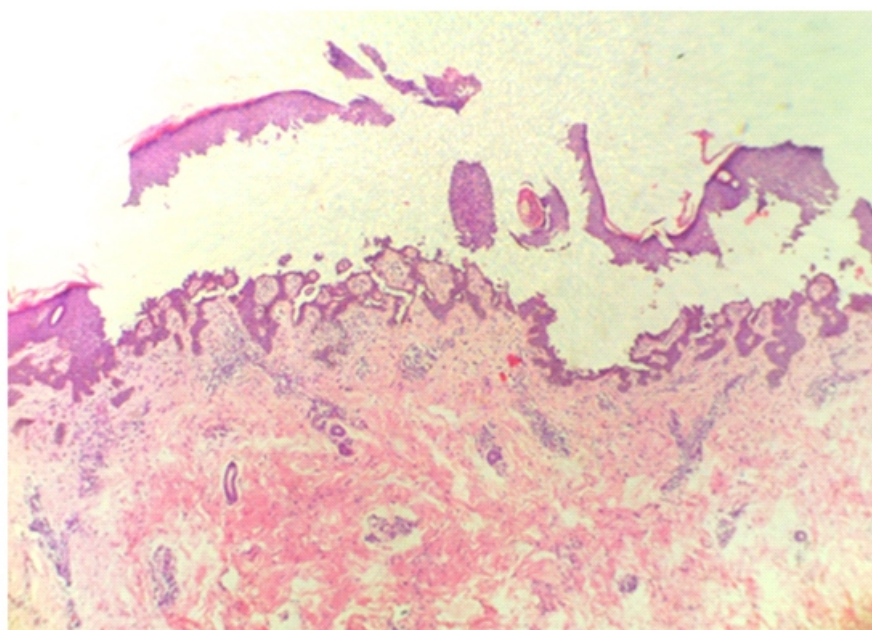


Figure 3 – Histology showing suprabasal acantholysis and acantholytic keratinocytes

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