

Case Report

DARIER'S DISEASE AND SCHIZOPHRENIA- A CASE REPORT

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ABSTRACT

Darier's disease is a rare autosomal dominant genodermatosis. There is a specific mutation in the ATP2A2 gene on chromosome 12q. Several neuropsychiatric manifestations have been described in association with Darier's disease. Most reports have come from western populations, with limited reports of Darier's disease and its neuropsychiatric associations among Asian people, although the demographic and clinical profiles are comparable. We present a case of 38 year old female from Kerala with Darier's disease presenting with schizophrenia spectrum disorder. Her first degree relatives have schizophrenia-like psychosis and dermatological manifestations suggestive of Darier's disease.

Keywords: Darier's disease, schizophrenia

INTRODUCTION

Darier's disease (also known as keratosis follicularis or dyskeratosis follicularis) is a rare autosomal dominant disorder. Darier's disease occurs worldwide, with an estimated incidence of 4 per million per decade and prevalence ranging from 1 in 30,000¹ to 1 in 100,000.² Men and women are affected equally. The age of onset is typically in the second decade of life. Clinically, Darier's disease is characterised by small, isolated papules that usually appear in childhood or teenage (10-20 years of age). These progressively enlarge and extend and are soon followed by thick and adherent grey-yellowish scales with a typical symmetric pattern. The sites of predilection are seborrhoeic areas, folds, and the face (scalp margins, forehead, ears, nasolabial furrows, and scalp). Nails and mucous membranes can be involved, too (particularly buccal mucosa, pharyngeal walls, oesophagus, and rectum). In addition, palms and soles are frequently involved, with typical small lesions of keratosis punctata or pits.³ Darier's disease is a chronic problem with many relapses during the summer season and variable pruritus, especially localised in folds or areas subject to repeated

trauma. Fetid odour occurs mainly when skin folds are affected.

There is a specific mutation in the ATP2A2 gene on chromosome 12q. The ATP2A2 gene encodes the sarcoplasmic/endoplasmic reticulum calcium-adenosine triphosphatase isoform 2 protein (SERCA2), a calcium pump with a central role in intracellular calcium signalling.⁴ Family members with confirmed identical *ATP2A2* mutations can exhibit differences in the clinical severity of disease, suggesting that other genes or environmental factors affect its expression.⁵ Although expressivity is variable, penetrance is high at 95%.⁶

Several neuropsychiatric conditions have been described in association with Darier's disease. However, these don't appear to be associated with a specific class of mutation and may result from an intrinsic but inconsistent effect of defective ATP2A2 expression. Descriptions of neuropsychiatric manifestations such as intellectual disability^{2,7,8}, epilepsy³, mood disorders^{9,10}, suicide^{2,11}, psychosis^{7,12}, and schizophrenia¹³ have been

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reported in patients with Darier's disease. But a comprehensive epidemiological data regarding neuropsychiatric manifestations are lacking. Reports of the association between Darier's disease and neuropsychiatric disorders have mostly come from western populations. We report the case of a 38-year-old woman with Darier's disease- hypertrophic form presenting with schizophrenia spectrum disorder.

CASE REPORT

A 38-year-old female patient from Kollam presented to us in April 2021 with four years of behavioural problems. She was educated up to plus one, married but separated from her husband, has three children, and worked in a cashew factory until three months back. She was diagnosed with Darier's disease, with initial skin manifestation at around 15 year of age and no prior history of any psychiatric illness. However, she has a family history of epilepsy in her sister, schizophrenia-like psychiatric illness in her father and brother, and dermatological manifestations suggestive of Darier's in her father and daughter. Father had illness onset at 55 years of age and her brother at 20 years. Father passed away, and her brother is 37 years old and is continuing medication. Her daughter, who is currently 14 years old, has dermatological manifestations for the last 7- 8 years.



Fig 1- Hyperkeratotic papular lesions with scaling over face, neck and anterior chest wall



Fig 2- Hyperkeratotic papular lesions over hand and

As per her aunt, the informant, she has a continuous illness of four years, with insidious onset, characterised by decreased social interaction, suspiciousness that her food is being poisoned, decreased self-care, sleep, and food intake, and muttering and smiling to self. She had psychiatric consultation locally at Kollam, had temporary improvement, but was on irregular medications (medication details not available). However, she was totally off medications for the past four months and had a worsening of her symptoms, hence bringing for admission.

On mental status examination, she was alert, oriented to time, place, and person; rapport could be established. The psychomotor activity was normal. There was prolixity. There were multiple non-systematised, non-bizarre, and bizarre delusions of persecution, grandeur, infidelity, and delusion of being pregnant by God. She had an anxious mood, affect was appropriate, reactive, of full-range, and mobile. She had second and third-person auditory hallucinations. Cognitive functions were intact, except impaired social, personal, and test judgement and grade 1 insight. Physical examination showed hyperkeratotic, hyperpigmented papular lesions over the face, neck, trunk, and upper and lower limbs, with pruritus. The nails and mucosa were spared.

Based on history and serial mental status examination and observation of ward behaviour, a psychiatric diagnosis of schizophrenia was made, with a differential diagnosis of schizoaffective disorder. Routine investigations, including CBC, biochemistry, thyroid

function test, etc., were done and were within normal range. She was started on risperidone 2mg, which was increased gradually and optimised at 6 mg during the one month of admission. Symptomatic treatment was given for the pruritus. Dermatology consultation was deferred due to the Covid situation. She showed significant improvement in psychopathology and her insight also improved by the time of discharge.

Informed consent was taken from the patient before taking the photographs.

DISCUSSION

There are reports in the literature about the association of Darier's disease with increased psychiatric morbidity, such as depression, suicidal ideation, and mood disorders. However, the most commonly observed neuropsychiatric manifestation in them was major depression. Few case reports highlight the occurrence of schizophrenia in Darier's disease. One of the arguments for the association between Darier's disease and neuropsychiatric disorders is the observation that the skin and brain share a common ectodermal origin. Four possible interpretations for this association are - the association may be purely chance, with no true biological basis (chance hypothesis), the psychiatric disorder could have been triggered by an understandable psychological reaction to the presence of chronic disfiguring skin disease and is unrelated to biological susceptibility (reactive hypothesis), the Darier mutation, through pleiotropic effect, could have increased vulnerability to neuropsychiatric illnesses (pleiotropy hypothesis)¹⁴ or there could be a genetic linkage between the Darier gene and a separate susceptibility gene for neuropsychiatric manifestation (linkage hypothesis).¹⁵ The Darier's disease locus was identified as the ATP2A2, which codes for sarcoplasmic/endoplasmic reticulum calcium-ATPase, SERCA2.¹⁶ This gene presents potential susceptibility to neuropsychiatric manifestation under the hypothesis that variations in SERCA2 have pleiotropic effects in the brain.

In this case, Darier's disease presents with schizophrenia; her first degree relatives have schizophrenia-like psychosis and dermatological manifestations suggestive of Darier's disease. Most of the reported cases in the literature are from the Western world. It was reported that the demographic and clinical

profiles of Asian patients with Darier's disease were comparable to that of the western population in terms of incidence rate, age of onset, distribution of disease patterns, and association with neuropsychiatric disorders⁽¹⁷⁾. The rarity of the case was the reason for us to present this case report.

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