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DARIER'S DISEASE – A RARE AUTOSOMAL DOMINANT GENODERMATOSIS: A CASE REPORT

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ABSTRACT Darier's disease, also known as Darier–White disease or keratosis follicularis, is a rare autosomal dominant genodermatosis characterized by greasy, hyperkeratotic papules predominantly in seborrheic areas, along with nail and mucosal changes. It has a prevalence of approximately 1 in 100,000. The disease typically manifests in adolescence and follows a chronic relapsing course. Here, we present a series of three clinically and histologically confirmed cases, emphasizing the importance of early diagnosis, genetic counseling, and symptomatic management. This case series underlines the diversity in clinical expression and the importance of recognizing rare genodermatoses.

KEYWORDS : Darier disease, keratosis follicularis, genodermatosis, ATP2A2, hyperkeratotic papules, acantholysis

INTRODUCTION

Darier's disease (DD) is a rare inherited skin disorder caused by mutations in the **ATP2A2** gene on chromosome 12q24.1, which encodes the SERCA2 calcium pump essential for desmosomal integrity and keratinocyte adhesion. Dysfunction of this pump leads to defective calcium signaling, resulting in acantholysis and dyskeratosis. It follows an **autosomal dominant** inheritance with variable penetrance and expressivity.

First described by Ferdinand-Jean Darier in 1889, the disease manifests as **greasy, warty papules**, especially in seborrheic areas such as the scalp, forehead, nasolabial folds, chest, and back. It may also involve **nails, mucosa, and palmar/plantar surfaces**. The disease exacerbates with **heat, sweat, friction, infections, UV exposure**, and emotional stress. While the diagnosis is often clinical, **histopathology** confirms acantholytic dyskeratosis with **corps ronds** and **grains**.

Case Descriptions

Case 1

A 62-year-old female presented with crusted, malodorous lesions over the **scalp, face, and flexures** since age 12. The lesions were **episodic**, worsened with **sun exposure and friction**, and associated with **mild pruritus**. She also had multiple skin-colored, wart-like papules over the **dorsum of hands and feet** for the past 8 years.

Family history revealed **similar lesions in her father, elder sister, and children**, suggesting a **dominant inheritance**. Nail changes included **subungual hyperkeratosis**, **V-shaped nicks**, and **longitudinal ridging**.

Cutaneous Examination

On clinical examination, multiple **hyperpigmented papules**, a few **pustules**, and **erosions** were noted over the **groins, abdomen, and inframammary folds**. **Hyperpigmented macules** were present over the **axillae** and **back**, with **honey-colored crusts** over the **scalp**. Palms and soles were spared. Dorsal hands and feet showed flat papules. Nail dystrophy with **subungual hyperkeratosis** and **V-shaped distal nicks** noted.

Histopathology

Skin Biopsy From Affected Areas Revealed:

- Suprabasal acantholysis
- Dyskeratosis
- Presence of **"corps ronds"** (round dyskeratotic cells with basophilic nuclei and clear halo in spinous layer)
- **"Grains"** in stratum corneum
- These features confirmed the diagnosis of **Darier's disease**.

DISCUSSION

Darier's disease stems from mutations in **ATP2A2**, affecting calcium ATPase function in the endoplasmic reticulum. This impairs **desmosomal integrity**, explaining the **acantholysis** and **keratinocyte dysadhesion**.

Clinical Features:

- Hyperkeratotic papules in seborrheic areas
- **Nail Changes:** V-shaped nicks, subungual hyperkeratosis, longitudinal ridging
- Mucosal papules (e.g., oral cobblestoning)
- Foul odor due to secondary bacterial colonization
- **Triggering Factors:** UV radiation, heat, friction, infections, and stress

Differential Diagnosis Includes:

- Hailey-Hailey disease (benign familial pemphigus)
- Seborrheic dermatitis
- Grover's disease
- Acrokeratosis verruciformis

Genetic counseling is crucial due to autosomal dominant inheritance. While **DNA testing** can confirm the mutation, it is not mandatory for diagnosis.

Management:

- **Topical Therapy:** keratolytics (salicylic acid, urea), topical corticosteroids, retinoids
- **Systemic Therapy:** oral retinoids (e.g., acitretin), antibiotics for secondary infections
- Lifestyle modifications: Avoiding heat, UV exposure, friction
- Psychosocial support: Due to visible disfigurement and chronicity
- Recent advances explore the **role of siRNA**, **gene editing**, and **targeted calcium signaling modulators**, but these remain experimental.

CONCLUSION

Darier's disease is a chronic, relapsing **genodermatosis** with significant psychosocial and physical morbidity. Early diagnosis via clinical suspicion and histopathology is essential. Management involves a **symptomatic approach**, family counseling, and prevention of aggravating factors. Our case series highlights the **classical presentation, hereditary pattern**, and the **importance of dermatologic vigilance** in recognizing such rare disorders.

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