Multiple hyperpigmented, warty and greasy papules

AK Douieb MD[1], Bayoumi Eassa MD[2]

[1]*Consultant, Department of Dermatology, HPLM, Larache, Morocco*
[2]*Department of Dermatology, Farwaniya Hospital, Kuwait*

A 54-year-old man presented with multiple yellow–brown, raised, keratotic, mildly greasy pruritic papules of 20 years duration. The lesions started on the chest and gradually progressed to involve the scalp, forehead, nasolabial folds, and groin area. Examination revealed multiple hyperpigmented, warty, greasy papules, some of them showing follicular appearance (Fig. 1). All routine hematological investigations were normal. General physical examination was normal. A positive family history was present with similar lesions in his son.

Skin biopsy was obtained from the keratotic papules and showed suprabasal cleft with few acantholytic keratinocytes. The upper part of the epidermis showed 2 types of dyskeratotic cells; corps ronds which were located in stratum granulosum and grains which were located in stratum corneum (Fig. 2).

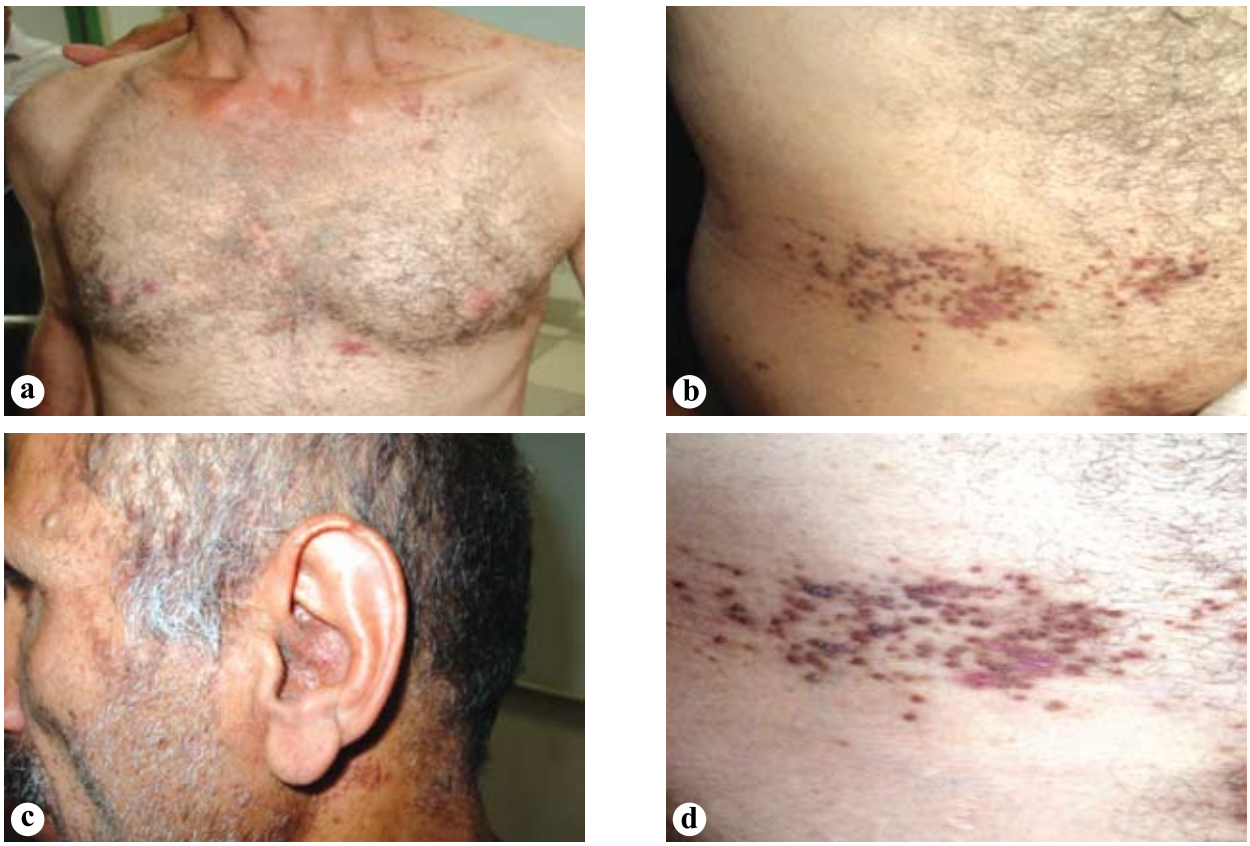

Fig. 1 a,b,c,d Clinical pictures showing multiple hyperpigmented, warty and greasy papules over trunk and face

Correspondence: *Dr. AK Douieb MD, Consultant, Department of Dermatology, HPLM, Larache, Morocco, Tel: 0021261204376*
Email: douieb@menara.ma

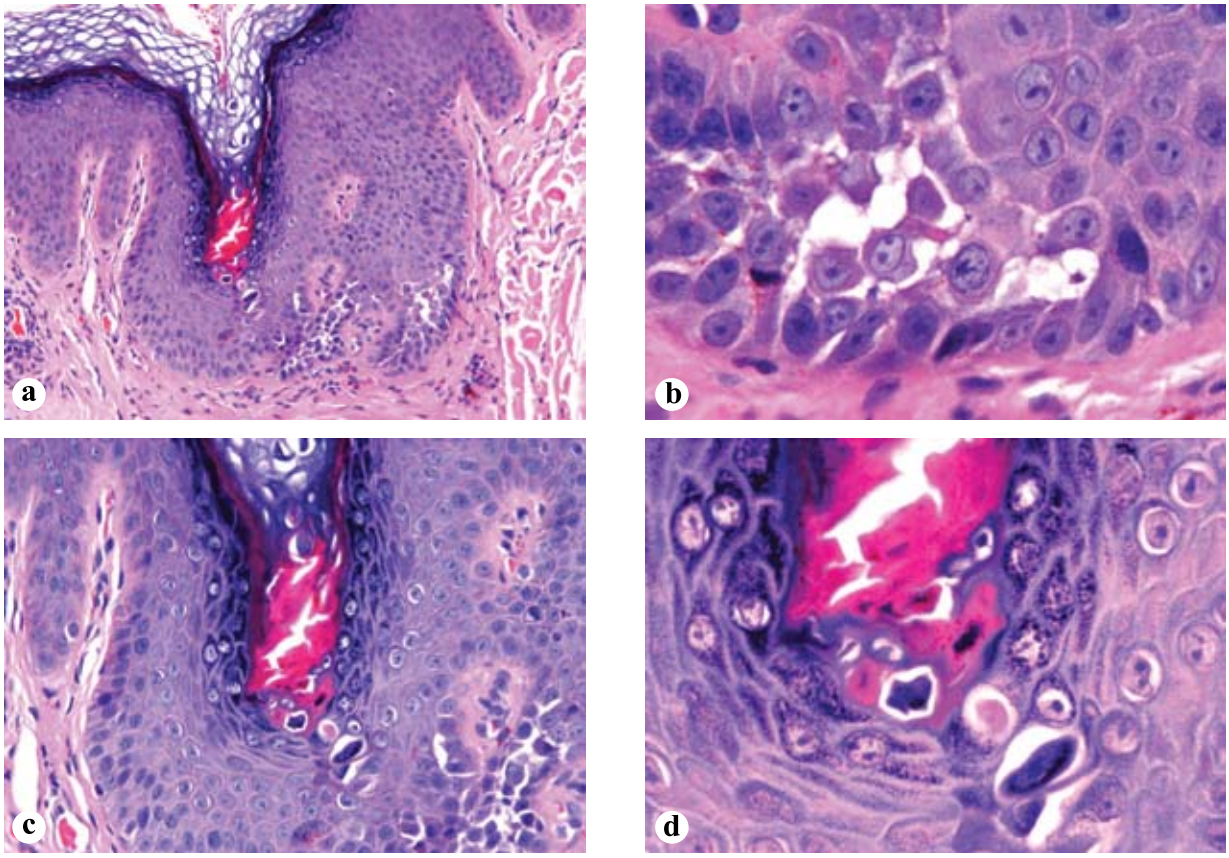

Fig. 2 a,b,c,d H & E section

What is your diagnosis?

1. Prurigo Nodularis
2. Lichen planus
3. Confluent and reticulated papillomatosis
4. Darier's disease (Keratosis follicularis)
5. Keratosis pilaris

The diagnosis is Darier's disease

DISCUSSION

Darier's disease (DD) which is also known as Darier-White disease or keratosis follicularis is a rare dermatosis with autosomal dominant inheritance with altered keratinisation of the epidermis, nails and mucous membranes.[1] The disease was first reported independently by Darier and White in 1889. White was first to recognize the genetic nature of DD by noticing that a mother and her daughter were affected. .[2-3] The disease commonly manifests from age 6-20 years; however, patients have presented as early as age 4 years and as late as age 70 years. It usually presents with multiple greasy, hyperkeratotic, firm skin coloured to brown papules over seborrhoeic areas, flexures, behind the ears, neck and acral areas. These papules may coalesce into plaques. According to the major areas affected, DD can be classified into seborrhoeic, flexural, acral or mixed pattern. Approximately 80% of patients have mild flexural involvement with scattered papules in the groin, axillae, or, in women, submammary skin.[4] Involvement of the hands is very common (approximately 95%). Lesions on the palms include punctate keratoses (80%), palmar pits (80%), and hemorrhagic macules (<10%). Acrokeratosis verruciformis–like lesions

(warty flat-topped papules on the dorsal hands) are present in approximately half the patients. Nails may develop characteristic red and white streaks, longitudinal ridges, and V-shaped distal notching. Oral involvement is detected in approximately 15% of patients, and usually appears as fine granular or coarse pebble stone lesions over the palate and less commonly, the tongue and buccal mucosa. Oral lesions may also affect the salivary glands and cause obstruction.[5] Histopathologically, the key features in diagnosing Darier's disease are focal acantholytic dyskeratosis with corps ronds and grains. Both corps ronds and grains are abnormal keratinocytes. Corps ronds are large keratinocytes with brightly eosinophilic cytoplasm and a large nucleus surrounded by a clear halo usually located in stratum spinosum and granulosum while grains are oval cells with elongated cigar-shaped nuclei and abundant keratohyaline granules usually located in stratum corneum.[6] The differential diagnoses of DD include eczema, Hailey-Hailey disease, Grover's disease for seborrhoeic or flexural lesions, acantholytic epidermal nevus for linear or segmental lesions, acrokeratosis verruciformis of Hopf and plane wart for acral lesions. Darier disease in a unilateral or localized pattern was first reported at the turn of the last century. This variant often lacked other features that were associated with typical Darier disease and the skin lesions were usually confined to a limited area.[7] Vesiculobullous variant of Darier's disease was first described by Pels and Goodman in 1939.[8] It can be confused with Hailey-Hailey disease. However, the warty malodorous greasy papules and vesicles with lack of maceration, the histological finding of marked hyperkeratosis, villi formation, and presence of dyskeratotic cells pointed towards the diagnosis of bullous Darier's disease. But the age of onset, typical flexural involvement, relapsing and remitting course of the vesicles and the lack of profound dyskeratosis and presence of foci of dilapidated brick wall appearance suggested Hailey-Hailey disease.[9] Other forms of DD can be recognized including cornifying, comedonal, haemorrhagic and hypopigmented, depigmented and acral, variants.[10-15]

The main genetic defect in DD is the involvement of ATP2A2 gene, mapped to chromosome 12q23-24.1. This gene encodes an endoplasmic reticulum calcium-transporting ATPase enzyme (SERCA2), which has a central role in intracellular calcium-mediated signalling. Defective SERCA2 function may alter the signalling mechanisms within keratinocytes. These changes impair desmosome assembly or interactions between the cytoskeleton and desmosomes. [16]

The management of DD can be divided into general advice, genetic counseling, topical remedies, systemic retinoid and surgical treatment. The main aims are symptomatic relief and treatment of complications. Basic measures for DD include sunscreen, cool cotton clothing, and avoidance of hot environments. Moisturizers with urea or lactic acid can reduce scaling and hyperkeratosis.

Topical therapy (mild or moderately potent topical steroid, topical retinoid such as isotretinoin gel, tretinoin cream and tazarotene gel). Oral retinoids (e.g. acitretin, isotretinoin, and etretinate) are considered the most effective treatment for DD. They reduce hyperkeratosis, smoothen papules, and reduce odor in more than 90% of patients. The main adverse effects, including mucosal dryness,

photosensitivity, hyperlipidemia, transaminitis, and skeletal hyperostosis. They are teratogenic, and appropriate counseling and contraception must be given. [17]

Oral antibiotics are often necessary to clear secondary bacterial superinfection. They may also be used as prophylaxis to prevent infection. Oral contraceptives have been reported to help in perimenstrual flares. Systemic steroids and cyclosporine were reported to be effective in reducing the inflammation in eczematous lesions. Surgical treatment includes electrosurgery, surgical excision with skin grafting and dermabrasion. Laser therapy such as carbon dioxide laser and Ebrium Nd:YAG laser were found to be effective. Photodynamic therapy with 5-aminolevulinic acid was used to treat the disease with improvement in more than 60% of cases.[18-20]

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