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Darier-White Disease: A Case Report

Masoud Golpour
Department of Dermatology, Pasdaran Boulevard, Booali-Sina Hospital,
Mazandaran University of Medical Science, Sari, Iran

Abstract: Darier-White Disease is a genetic disorder that involved the keratinized and non-keratinized epithelium of mucous membrane, cornea and submandibular glands. It is manifested in summer and predisposed by warm and wet weather conditions. The complications of disease are aggravated by bacterial and herpes simplex virus infections. Diagnosis is based on positive family history, clinical and histopathological characteristics of the disease. Although, surgical treatment is useful for hypertrophic kinds of the disease, systemic Isotretinoin is a choice treatment. We herein present two patients with Darier-White Disease. Case one was a 30 year-old man with desquamative papules for 15 years. The surface of lesions was greasy and rough. The lesions were on face, auxiliary and upper chest area. The diagnosis was done after biopsy from forehead lesions. Case two was a 22 year old man with positive history of lesions on hands from childhood. The spreading papules were appeared in neck area during recent year. Patient referred with lesions on hands, wrist, posterior side of elbow, scapulae, neck and anterior and posterior of the trunk. The diagnosis was confirmed after biopsy from abdominal surface lesions. There is no cutaneous malignancies report related to Darier's disease in prior studies. Although, Basal Cell Carcinoma (BCC) and a rare kind of sweet gland's tumor were reported, squamous cell carcinoma in digestive system and skin and hyperkeratosis in foot nail was reported in heterozygote mice. Differentiation between human and mice is needed future studies.

Key words: Darier-White Disease (DWD), pathology, treatment, diagnosis, biopsy

INTRODUCTION

Darier-White Disease (DWD) is an autosomal dominant genodermatosis without evidence for X-linked or autosomal recessive forms of the disease (Constantinidis and Tissot, 1981; Cooper and Burge, 2003; Zeglaoui *et al*., 2005; Tavadia *et al*., 2002). The prevalence of DWD was reported one in 100,000 in Denmark and one in 36,000 in England. DWD is not present at birth and generally begins in the first or second decade. Male and female are equally involved (Tumer and Horn, 1997; Koh *et al*., 1996; DiDonato and Sarkar, 1997). DWD is usually present in the summer and is aggravated with heat and humidity (Davis, 1987). Bacterial infections are the common causes of disease and exacerbated by herpes simplex virus (Cuajungco and Lees, 1977). DWD dose not seem to be a predisposing factor for cutaneous malignancies, though basal cell carcinomas and a rare sweat gland tumor was reported (Salmenpera, 1997; Choo and Klug, 1997). Associated diseases consist of Rhinitis pigmentosa and occasional asymptomatic bone cysts (Choo and Klug, 1997; Koh *et al*., 1996). There is no preventive method for the disease (Prasad, 1985). DWD can involve forehead, scalp, chest, trunk and back. Although, these areas have many sebaceous glands, lesions also occur commonly in sites without sebaceous glands such as palms and soles (Sandstead, 1995), besides, in keratinizing and non-keratinizing epithelial, such as mucous membrane, cornea and submandibular glands (Hassan *et al*., 2000; Williams, 1983). Clinical diagnosis of small lesions in adults may be difficult and may need biopsy (Vallee and Auld, 1990). Seborrheic dermatitis due to distribution and waxy appearance of the lesions is considered in differential diagnosis, as well as benign familial pemphigus, mainly pemphigus foliaceous can be similar to the disease on clinical and histological grounds. Positive family history, clinical manifestation and histological features made diagnosis of the disease (Tumer and Horn, 1997; Frederickson, 1989; Ripa and Ripa, 1995; Collipp, 1982; Klug and Schwabe, 1995). Sunscreens (at least SPF 30) are necessary for treatment of the disease (Berg, 1990). This genetic disorder affecting the epidermis is enhanced by topical or systemic retinoids including topical Tazarotene, Adapolene and Tigazone (Berg, 1990; McMillan and Rowe, 1983). Systemic Isotretinoin is the first choice of systemic therapy (Cooper and Burge, 2003). If the disease is resistance to the first therapy, Acitretin is suitable. In cases of long-term therapies, Tazarotene gel can be used in addition to systemic retinoids. If the disease precipitates by

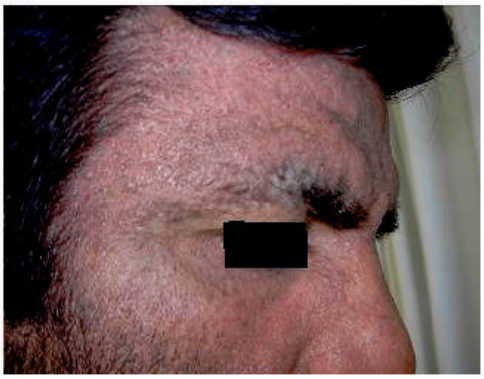

Fig. 1: Papulovegetative lesions in forehead with greasy and Seborrheic surfaces

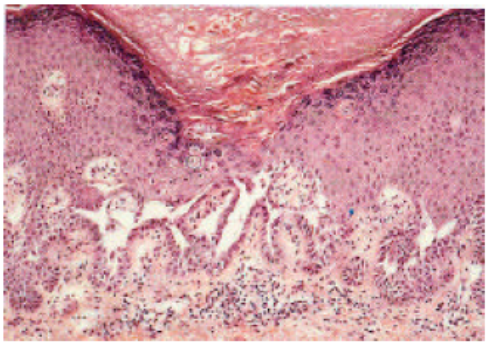

Fig. 2: Hyperkeratosis, Parakeratosis, acantholytic cells, diskeratosis and Lymphatic infiltration associated with melanophage in dermal area (Hematoxilin and Eosin)

bacterial infections, appropriate antibiotic therapy will be essential and can lead to remarkable improvement (Vilanova *et al*., 1997; Heinkin and Bradley, 1970). We present here two cases of Darier-white disease that referred to dermatology clinic at Boo-Ali Sina hospital in Sari/ Iran.

Case 1: A 30 year-old man presented with distributed malodorous papulovegetative lesions in forehead, auxiliary and superior part of trunk. The lesions first appeared greasy and Seborrheic (Fig. 1).

The patient complained of slight itching and burning sensation. The onset of the disease was 15 years ago. Seborrheic papules in face were the first manifestation. The lesions appeared in auxiliary and superior part of trunk several months later. The patient had no history of other disease and no family history of Darier-white disease. Hematology tests were normal. There was no significant problem at physical exam. Biopsy was

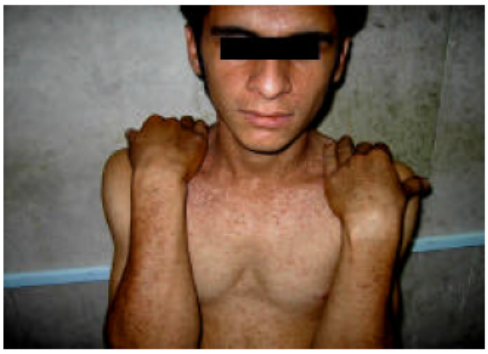

Fig. 3: Multiple distributed papules located on hands, wrist, posterior part of elbow, scapula, neck and anterior part of trunk

taken from forehead lesion and revealed hyperkeratosis, Parakeratosis and epidermis acanthosis. Acantholytic cells and diskeratosis were seen. Lymphatic infiltration associated with melanophage revealed in dermal area (Fig. 2). Histopathological study confirmed the diagnosis of DWD.

Case 2: A 22 year old man who referred with multiple distributed papules located on hands, wrist, posterior part of elbow, scapula, neck and posterior anterior parts of trunk (Fig. 3).

The lesions on hand appeared from childhood. The patient reported the lesion on neck from last year. He had no history of other diseases. Family history of Darier's disease was not found. At physical examination, no problem was detected. Hematology study was normal. Biopsy was obtained from abdominal lesion and showed hyperkeratosis, Parakeratosis, acantholytic, papillomatosis epidermis and acantholytic cells. There was mild lymphatic infiltration. Diagnosis of Darier's Disease was confirmed histopathologically.

DISCUSSION

Darier's disease is an autosomal dominant disorder with worldwide distribution. The prevalence of DWD is estimated to vary from one in 36,000 to one in 100,000 (Tavadia *et al*., 2002; Loche *et al*., 1999). In Godic *et al*. (2005) study, Darier's disease was detected in 77 cases (Godic *et al*., 2005). Also, in a study of Goh *et al*. (2005) in Singapore from 1982-2002, 24 of patients had Darier's disease. Our study emphasizes the rarity of Darier-White disease, whereas only 2 cases among 2470 biopsies were diagnosed during 10 years clinical study. DWD manifests by multiple distributed,

crusted, pruritus papules that are occasionally malodorous (Cuajungco and Lees, 1977). The distribution of the lesions is related to Seborrheic areas, while the chest, back, ears, nasolabial folds, forehead and groin are involved commonly (Constantinidis and Tissot, 1981; Tumer and Horn, 1997; Koh *et al*., 1996; Cuajungco and Lees, 1977). The lesions may first appear as colored papules that are quickly covered with rough-textured, scaly crust (Koh *et al*., 1996; Cuajungco and Lees, 1977; Salmenpera, 1997; Vilanova *et al*., 1997). The lesions may joint together into large plaques. Then the plaques become quite thick, forming malodorous hypertrophic warty masses in intertriginious areas. Permanent scarring alopecia may occur because of extensive scalp involvement (Constantinidis and Tissot, 1981; Cuajungco and Lees, 1977; Sandstead, 1995; Ripa and Ripa, 1995; Goh *et al*., 2005). The disease first reported in an American man in 1889, when he was entered in the Northern army at the age of 22. His eruption appeared under his knapsack after a long march. Lesions had precipitated by oral lithium and phenol or ethyl chloride spray (Tumer and Horn, 1997; DiDonato and Sarkar, 1997; Cuajungco and Lees, 1977; Salmenpera, 1997; Prasad, 1985; Heinkin and Bradley, 1970; Ecker and Schroeder, 1978). Cutaneous malignancies are rarely reported with Darier's disease. Subungoual and scrotal Papilloma cyst were reported in two patients (Ripa and Ripa, 1995; Berg, 1990). As mentioned above, DWD is an inherited autosomal dominant trait and new mutations are common with high penetration over 95%. A various set of mutations in Ca^{2+}-ATPase isoform 2 (SERCA2) has been identified (Tumer and Horn, 1997; Frederickson, 1989; Collipp, 1982; Ecker and Schroeder, 1978). Premature and abnormal keratinization and loss of epidermal adhesion with acantholysis are visible. Electron microscope studies demonstrate basal cell vacuolization and decreasing numbers of desmosomes adhesion on the lateral borders of basal cells (DiDonato and Sarkar, 1997; Ripa, 1995; Withers *et al*., 1968). Tazarotene gel is effective in children as well as in adults and Sunscreens (at least SPF30) are necessary (Vallee and Auld, 1990; Vilanova *et al*., 1997). Diagnostic and therapeutic managements in DWD should be included biopsy and pathological assessment of the lesion. Early diagnosis, current drugs therapy and sunscreens are important in treatment of the DWD. Further studies are needed to identify the relationship between DWD and cutaneous malignancies.

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