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CASE REPORT

INFLAMMATORY VITILIGO VERSUS HYPOPIGMENTED MYCOSIS FUNGOIDES IN A 46 YEAR - OLD IRANIAN WOMAN (HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY): A CASE REPORT AND REVIEW OF THE LITERATURE

[1]Kamyab Hesari Kambiz, [2,*]Montazer Fatemeh and [3]Safaeii Naraghi Zahra

[1]Department of Pathology, Razi Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran
[2]Department of Pathology, Gastrointestinal Cancer Research Center, Imam Hospital, Mazandaran University of Medical Science, Sari, Iran
[3]Department of Pathology, Razi Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran

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ABSTRACT

The diagnosis fundament of vitiligo is focusing clinical manifestations followed by biopsy that is helpful for discriminating disorder from other clinical conditions characterized by hypo pigmentation. The rare inflammatory variant of vitiligo may be difficult to distinguish from hypo-pigmented mycosis fungoides (MF) on clinical, histological and even immunohistochemical grounds. Both diseases show dermal lymphocytic infiltration, exocytosis, interface dermatitis and mild spongiosis (particularly when biopsies are taken from the periphery of early vitiliginous lesions or from lesions with an inflammatory borders). Also both disorders show a predominance of CD8+ T cells in tissue samples. We present a case with clinical findings of several depigmented patches on the forehead, eyelids, and dorsal hands, the near-total loss of melanocytes evident with Melan-A staining, and PCR findings demonstrating a lack of monoclonality, although according to combination of clinical, histological, immunohistochemical and molecular study, inflammatory vitiligo was favored but hypo pigmented MF could not ruled out definitely.

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INTRODUCTION

Vitiligo is an acquired pigmentary disorder involves both skin and mucous membranes manifested by depigmented patches and macules (Ortonne *et al.,* 2008). This phenomenon is commonly associated with some underlying disorders such as autoimmune disorders. The diagnosis fundament of vitiligo is focusing clinical manifestations followed by biopsy that is helpful for discriminating disorder from other clinical conditions characterized by hypo pigmentation (Kovacs *et al*., 1998). For confirming diagnosis, microscopic examination, Fontana-Masson stains and immunohistochemistry testing showed specific skin involvement including full lack of melanocytes in associated with total losing pigmentation in epidermal layer (McKee *et al.,* 2005). Along with hypopigmentary changes, other histologic findings include perivascular and perifollicular lymphocytic infiltration, melanocytes and keratinocytes degeneration, increasing Langerhans cells count, and epidermal vacuolization (Moellmann *et al.,* 1982). Although a variety of scenarios have been pointed to describe causes of vitiligo including cytotoxic, oxidant-antioxidant, autoimmune, and neural mechanisms, recent researches have suggested that some local triggers may alert immune innate system of the skin that precede adaptive immune responses targeting melanocytes (Alain Taïeb, 2012).

Corresponding author: Montazer Fatemeh
Department of Pathology, Gastrointestinal Cancer Research Center, Imam Hospital, Mazandaran University of Medical Science , Sari, Iran

CASE PRESENTATION

A 46-year-old Iranian female presented to our office complaining of a 5-year history of white patches on her face, neck, and trunk. Past medical history was insignificant with a negative review of systems. On physical examination, speckled, depigmented macules and patches on the eyelids, forehead, cheeks, neck, and lower trunk were appreciated. In addition, hypopigmented patches with scaly borders were observed. No evidence of poikiloderma, hypoesthesia, and dysesthesia of the patches were noted.

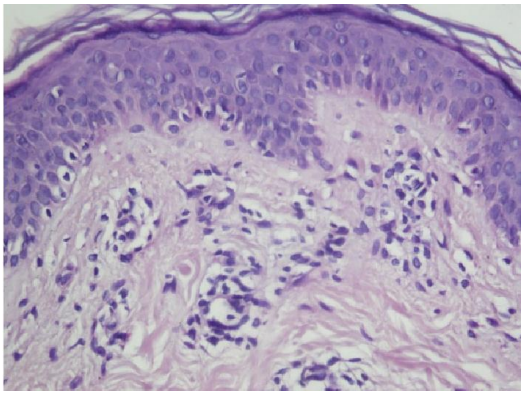

Fig. 1. Punch biopsy [H&E, 200X]

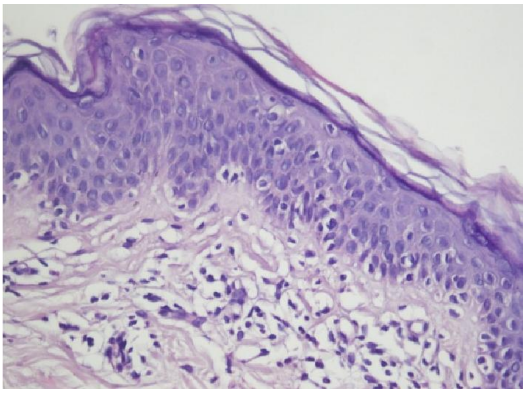

Fig. 2. Punch biopsy [H&E, 400X]

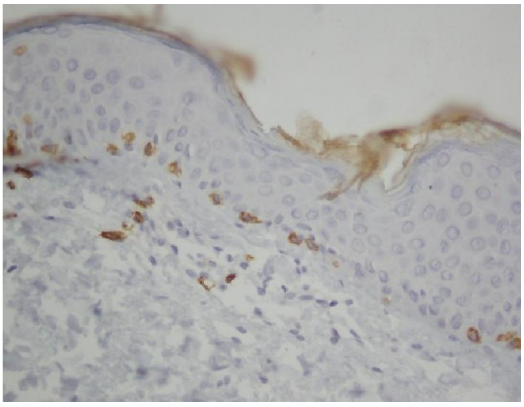

Figure 3a.

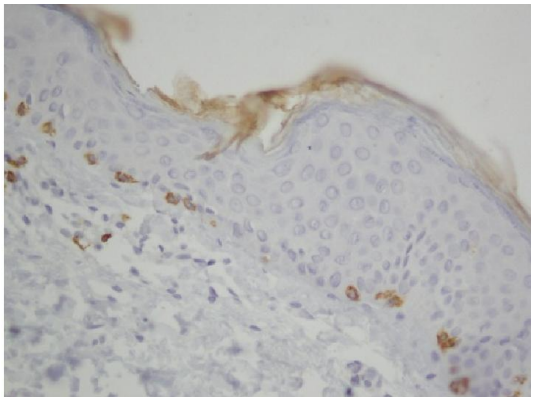

Figure 3b.

Fig. 3a, 3b. Punch biopsy. CD4+ (a) to CD8+ (b). Ratio approximately 1:1 (400X)

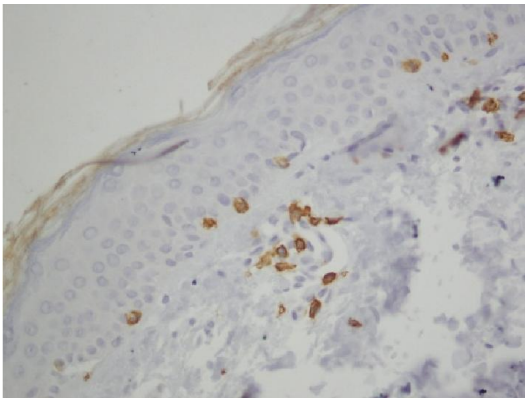

Fig.4. CD7 Stain positive in approximately 30% of intraepidermal lymphocytes (400X)

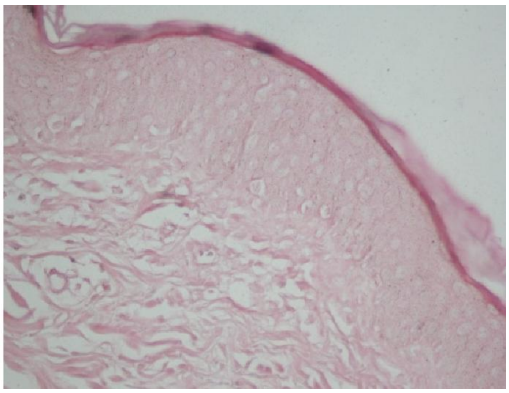

Fig. 5. Fontana Masson stain, complete loss of melanin pigment

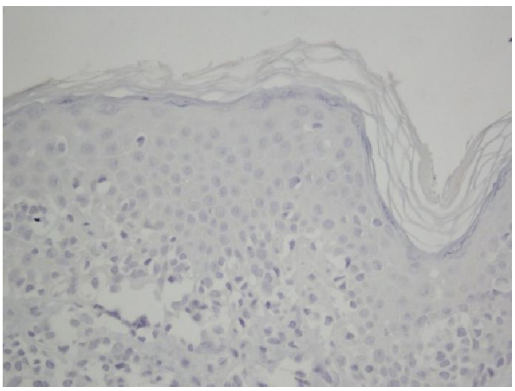

Fig. 6. Melan A. nearly completes loss of Melanocytes

Loss of hot or cold sensation was not revealed within the patches. An in office KOH was negative for fungal organisms. The clinical diagnosis was vitiligo and for ruled out of pigmented MF, a punch biopsy was taken from the lower trunk hypo pigmented patch. Microscopic assessment showed mild spongiosis in combination with superficial perivascular lymphocytic inflammation in papillary dermis, multifocal vascular alteration of the dermoepidermal junction, focal wiry bundles of collagen in the papillary dermis as well as mild lymphocytic exocytosis (Fig. 1, 2). CD4 and CD8 stains demonstrated a helper: suppressor ratio of equal to 1:1 and a CD7 stain demonstrated staining of approximately 30% of lymphocytes (Fig. 3a-b, 4). Further staining with Fontana Masson demonstrated a complete loss of melanin pigment and

also nearly completes loss of melanocytes on Melan-A staining (Fig. 5, 6). A polymerase chain reaction (PCR) assay for rearranged T-cell receptor gamma genes was obtained which show polyclonality. Given the clinical findings of several classic appearing depigmented patches on the forehead, eyelids, and dorsal hands, some histologic findings, the near-total loss of melanocytes evident with Melan-A staining, and PCR findings demonstrating a lack of monoclonality, the diagnosis of inflammatory vitiligo was favored but Hypo pigmented MF could not be ruled out definitively. Therefore close follow up of the patient should be considered.

DISCUSSION

Vitiligo is a partial common idiopathic skin disease with a worldwide prevalence of 0.5% to 2.0%, losing melanocytes led to appearance of depigmented patches (Alain Taïeb, 2012). This clinical phenomenon can be appeared in almost all skin areas especially face, neck, trunk, and extremities. In this regard and similar to some clinical manifestations, main differential diagnosis of vitiligo include hypopigmented mycosis fungoides, tineaversicolor, pityriasis alba, and other autoimmune and inflammatory skin disorders (Alain Taïeb, 2012). Vitiligo typically demonstrates unremarkable histopathological changes other than an absence of melanocytes. However, when biopsies are taken from the periphery of early depigmented lesions or from lesions with an inflammatory border, a dermal lymphocytic infiltrate, exocytosis, interface dermatitis, and mild spongiosis may be seen. Most reports of inflammatory biomarkers could document both CD4+ and CD8+ T-cells dermal infiltration with elevated CD8/CD4 ratio, Although a CD4 predominant infiltrate has also been reported (Khopkar *et al.,* 2011), but similar to our report the CD4+ and CD8+ T-cells accounts may be remained similar (Alain Taïeb, 2012; Petit *et al.,* 2003). One of the main differential diagnosis of inflammatory vitiligo is hypopigmented mycosis fungoides that their discrimination seems to be difficult. Hypopigmented mycosis fungoides is a rare variant of patch-stage MF and predominately seen in young patients with dark skin (Koores *et al.,* 2012; Karaphanth *et al.,* 2000). The lesions appear asymptomatic or slightly pruritic hypo pigmented patches that may or may not be accompanied by typical patches and plaques of classic MF. The underlying mechanism leading to hypopigmentation has been a subject of controversy. Some studies have found degenerative changes in melanocytes to nonspecific cellular injuries while others demonstrated impaired melanosome transfer to keratinocytes. A part from prominent pigment incontinence, Hypo pigmented MF is distinguishable from classic MF histopathologically. Although a frequent CD8+ phenotype has been described in the former (similar to vitiligo), the two variants share similar clinical course and prognosis (10). Distinction from vitiligo can be challenging and may only be resolved upon long term follow - up (EL-Shabrawi-Caelen *et al.,* 2002).

On histopathology early patch stage of MF show patchy band like lymphocytic infiltrate within papillary dermis, often associated with coarse fibrosis. Often, only a few of the atypical T-cells are present in the dermis. The presence of clustered epidermotropic atypical lymphocytes known as pautrier micro abscesses is uncommonly observed in early patch stage MF. Helpful clues for the diagnosis of MF in this stage include the linear accumulation of atypical lymphocytes along the basement membrane zone of epidermis or a single cell pagetoid infiltrate of atypical lymphocytes into epidermis without spongiosis. For differential diagnose of these two entities, some definitive histopathological features of each have been presented. For vitiligo, melanocytes are usually totally lost, but hydropic degeneration is rarely occurred, in contrast, in hypopigmented mycosis fungoides, melanocytes are partially lost and hydropic degeneration is frequent (El-Darouti *et al.,* 2006). Also, lymphocytes in papillary dermis are less commonly infiltrated in vitiligo than in hypo-pigmented mycosis fungoides (EL-Shabrawi-Caelen *et al.,* 2002). Moreover, dermal wiry fibrosis is less frequent in vitiligo compared to mycosis fungoides. In addition to the histopathological differences, T-Cell receptor gene rearrangement study with PCR can be useful for detecting Hypopigmented MF. However, only 50% of patch-stage MF lesions are reported to demonstrate monoclonality. Similarly monoclonality may also be seen in benign disorders, including inflammatory vitiligo. Therefore, Hypopigmented MF cannot be definitively ruled out based on T-Cell receptor gene rearrangement El-Darouti *et al.,* 2006).

A 2006 study by EL-Darouti *et al*. sought to identify some defining histopathological features of each to aid in differentiating the two entities. They compared biopsy specimens of 26 patients with vitiligo to 28 patients with Hypopigmented MF, and determined several statistically significant differences. According to their study some histologic findings favor of vitiligo such as total loss of melanocytes, BM thickening, rare basal layer hydropic degeneration and lower density of dermal infiltration .Compared with hypopigmented MF which show partial loss of melanocytes, more frequent hydropic degeneration and lymphocytes in papillary dermis, dense dermal infiltrate and frequent dermal wiry fibrosis.None of these features were 100% specific however (EL-Shabrawi-Caelen *et al.,* 2002). InSoro report in 2013 (El-Darouti *et al.,* 2006), a 58-year-old Indian female was reported with similar manifestations of inflammatory vitiligo and hypo pigmented mycosis fungoides indicated that the difficulty in differentiating between these two diseases and examine some characteristic clinical ,and histopathological features of each as well as immuno histochemical and molecular study. Although inflammatory vitiligo was favored, but a conclusive diagnosis cannot be made, necessitating close follow-up of the patient and monitoring for progression of their disease over time. In Petit *et al* report in 2003 (Luis *et al.,* 2013), two cases of an inflammatory vitiligo-like condition that simulated mycosis fungoides are reported. Both patients presented acquired hypo pigmented maculae sharply limited by an erythematous and popular border. The clinical aspect was suggestive of inflammatory vitiligo. Mycosis fungoides was suspected on skin specimens showing a dense band-like lymphocytic infiltrate with discrete nuclear atypia and marked exocytosis. This infiltrate was made of CD3 positive lymphocytes as well as CD8 positive lymphocytes were numerous in one case, few in the other. There was a loss of melanocytes and absence of dominant T-cell clones in both cases. Finally according to

these findings mycosis fungoides was ruled out and inflammatory vitiligo was favored. By reviewing these cases, it seems that the main problem to diagnose inflammatory vitiligo is its similar manifestations in some clinical, histological, immunohistochemical and also molecular findings, in comparison with hypopigmented mycosis fungoides. In this regard, some differentiates clinical manifestations such as presence of erythematous lesions, poikiloderma and scaling favors of second disease. Also some histopathology findings such as complete absence of melanocytes, basement membrane thickening as well as focal epidermotropism, in contrast to diffuse epidermotropism in MF, may be helpful for diagnosing inflammatory vitiligo. Finally, because none of histological findings which discussed previously were100% specific and this fact that also monoclonality in T-cell gene rearrangement study favors of MF, but is only 50% sensitive and not entirely specific, often a definite diagnosis cannot be made. Therefore similar to previous study we recommend that close follow up and monitoring for progression of disease over time is necessary.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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