DERMOSCOPY OF THE MONTH

Multiple Eruptive Dermatofibromas in Patient with Systemic Lupus Erythematosus

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Abstract

Introduction. Multiple eruptive dermatofibromas are described in association with different immune-mediated conditions like SLE, pemphigus, myasthenia gravis, HIV infection, organ transplantation, acute myeloid leukemia, ulcerative colitis, atopic dermatitis and immunosuppressive therapy. **Case Report.** A forty-five year-old woman presented at our Department with over 20 dermatofibromas on her trunk and extremities developed spontaneously over the last 3 years, out of which more than 10 lesions developed over the previous year. The patient was diagnosed with systemic lupus erythematosus before the onset of lesions and was treated with different immunomodulatory agents (corticosteroids, methotrexate, antimalarials, azathioprine, belimumab, anti IL-6 antibody). Dermoscopy of different lesions revealed different dermatoscopic patterns without pattern predominance. A biopsy specimen of one lesion confirmed the diagnosis. **Conclusion.** There are few cases reports describing a possible link between systemic lupus erythematosus and multiple dermatofibromas. The mechanism is still unknown but is believed to be due to the altered immunity in immune-mediated diseases.

Key words: Lupus Erythematosus, Systemic; Histiocytoma, Benign Fibrous; Immunosuppressive Agents; Autoimmune Diseases; Immunomodulation; Dermoscopy

Introduction

Dermatofibromas, also known as fibrous histiocytomas, represent dermal tumors originating from proliferation of fusiform cells corresponding to fibroblasts, histiocytes, blood vessels and collagen (1). The lesions are usually tan brown, pink-red, the skin being blue in some cases, rounded firm papules from 3 mm to 2 cm in diameter. They usually appear on the lower extremities of young females (2). As suggested by some authors, multiple dermatofibromas or multiple eruptive dermatofibromas are defined as the presentation of more than 15 dermatofibromas or 5-8 dermatofibromas developed in less than 4 months. Presentation of multiple dermatofibromas is reported to be linked to altered immunity or autoimmune diseases (3).

Case Report

A 45-year-old female patient presented with a 3-year history of numerous dark pigmented nodules developing continually, including the previous 6 months. In 1994, the diagnosis of chronic cutaneous lupus was confirmed. In 2005 polyarthrititis, erythema, leukopenia and lymphopenia, positive antinuclear antibodies and increased level of anti-double-stranded DNA were found, confirming the diagnosis of systemic lupus erythematosus. Treatment was started with prednisone in tapering doses and azathioprine 100 mg per day. Further on, from September 2006, the patient was treated sequentially with different immune modulatory agents - antimalarials, methotrexate, belimumab within a clinical study, anti-IL-6 antibody and thalidomide while prednisone was maintained at a

Figure 1. Multiple dermatofibromas on the trunk (A) and lower extremities (B)

low dose of 10 mg daily. SLE activity fluctuated during the disease course, with neurological manifestations (epileptic attacks and nerve palsies), serositis and cutaneous lesions, but since April 2018 the disease activity has been low and the patient is on the maintenance dose of prednisone 10 mg daily.

In October 2019 at the regular follow-up, the patient was seen by a dermatologist and she complained of the appearance of more than 20 subcutaneous nodules, not accompanied by itching or other symptoms. On clinical examination, hyperpigmented and skin-colored subcutaneous nodules were present, and on palpation a dimple sign was present (**Figure 1A and B**). On dermoscopy, homogenous brown with central white patch was present on hyperpigmented macules, while homogenous slight brown pigmentation was evident on skin colored nodules.

One of the nodules was excised and histologic examination showed dermal bundle proliferation consisting of histiocyte and partly spindle cells fused in hyalinized stroma. This proliferation was not in contact with epidermis which showed signs of acanthosis and hyperpigmentation of stratum basale - confirming the diagnosis of dermatofibroma.

Discussion

The definition of multiple dermatofibromas or multiple eruptive dermatofibromas is arbitrary, and it implies the presence of more than

15 dermatofibromas or multiple dermatofibromas developed in less than 4 months (3). Presentation of multiple dermatofibromas is reported to be linked to altered immunity or autoimmune diseases such as lupus erythematosus, myasthenia gravis, pemphigus vulgaris, HIV infection, organ transplantation, acute myeloid leukaemia, ulcerative colitis and atopic dermatitis (3). In our patient, MDF appeared after years of treatment with various disease modifying agents, including biologic therapy (belimumab and anti-IL6 antibody). Pathophysiology of dermatofibroma development is yet to be discovered, but it is shown that there could be mast cell (6) involvement leading to acanthosis of the overlying epidermis, basal melanosis and mononuclear recruitment. Other studies have shown the involvement of interleukin-1 in process, through autocrine role in fibroblast proliferation. Also, elevated levels of basic fibroblast growth factor and platelet-derived growth factor are found in patients with SLE but multiple dermatofibromas may affect fibroproliferative response and lead to growth of dermatofibromas (7, 8). Abortive immune reactive process triggered by drugs that down-regulate T cells could be the reason why there are several case reports of patients treated with oral prednisone (9) or in patients with Hodgkin lymphoma treated with the antibody-drug conjugate brentuximab vedotin, a CD30 directed antibody (10) which presented with multiple dermatofibromas; though the link is still unknown.

Figure 2. Patterns of dermatofibroma. A, peripheral delicate pigment network and central white scar like patch. B, total delicate pigment network. C, peripheral delicate pigment network and central white network. D, total homogeneous pigmentation.

In HIV infection, antiretroviral therapy (ART) is used to suppress viral load which leads to restored immune function. However, antiretrovirals could also lead to paradoxical exacerbation of existing co-morbidities or development of new conditions, also known as immune reconstitution associated disease (IRAD), and multiple dermatofibromas could be one of them (4).

Multiple eruptive dermatofibromas were also described during pregnancy. Pregnancy can be considered as an altered immune state due to several mechanisms that are involved in survival of human fetal allograft in a potentially hostile immunological environment. The state of maternal-fetal tolerance is yet to be studied but more notice is given to the regulatory T cells (5).

Dermoscopy of dermatofibromas shows different pattern variations classified by Zaballos et al in 10 patterns. The major described appearance of dermatofibromas is a periph-

eral delicate pigment network and central white scar-like patch, which was found in 34.7% of cases (**Figure 2.A**), followed by total delicate pigment network in 14.6% of cases (**Figure 2.B**), peripheral delicate pigment network and central white network in 9% of cases (**Figure 2.C**), total homogeneous pigmentation in 4.8% cases (**Figure 2.D**). In our patient several different patterns were found, without predominance (11).

In conclusion, multiple dermatofibromas could be regarded as a sign of altered immune response. Autoimmune diseases or altered immunity due to immunosuppressive drugs must be excluded in patients presenting with multiple dermatofibromas, with systemic lupus erythematosus and HIV infection being the most common. Different dermoscopic patterns can be found in patients with MDF without predominance, which is in contrast to the patients with multiple melanocytic

nevi where predominant dermoscopic pattern can be found.

Abbreviations

MDF – multiple dermatofibromas

SLE – systemic lupus erythematosus

HIV – human immunodeficiency virus

ART – antiretroviral therapy

IRAD – immune reconstitution associated disease

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Eruptivni dermatofibromi kod pacijenta sa sistemskim eritemskim lupusom

Sažetak

Uvod. Pojava eruptivnih multiplih dermatofibroma povezuje se sa različitim imunoposredovanim bolestima kao što su sistemski eritematozni lupus, mijastenija gravis, HIV infekcija, transplantacija organa, akutna mijeloidna leukemija, ulcerativni kolitis, atopijski dermatitis i imunosupresivna terapija. **Prikaz slučaja.** Bolesnica starosti 45 godina, koja boluje od sistemskog eritemskog lupusa lečenog različitim imunomodulatornim agensima (kortikosteroidi, azatioprin, metotreksat, antimalarici, belimumab, anti-IL-6 antitelo), primetila je spontanu pojavu preko 20 dermatofibroma na koži trupa i ekstremiteta u poslednje tri godine, od toga više od 10 u poslednjih godinu dana. Dermoskopijom više promena uočeni su različiti dermoskopski obrasci dermatofibroma bez predominantnog obrasca. Biopsijom lezije histopatološki je potvrđena dijagnoza dermatofibroma. **Zaključak.** Pojava multiplih dermatofibroma opisana je udruženo sa sistemskim eritemskim lupusom i kod primene imunosupresivnih lekova. Mehanizam nastanka i dalje nije poznat, ali se povezuje sa različitim imunoposredovanim oboljenjima.

Ključne reči: Sistemski eritemski lupus; Benigni fibrozni histiocitom; Imunosupresivni lekovi; Autoimune bolesti; Imunomodulacija; Dermoskopija

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