Multiple Eruptive Dermatofibromas: Case Report

Multipl Erüptif Dermatofibroma

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ABSTRACT Dermatofibroma is a common, benign tumor of the dermis, often appearing as a solitary lesion of unknown etiology that presents on the lower extremities in adults. Multiple and eruptive dermatofibromas are unusual. Although the etiology of multiple eruptive dermatofibromas is unknown, most patients have underlying diseases of immune-mediated origin, such as autoimmune diseases, immunosuppressive treatments, HIV infection, and hematologic malignancies. Herein, we report an unusual case of multiple eruptive dermatofibromas that presented with nearly 100 well-circumscribed firm, tan to brown round papules (1-10 mm in diameter) all over the body, including the face, palms, and soles. The number of lesions increased gradually over a 2-year period, without any symptoms. Comprehensive clinical and laboratory diagnostic evaluation showed no evidence of an underlying disorder. Histopathological examination of one of the lesions from the patient's thigh revealed dermatofibroma. Based on these clinical and histopathological findings, the patient was diagnosed as a rare case of multiple eruptive dermatofibromas not associated with an underlying disease.

Key Words: Neoplasms, multiple primary; histiocytoma, benign fibrous

ÖZET Dermatofibroma erişkinde alt ekstremitelerde oluşan, etyolojisi bilinmeyen ve çoğunlukla soliter tek bir lezyon şeklinde ortaya çıkan dermisin sık görülen benign tümörlerindendir. Multipl ve erüptif formlarına ise nadiren rastlanmaktadır. Multipl erüptif dermatofibromaların etyolojisi tam olarak bilinmemekle birlikte, bu hastaların çoğunda otoimmun hastalıklar, immünsüpresif tedavi, HIV infeksiyonu ve hematolojik maligniteler gibi altta yatan immün sistem aracılı bir hastalık vardır. Burada, iki yıllık bir periodda yüz, avuç içi ve ayak tabanları da dahil olmak üzere tüm vücutta yaklaşık 100 adet, iyi sınırlı, sert, deri rengi ile kahverenkli, çapları 1-10 mm arasında ölçülen multipl eruptif dermatofibromaları olan bir olguyu sunduk. Lezyonların sayısı iki yıllık bir period içinde giderek artmıştı.Yapılan geniş kapsamlı klinik ve laboratuar çalışmaları sonucunda hastada altta yatan herhangi bir hastalığa ait bir delil gösterilemedi. Üst bacakta lezyondan alınan biyopsi örneğinin histopatolojik incelemesi dermatofibroma olarak belirlendi. Bu klinik ve histopatolojik bulgularla hastaya, herhangi bir altta yatan hastalıkla birliktelik göstermeyen nadir bir multipl eruptif dermatofibroma olgusu tanısı konuldu.

Anahtar Kelimeler: Tümörler, çoklu primer; histiyositom, benign fibröz

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Dermatofibromas are benign tumors of fibrohistiocytic origin that usually occur on the legs of middle-aged females.[1,2] They mostly present in healthy individuals as a local tissue response to some type of inflammation or trauma.[3] In general, they present as violaceous to reddish-brown round papules or nodules of variable size, and sometimes have a yellowish

hue. They may be elevated or slightly depressed. The "dimple" sign, which was first proposed by Fitzpatrick, is the depression in the center of a dermatofibroma that forms when it is grasped between the thumb and index finger, and is characteristic of dermatofibromas. In contrast to the high prevalence of solitary lesions, the growth of multiple lesions with an eruptive feature is rarely encountered.[4,5] Although the pathogenesis remains uncertain, multiple eruptive dermatofibromas (MEDF) has been frequently described in association with altered immunity, such as systemic lupus erythematosus,[6] HIV infection,[7] hematologic malignancy,[8] pregnancy,[9] and iatrogenic immunosuppression.[10] Nonetheless, patients with MEDF and the lack of an associated condition have also been reported.[4] Herein we report the case of a 16-year-old MEDF patient with no evidence of an underlying disease.

CASE REPORT

A 16-year-old male presented to our dermatology outpatient clinic with multiple lesions over his entire body that gradually developed during a 2-year period. The patient first recognized a few lesions on his chin, and then experienced a continuous gradual increase in the number and diameter of the lesions on his extremities, chin, palms, and soles during this 2-year period. None of the lesions spontaneously regressed following this 2-year period. He did not experience any pain, itching, or burning. The past medical histories of the patient and his family were unremarkable, except that the patient had undergone 3 or 4 cryotherapy sessions for the lesions he presented with, without any improvement. Moreover, the patient's history of drug intake was negative. On dermatological examination he had approximately 100 well-circumscribed, firm, tan to brown round papules (1-10 mm in diameter) located over his extremities (Figure 1-3), as well as 1-mm light-brown, flat papules on his face, palms, and soles. When the eruptive and widespread nature of the lesions were taken into consideration, the differential diagnosis before biopsy included generalized eruptive histiocytoma, eruptive dermatofibroma, xanthoma disseminatum, lichen nitidus, as well as verruca vulgaris. However, no improvement with cryotherapy sessions abolished the idea of verruca vulgaris somewhat as the differential diagnosis.

Histopathological examination of 1 of the papules on the patient's thigh showed proliferation of spindle-shaped fibroblasts interspersed between collagen bundles, and scattered histiocytes and multinuclear giant cells within the dermis (Figure 4). Immunohistochemical staining for S100 and CD68 were negative, while vimentin staining was diffusely positive (Figure 5). The patient's clinical and immunohistopathological features were consistent with MEDF.

On physical examination no signs of autoimmune disease were observed. Routine laboratory investigation results, including full blood count, erythrocyte sedimentation rate, urea, creatinine, liver function tests, lipid profile, and C-reactive protein level, were normal, as were serum T3, T4, and thyroid-stimulating hormone levels. HIV test, rheumatoid factor, and antinuclear antibody results were negative, and chest X-ray was normal.

As there is no specific treatment modality reported for MEDF, we decided to follow-up the patient without any treatment. During a 6-month observation period none of the lesions disappeared or decreased in size. The patient was then lost to follow-up.

DISCUSSION

MEDF was first reported by Baraf and Shapiro[4] as the presence of at least 15 dermatofibromas in a patient; however, 15 lesions was chosen arbitrarily. Moreover, Ammirati et al.[11] defined MEDF as the presence of 5-8 dermatofibromas that appear within a 4-month period. Our patient had nearly 100 lesions that appeared during a 2-year period, which clearly demonstrates the eruptive nature of MEDF. MEDF most commonly occurs on the legs, trunk, and arms.[12] The literature includes only a few MEDF cases in which the lesions occurred on unusual areas, such as the face,[13] palms, and soles.[14] Our case is interesting because dermatofibromas were observed over the patient's entire body, and included unusual localizations-the face, palms, and soles.

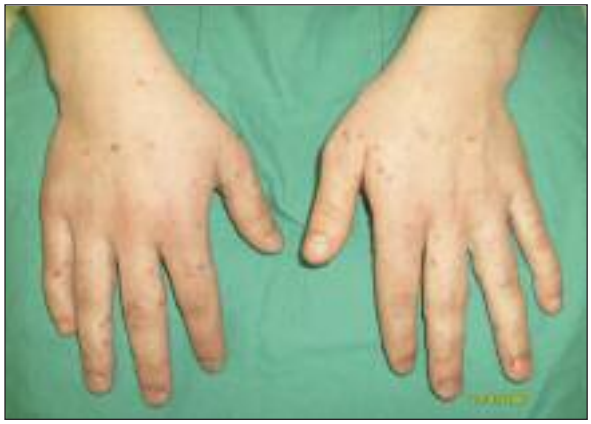

FIGURE 1: Multiple tan to brown papules on the dorsum of the patient's hands.

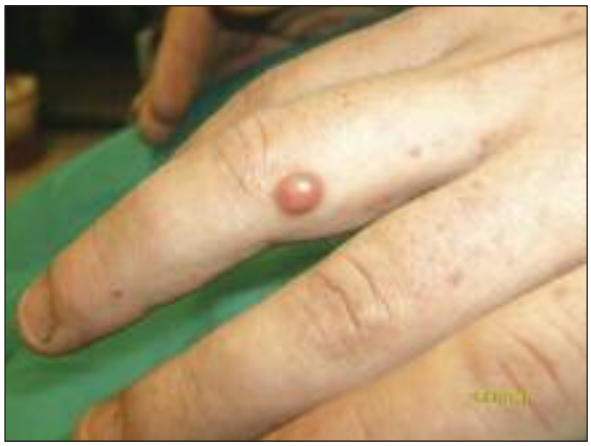

FIGURE 2: A large tan to brown papule on the lateral side of the patient's middle finger.

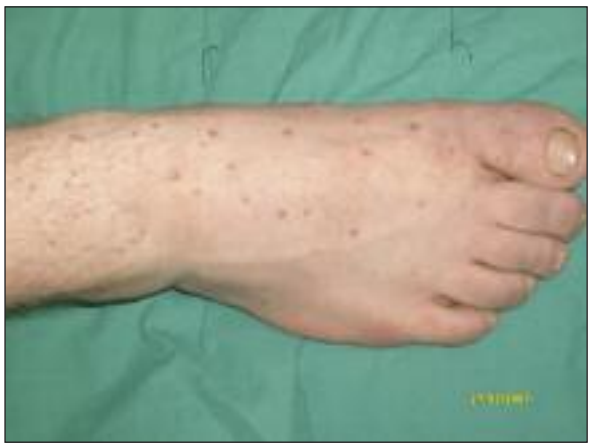

FIGURE 3: Multiple tan to brown papules on the dorsum of the patient's feet.

Niiyajama et al.[12] also reported that cases presenting with unusual lesion localization had no associated underlying diseases, as did the presented case.

MEDF should be differentiated from generalized eruptive histiocytoma, which is generally only possible with biopsy. Clinically, generalized eruptive histiocytoma is characterized by recurrent crops of red to brown papules distributed on the face, trunk, and proximal extremities, as well as on mucosal surfaces. The lesions tend to resolve spontaneously, leaving scars or hyperpigmented macules. Histopathological examination of MEDF reveals mostly fibrocytes or fibroblasts, while histiocytomas primarily contain monomorphous vacuolated macrophages.[15] Moreover, histiocytes stain positively for lysozyme, α1 antitrypsin, CD11b, CD14b, CD68, and factor XIIIa.[16,17] Xanthoma disseminatum may also resemble MEDF, although the

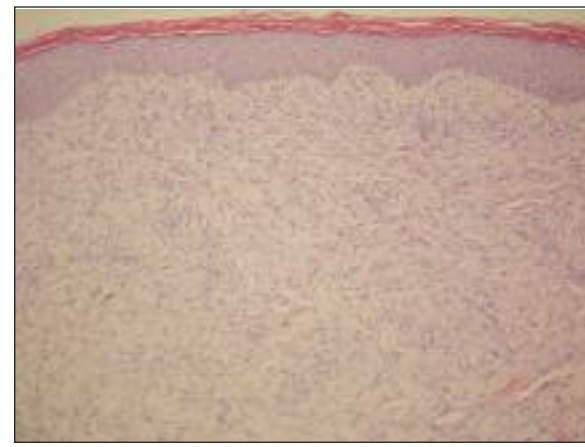

FIGURE 4: A dermal nodule composed of spindle-shaped fibroblasts under the epidermis (H&E, 100×).

FIGURE 5: Tumor cells are diffusely positive for vimentin (immunoperoxidase, ×100).

characteristic laryngeal, eye, and oral lesions, and the tendency for plaque formation and diabetes insipidus have not been described in MEDF.[18]

There are several reports that indicate patients with MEDF often have various underlying diseases. Huang et al.[10] reviewed 62 cases of MEDF published between 1973 and 2006. Among the 62 cases, 41 (66%) had underlying diseases. Most MEDF cases in the literature are associated with autoimmune diseases, such as systemic lupus erythematosus,[6,19] myasthenia gravis,[20] pemphigus vulgaris,[21] and dermatomyositis.[10] Other associated conditions include pregnancy,[9] HIV infection,[7] atopic dermatitis,[22] and hematologic malignancies.[23] Nevertheless, a review[12] of 50 MEDF patients reported that 22 of the patients did not have an underlying abnormality. To the best of our knowledge only 3 MEDF cases (presenting with >100 lesions) without an underlying abnormality have been reported.[24,25]

The pathogenesis of MEDF remains unknown. Several hypotheses for explaining the occurrence of multiple eruptive lesions have been proposed. The nature of dermatofibroma, as a neoplasm or a reactive process, has been debated for decades. As triggering events, insect bites,[26] local trauma, and infectious agents[7] have been considered. One recent report suggests that dermatofibroma represents an abortive immunoreactive process mediated by dermal dendritic cells.[27] According to this hypothesis, the development of multiple dermatofibromas in immunodeficient states might be facilitated by the inhibition of down-regulatory T cells.[19] Additionally, mast cells are present in large numbers in the early stage of dermatofibroma development, and the presence of these lesions was attributed to reactive hyperplasia associated with systemic autoimmune disorders.[28] Morever, platelet-derived growth factor and basic fibroblast growth factor, which stimulate fibroblasts, have been detected.[29] Familial cases have also been reported, suggesting a genetic role in its etiology.[22,30] Although the presented case could not recall any apparent triggering event, there might have been a minor stimulus that the patient was not aware of.

In conclusion, MEDF, although rare, can be encountered in otherwise healthy individuals. As such, it is prudent to exclude any underlying diseases before making a definitive diagnosis.

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