

CLINICAL REPORT

Ultraviolet Light-induced Köbner Phenomenon Contributes to the Development of Skin Eruptions in Multicentric Reticulohistiocytosis

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Multicentric reticulohistiocytosis is a rare systemic disease of unknown aetiology characterized by erosive arthritis and cutaneous lesions consisting of multiple reddish-brown papules and nodules, mainly involving the face and distal upper extremities. It has been suggested that skin eruptions in multicentric reticulohistiocytosis are associated with Köbner phenomenon due to their characteristic distribution, such as on the dorsal aspects of the hands and fingers. We report here a case of a Japanese woman with multicentric reticulohistiocytosis, in whom erythematous macules and papules were widely distributed over the face, ears, neck and the V-area of the chest. Notably, repeated irradiation of ultraviolet (UV) B on the uninvolved back skin resulted in the induction of erythematous macules with infiltration of reticulohistiocytes, indicating the association of UVB-induced Köbner phenomenon with the development of skin lesions, especially on the sun-exposed area. This is the first known report demonstrating the contribution of UV-light-induced Köbner phenomenon for the development of skin eruptions in patients with multicentric reticulohistiocytosis. Key words: multicentric reticulohistiocytosis; Köbner phenomenon; ultraviolet B; corticosteroid; methotrexate; sun protection.

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Multicentric reticulohistiocytosis (MRH) is a rare systemic disease of unknown aetiology characterized by mucocutaneous papulonodules and erosive arthritis. The cutaneous lesions consist of multiple reddish-brown papules and nodules, mainly involving the face and distal upper extremities. The arthritis preferentially involves the interphalangeal joints of the hands and can lead to joint destruction and deformities. All of these clinical symptoms are directly caused by the infiltration of reticulohistiocytes, which are histologically characterized by histiocytic multinucleated giant cells with eosinophilic ground glass cytoplasm (1). Although it has been suggested that skin eruptions in MRH are closely associated with Köbner phenomenon due to their characteristic dist-

tribution on the dorsal aspects of finger joints and over the sun-exposed areas (1, 2), thus far there has been no clear evidence proving the contribution of Köbner phenomenon to the development of skin lesions in this disorder. We report here a case of MRH, in which repeated irradiation of ultraviolet B (UVB) on the uninvolved back skin resulted in the induction of erythematous macules with the infiltration of reticulohistiocytes.

CASE REPORT

A 54-year-old Japanese woman visited our hospital with multiple skin lesions on the distal interphalangeal joint of the fingertips and chronic multiple symmetrical arthralgia of one year's duration. She had been treated with methotrexate (4 mg/week) for the previous 3 months based on the initial diagnosis of rheumatoid arthritis, but no significant effect was observed. Her skin lesions consisted of multiple pruritic reddish papulonodules over the dorsal areas of the hands, fingers, elbows and knees, multiple small whitish papules on the oral mucosa of the upper lip, and erythematous macules and papules over the face, ears, neck and the V-area of the chest (Fig. 1a). The lymph nodes were not palpable, and there were no other abnormal findings on physical examination except for the skin lesions and the joint involvement. There was no family history of collagen diseases. Laboratory studies revealed elevated erythrocyte sedimentation rate (70 mm/h), C-reactive protein (0.91 mg/dl) and CH50 (59.1 U/ml), reflecting the moderate inflammation of the joints. The antinuclear-antibodies titre was 1:320 with a speckled pattern. The patient had positive serological test results for anti-SS-A antibodies (133.4 U/ml; <29.0 U/ml), rheumatoid factor (30 IU/ml; <20 U/ml), and anti-CCP antibodies (31.3 U/ml; <4.4 U/ml), while antibodies against U1RNP, double-strand DNA and Sm antigens were negative. Other laboratory evaluation, including complete blood count and blood biochemical values, were all within normal limits. Urinalysis was normal and tumour markers were within normal ranges. A complete medical examination, including computed tomography (CT) examination of the chest, pelvis and abdomen, revealed no evidence of internal malignancy. Her hand X-rays showed well-circumscribed erosions in the distal interphalangeal joints. Histopathological

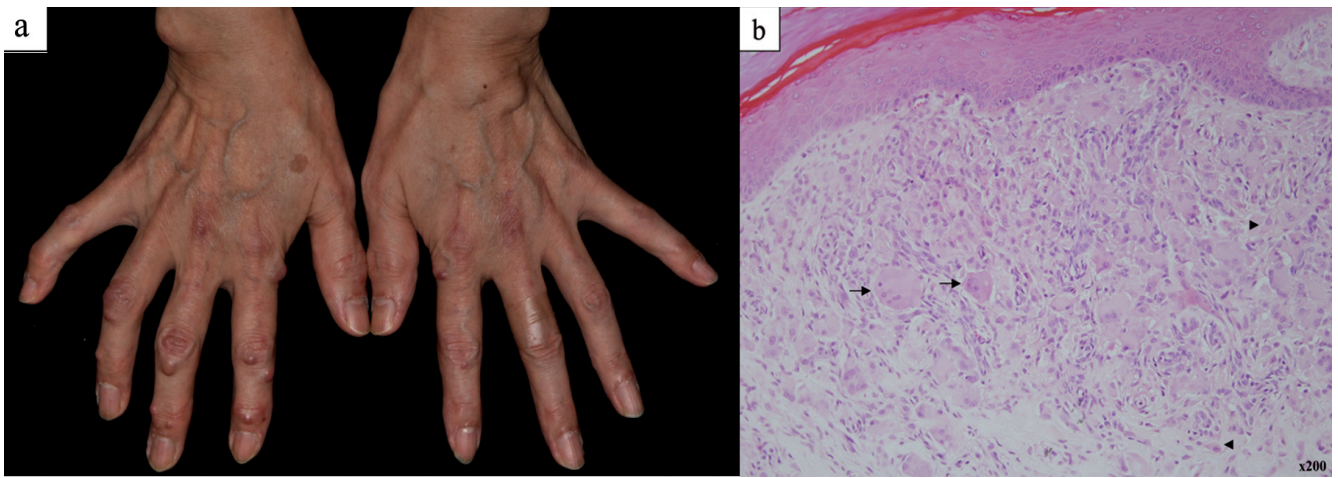


Fig. 1. Clinical and histopathological manifestations on admission. (a) Multiple pruritic reddish papulonodules disseminated over the dorsal areas of hands and fingers, especially around the joints. (b) Reticulohistiocytes (arrowheads) and giant cells (black arrows) were widespread throughout the dermis. Hematoxylin and Eosin.

examination of papules on the hand and erythematous macules on the face showed dermal infiltrates consisting of multinucleated histiocytic giant cells with an eosinophilic “ground glass” cytoplasm, which are positive for CD68 and negative for S100 (Fig. 1b). Neither lymphocytes extending to the dermo-epidermal junction nor vacuolar changes in the basal-cell layer were seen. Based on these clinical, laboratory and histopathological findings, the patient was diagnosed as having MRH.

Since the characteristic distribution of the eruptions over the face, ears, neck and the V-area of chest suggested the contribution of sunlight-induced Köbner phenomenon for the development of skin lesions, a

photo test was performed. Fifteen J/cm² of UVA and 0.8 MED of UVB (50 mJ/cm²), as well as visible light, were applied to the uninvolved skin on the back for 3 consecutive days. As expected, 2 days after the completion of irradiation, diffuse erythematous macules with multiple small papules were developed on the UVB-irradiated site. Histopathological examination showed infiltrates including reticulohistiocytes and multinucleated histiocytic giant cells as well as lymphocytes in the papillary and upper reticular dermis. Furthermore, reticulohistiocytes and histiocytic giant cells were also widely distributed throughout the reticular dermis (Fig. 2a–c). All of these reticulohistiocytes and histiocytic giant cells were positive for CD68 and

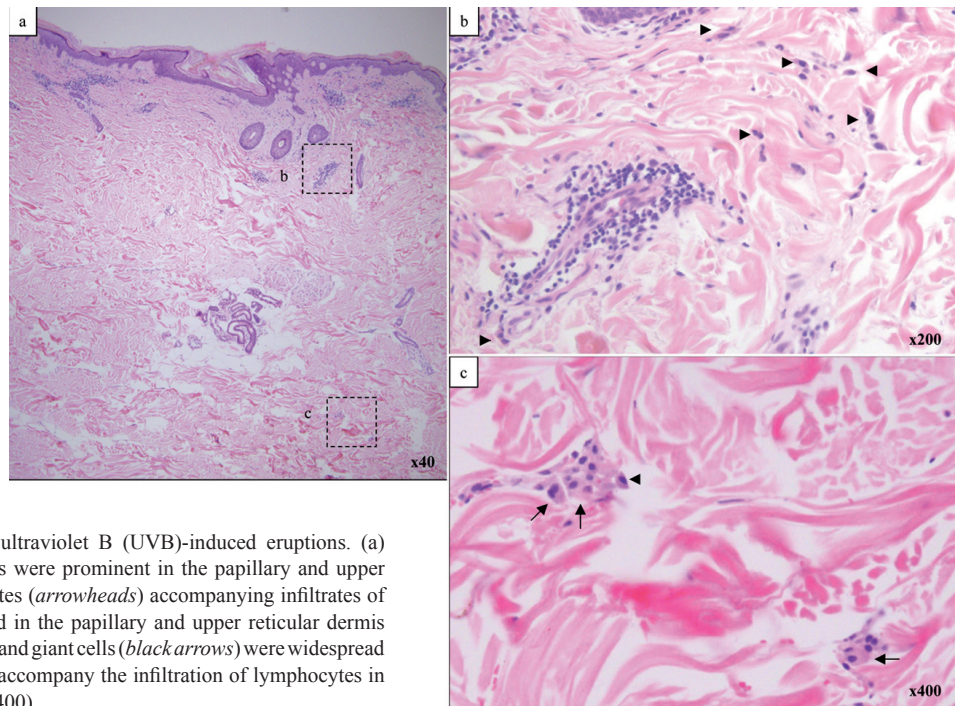


Fig. 2. Histopathological features of the ultraviolet B (UVB)-induced eruptions. (a) Perivascular infiltrate of inflammatory cells were prominent in the papillary and upper reticular dermis. (×40) (b) Reticulohistiocytes (arrowheads) accompanying infiltrates of lymphocytes and histiocytes were observed in the papillary and upper reticular dermis (×200) (c) Reticulohistiocytes (arrowheads) and giant cells (black arrows) were widespread throughout the dermis. These cells did not accompany the infiltration of lymphocytes in the deep dermis (Hematoxylin and Eosin ×400).

negative for S100, and were morphologically similar to those seen in papules on the hand and erythematous macules on the face. Collectively, we concluded that UVB-induced Köbner phenomenon contributed to the development of skin lesions in the present case. The patient was treated with oral methotrexate (6 mg/week) and prednisone (10 mg/day) in combination with sun-protection clothing and the appropriate broad-coverage sunscreens. Her joint pain disappeared with gradual regression of the skin lesions over a period of 2 weeks (Fig. 3). Some skin lesions remained on the anterior neck due to incomplete sun protection being used in this area. No exacerbation was observed in a follow-up period of 6 months.

DISCUSSION

MRH is classified into Class II or non-Langerhans' cell histiocytosis, characterized by an extensive papulonodular cutaneous eruption as well as a severe, sometimes destructive, arthropathy (3). The onset of MRH is usually insidious. The majority of patients present with initial articular signs and symptoms and the skin manifestations usually present months to years later

(a mean of 3 years) (4), which is the main reason why patients with MRH are often misdiagnosed as having rheumatoid arthritis, as in the present case. The typical cutaneous manifestations consist of flesh-coloured to reddish-brown papules and nodules, commonly located on the mucous membranes, face, neck and hands (3). The presence of the photo-distributed eruption and the presence of papulonodular lesions on the dorsum of the hands and interphalangeal joints, mimicking Gottron's papules with periungual telangiectasia, might cause the confusion of MRH with dermatomyositis (2, 5). We excluded the coexistence of dermatomyositis and cutaneous lupus erythematosus due to the lack of histopathological changes characteristic for these diseases, such as liquefaction degeneration, keratotic scaling and follicular plugging.

Since the distribution of the eruptions over the neck and face suggested sunlight-induced Köbner phenomenon, we performed a photo test. Diffuse erythematous macules with small papules, similar to the eruptions on her face and neck, appeared after repeated irradiation of UVB. Histological examination revealed the infiltration of reticulohistiocytes and histiocytic giant cells throughout the dermis and the perivascular infiltration of mononuclear cells in the papillary and the upper reticular dermis. The most important observation here was that reticulohistiocytes and histiocytic giant cells were observed in the middle and deep dermis, where UVB light cannot reach, without accompanying mononuclear cell infiltration. This finding suggests that non-specific inflammation in the papillary dermis caused by repeated irradiation of UVB triggered the infiltration of reticulohistiocytes into the whole dermis of the irradiated area, indicating that this skin eruption developed as a result of UVB-induced Köbner phenomenon.

The Köbner phenomenon was first described in psoriatic skin by Köbner (6) in 1876. He found new psoriatic lesions on normal healthy skin after horse bites. He observed further that this phenomenon could be provoked by puncturing the normal-appearing skin in psoriatic patients after certain latent periods (3 weeks to several months). This phenomenon has been further reported in various systemic diseases, including lichen planus, vitiligo vulgaris, autoimmune blistering dermatoses, systemic lupus erythematosus, discoid lupus erythematosus, systemic sclerosis, dermatomyositis, and sarcoidosis (6–13). The factors provoking Köbner phenomenon have been reported to be: needling, scratches (9), trauma (11), sun exposure, X-rays, heat, cold, pressure, drug administration, silica granulomas, tattooing, scars, and inflammatory dermatoses (6, 7, 10, 12, 13). There have been two reports regarding presumed Köbner phenomena triggered by trauma in MRH (14, 15). However, as far as we know, this is the first report proving the contribution of UVB-induced Köbner phenomenon to the development of skin eruptions in



Fig. 3. Efficacy of the combination therapy of oral methotrexate and prednisone with sun-protection clothing and sunscreens. (a) Before the treatment: erythematous macules and papules were widely distributed over the neck. (b) After the treatment: skin lesions regressed on the posterior neck, but remained slightly on the anterior neck, where the sun protection was incomplete.

MRH. Since the combination therapy of oral corticosteroid and methotrexate with sun-protection clothing and sunscreens may be useful for the treatment of skin symptoms of MRH, it is important for us to be aware of the involvement of sunlight-induced-Köbner phenomenon in the pathogenesis of this clinical entity.

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