

Febrile Ulceronecrotic Mucha-Habermann Disease

To the Editor:

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD), first reported by Degos et al¹ in 1966, is a rare subtype of pityriasis lichenoides et varioliformis acuta. It consists of an acute and severe generalized lesion of purpuric and ulceronecrotic papulonodules and/or plaques associated with systemic involvement.^{2,3} Cutaneous lesions always are present prior to the acute fulminating course.^{4,5} According to a search using PubMed for articles indexed for MEDLINE and the Chinese National Knowledge Infrastructure for content written in Chinese using the term *febrile ulceronecrotic Mucha-Habermann disease*, 62 cases,^{2,23} including 1 boy,⁶ have been reported, with 9 reported deaths in adults.^{2,7,8} The disease has no ethnic or geographic dispositions. Herein, a rare case of FUMHD recurring after initial therapy with methylprednisolone is presented; the patient was successfully treated with methylprednisolone combined with methotrexate sodium.

A 15-year-old adolescent girl presented with a 14-day history of an abrupt onset of low-grade fever (37.5°C–37.8°C), abdominal pain, diarrhea 4 to 5 times daily, and scattered asymptomatic erythematous papules over her abdomen that worsened progressively within a few days. Ten days later the rash suddenly became worse and more extensive, evolving to central ulceration followed by skin necrosis, and accompanied by itching and persistent fever. The lesions were unresponsive to antibiotics, including clarithromycin and cephalosporins. She had no headache or sore throat since her outbreak, and she was not taking medication. She had intermittent abdominal pain and diarrhea for the last 10 years, which was attributed to an allergy to capsicum. No other family members were similarly affected. Physical

examination showed that the patient was 155-cm tall and weighed 34 kg. Axillary temperature was 37.5°C. There were numerous discrete, oval-shaped, variously sized, partially confluent, erythematous macules, papulonodules, and/or papules distributed over the neck, trunk, and proximal extremities; most lesions with red halos had central necrosis (Figure 1). The palms, soles, mouth, and genitals were not involved. A colonoscopy showed normal appearance of colonic mucosa. The leukocytes with normal differential counts increased to $25.3 \times 10^9/L$ (reference range, $4.0\text{--}11.0 \times 10^9/L$). Serum globulin was 43.9 g/L (reference range, 20–35 g/L). Decreased serum albumin (20 g/L [reference range, 38–55 g/L]) and C3 (0.3 g/L [reference range, 0.87–1.41 g/L]) also were present. Other results including blood chemistry; anti-streptolysin O; IgA, IgG, and IgM rheumatoid factor; anti-human immunodeficiency virus antibody; herpes simplex virus type 1 and type 2 IgM; *Treponema pallidum* particle agglutination test; anti-DNA antibody; double-stranded DNA antibody; C-reactive protein; erythrocyte sedimentation rate; stool routine test including occult blood; aspartate aminotransferase and alanine aminotransferase; and antineutrophil cytoplasmic antibodies (perinuclear and cytoplasmic) were negative or normal. The repeatedly smeared slides of bone marrow were normal. A biopsy from a fully developed lesion revealed focal but full-thickness epidermal necrosis, bandlike lymphocytic and neutrophilic infiltration in the superficial dermis (Figure 2A), and periadnexal (Figure 2B) and perivascular (Figure 2C) inflammatory infiltration. The infiltrate included lymphocytes and neutrophils, with predominantly lymphocytes (Figures 2B–2D). Erythrocyte extravasation was present in the superficial dermis and epidermis (Figure 2D), and interface damage also was present. Immunohistochemical staining showed CD4⁺ and CD8⁺ lymphocytes were present in the necrotic lesion and superficial dermis. Periadnexal and perivascular lymphocytic infiltration also was observed with CD4⁺ and CD8⁺ immunopositivity. CD8⁺ cells were predominant. Colonic biopsy showed many eosinophilic and lymphocytic infiltrations in the mucosa.

The patient was diagnosed with FUMHD. Monotherapy with oral methylprednisolone 8 mg

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Figure 1. Diffuse polymorphous erythematous macules, papules, and necrotic lesions distributed over the body (A). Lesions with red halos had central necrosis (B).

3 times daily resulted in remarkable response with rapid resolution of abdominal manifestations, reepithelialization of ulcerations, and normalization of body temperature 3 days later. Five days later most of the ulcerations healed with hyperpigmentation and atrophic scars, serum albumin increased to 31.9 g/L, and leukocyte counts decreased to $19.2 \times 10^9/L$. Six weeks later when methylprednisolone was decreased to 8 mg daily, the symptoms recurred and progressed more rapidly. Laboratory results showed leukocytosis and hypoalbuminemia again but normal globulinemia. Oral methylprednisolone 24 mg daily was restarted, which resulted in a poor response. Two days later, intravenous methylprednisolone 120 mg daily was started, which resulted in excellent response after the first treatment. Following 3 days of high-dose therapy, oral methylprednisolone 24 mg daily and intravenous methotrexate 10 mg weekly was started; the lesions responded but not as well as when the patient initially was treated with methylprednisolone 24 mg only. Methotrexate was stopped after 10 weeks at a total dosage of 100 mg, and the steroid was subsequently tapered off and discontinued 6 months later. After treatment the lesions resolved, leaving behind atrophic scars and hyperpigmentation; abnormal laboratory findings also recovered. The residual atrophic scars recovered and hyperpigmentation gradually disappeared at 2-year follow-up. The lesions did not recur after all medications were discontinued.

Febrile ulceronecrotic Mucha-Habermann disease is differentiated from pityriasis lichenoides et varioliformis acuta by a rapid progression of necrotic papules to large coalescent ulcers with necrotic crusts, hemorrhagic bullae, and pustules frequently associated with systemic symptoms,^{8,9} including high fever¹⁰; sore throat¹⁰; sepsis⁸; and gastrointestinal,^{8,9} hepatic,^{2,9} neurologic,⁸ and pulmonary^{2,13} involvement. Cardiomyopathy,⁸ rheumatologic manifestations,⁸ megaloblastic anemia, pancytopenia,⁸ and diffuse intravascular coagulation^{8,16} also may be present. The oral and genital mucosa,⁸ intertriginous areas,¹⁰ lips and prepuce,¹⁴ and palms and soles¹⁴ may be similarly affected. Necrotic lesions may be painful and extensive, sometimes accompanied by secondary infection, but always heal with hypopigmentation and atrophic scars.⁸ The condition has a predilection for males,^{8,9,16} though the reason remains unclear. The mean age at presentation is 27.4 years, ranging from 4 to 82 years,⁸ with most patients younger than 35 years.⁸ It is a potentially fatal condition for patients aged 26 to 82 years.^{2,7,8} No deaths have been reported in children, though severe conditions including central nervous system involvement have been described in pediatric cases.^{8,13} Frequently, abnormal laboratory findings include leukocytosis, elevated erythrocyte

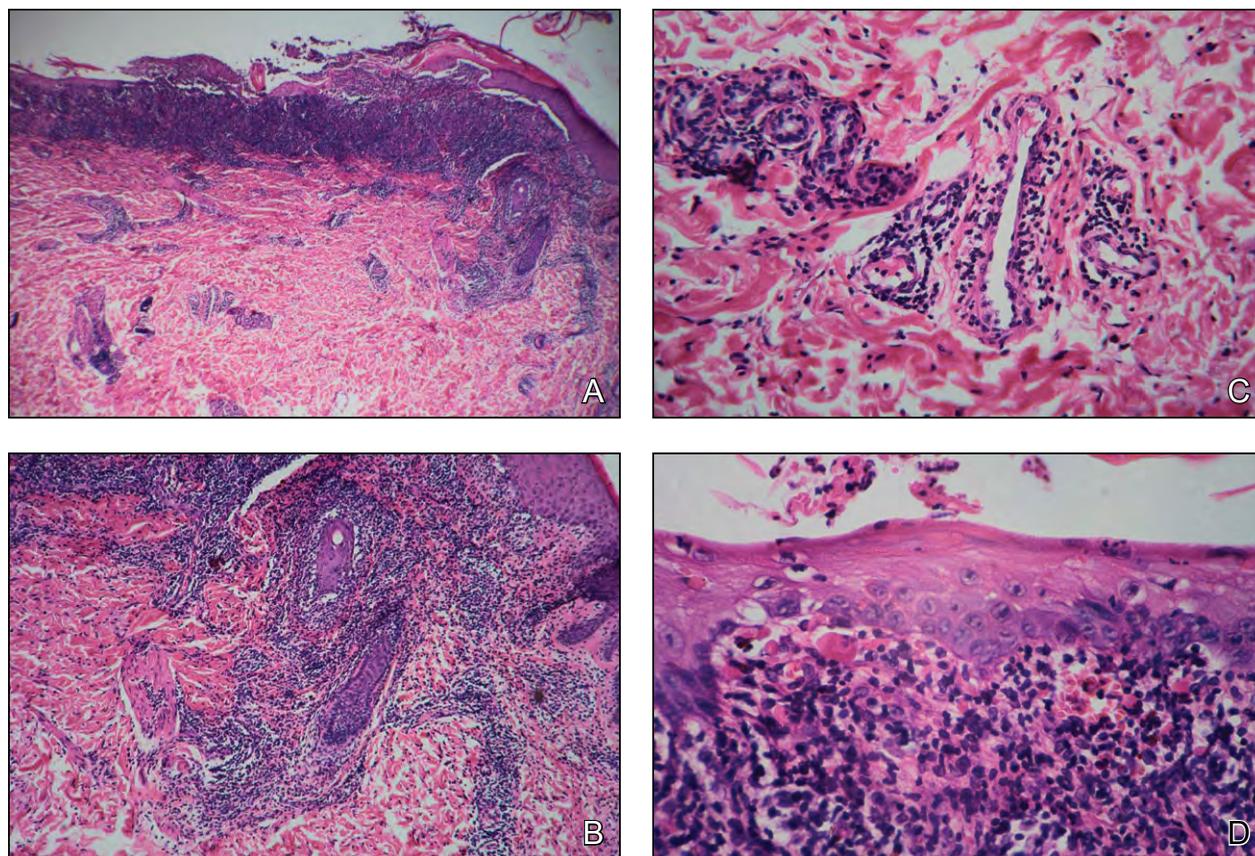


Figure 2. Histopathology of a necrotic lesion showed focal but full-thickness epidermal necrosis, bandlike lymphocytic and neutrophilic infiltration in the superficial dermis (A), periadnexal (B) and perivascular inflammatory infiltration (C), and erythrocyte extravasation in the superficial dermis (D)(H&E; original magnifications $\times 40$, $\times 100$, $\times 250$, and $\times 250$, respectively). The infiltrate included lymphocytes and neutrophils, with predominately lymphocytes (B–D).

sedimentation rate and C-reactive protein, anemia, mild hypergammaglobulinemia, and hypoproteinemia with or without hypoalbuminemia.⁹ The present case was representative because she shared most of the usual symptoms, though there was an absence of palm, sole, mouth, and genital involvement. Important clinical findings for the patient were leukocytosis, and the lesions healed with hyperpigmentation, which may recover gradually. Although she had typical abdominal symptoms, the colonoscopy and biopsy results suggested an allergy to capsicum, not FUMHD.

The etiopathology remains unknown, though infectious theory including bacteria,⁷ adenovirus, cutaneous cytomegalovirus,^{8,12} reactivated Epstein-Barr virus,^{8,10,15} asymptomatic varicella-zoster virus,^{11,12} and herpes simplex virus¹² have been considered. The presence of clonal T-cell receptors also was considered due to the prognosis and severity of the disease.^{7,9,11,12} The present case did not respond to antibiotics and had negative serology of herpes simplex virus type 1 and type 2 IgM. Resolution was achieved with

corticosteroid and methotrexate combination therapy. The results suggested that immunoreaction may play an important role in its pathogenesis.

Although no definite therapy is recommended for all patients at present,⁸ several agents, such as systemic oral and intravenous corticosteroids, antibiotics, antiviral treatments, dapsone, methotrexate, psoralen plus UVA,^{8,10,15} cyclosporine,^{8,13} methotrexate combined with prednisone,¹⁴ and intravenous immunoglobulin in combination with methotrexate and prednisone,³ are optional therapies with variable effects. This case report suggests an oral corticosteroid and methotrexate would be a good selection in managing FUMHD. Because FUMHD is a rare and sporadic disease with an unknown etiopathology and most cases were treated with multiple agents in various combinations, it is still hard to evaluate which defined medication or combination therapy is optimal for the treatment of FUMHD.^{8,9}

Because the disease is potentially life threatening, it is important for clinicians to be aware of the

symptoms in the early stage and start treatment as soon as possible.⁸

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