A fatal case of febrile ulceronecrotic Mucha-Habermann disease in a child

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Key words: children; fatal outcome; febrile ulceronecrotic Mucha-Habermann disease.

INTRODUCTION

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) is a rare, potentially fatal, severe variant of pityriasis lichenoides et varioliformis acuta (PLEVA). Lesions of FUMHD usually start with erythematous papules and plaques that rapidly progress to form large, often coalescing necrotic ulcers with hemorrhagic crusts. The skin findings are typically accompanied by systemic symptoms including high fever, abdominal pain, diarrhea, arthritis, pulmonary involvement, central nervous system symptoms, and sepsis. These systemic manifestations can lead eventually to serious complications or even a fatal outcome.[1-3]

Fatal cases were confined to adults (9 deaths of about 70 reported cases). On the contrary, children with FUMHD tend to have a more favorable outcome than adults, and no deaths have so far been reported in children.[2,3] Here we report the first case, to our knowledge, of a child with FUMHD complicated by sepsis that resulted in multiple organ failure and death.

Abbreviations used:

ABS:	antibiotics
DDS:	diamino-diphenyl sulphone
FUMHD:	Febrile ulceronecrotic Mucha-Habermann disease
IVIG:	intravenous immunoglobulins
MI:	mucosal involvement
MTX:	methotrexate
PLEVA:	pityriasis lichenoides et varioliformis acuta
SI:	systemic involvement
SS:	systemic steroids

CASE REPORT

A 9-year-old boy presented with a 1-month history of a painful skin eruption that started on the abdomen then progressed over a few weeks to cover almost the entire body. The eruption was associated with fever (39°C) and generalized malaise. Skin examination found widely distributed erythematous macules, papules, and necrotic plaques with hemorrhagic crusts (Fig 1). Flexural accentuation of the lesions was noticed in the axillae, groin, and neck (Fig 2). The oral mucosa was also involved with small painful ulcers on the tongue and inner lip (Fig 3).

Results of routine laboratory investigations were normal except for mild leukocytosis, elevated erythrocyte sedimentation rate and C-reactive protein, and anemia. A skin biopsy specimen taken from a necrotic plaque showed focal full-thickness epidermal necrosis, exocytosis, and vacuolar interface dermatitis consistent with PLEVA. The dermis showed prominent superficial and deep perivascular lymphocytic infiltrate and focal hemorrhage (Fig 4). Based on correlation of the clinico-pathologic features, the diagnosis of FUMHD was made. The patient was admitted to the hospital and received systemic antibiotics (azithromycin, 250 mg/d) and systemic steroids (30 mg/d) with almost no response. However, he left the hospital after 10 days and returned 3 weeks later. During this period, he had been treated at another hospital with intravenous immunoglobulins (IVIG) and cyclosporine that had been stopped after 1 week because of worsening skin lesions and impaired renal function.

Despite these treatments, the ulceronecrotic papules and plaques increased in number and size and became confluent, covering almost the entire body surface (Fig 5). The ulcerative lesions became secondarily infected with *Pseudomonas aeruginosa*, which was cultured from the skin and blood. This

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Funding sources: None.
Conflicts of interest: None declared.
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JAAD Case Reports 2016;2:181-5.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2016.03.002

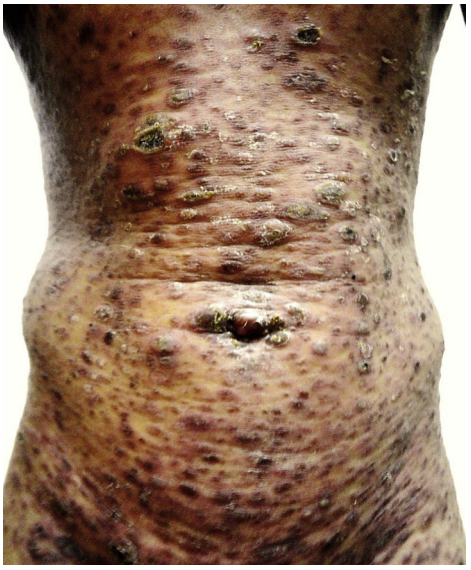

Fig 1. Febrile ulceronecrotic Mucha-Habermann disease. Generalized ulceronecrotic papules and plaques covering the whole trunk.

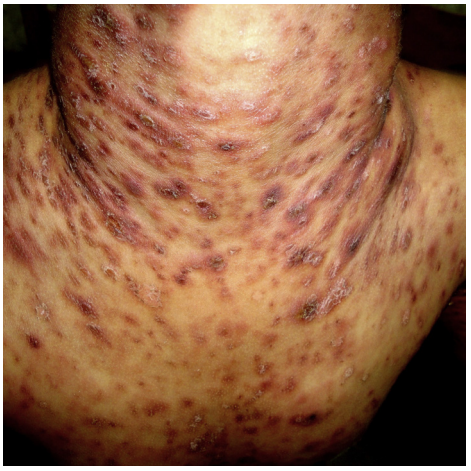

Fig 2. Flexural accentuation of the ulceronecrotic lesions on the neck.

infection resulted in the development of gangrenous ulcers covered with central black eschars and surrounded by erythematous borders, features consistent with those of ecthyma gangrenosum classically associated with *Pseudomonas* septicemia (Fig 6).

Accordingly, the patient was transferred to the intensive care unit and given systemic vancomycin and gentamycin. Over the next few days, he continued to deteriorate and showed signs of systemic inflammatory response syndrome including tachypnea, tachycardia, and hypothermia. Supportive measures and intravenous fluids were given, but refractory hypotension, myocardial dysfunction, and generalized edema followed.

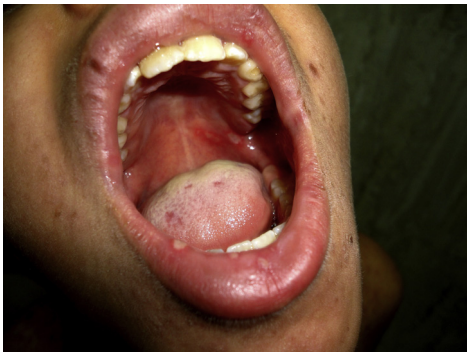

Fig 3. Mucosal erosions on the tongue and lips.

Fulminant sepsis led eventually to multiple organ failure and death.

DISCUSSION

An up-to-date literature review of FUMHD found that about 36 pediatric cases are reported. Analysis of these cases found an age range of 21 months to 18 years, a higher incidence in boys than girls (27 vs 9, respectively), and a suspected etiology in only 6 cases. Generalized ulceronecrotic lesions associated with fever and histopathology consistent with PLEVA were found in all patients. Mucous membrane involvement was found in 10 cases (28%), and systemic involvement was observed in 16 cases (45%). Combined therapy was the rule except in 2 patients, and complete recovery occurred in all cases.[1-3]

FUMHD in children differs from that in adults by its more rapid transformation from PLEVA to FUMHD, less mucosal involvement, more frequent vasculitis, and more favorable outcome than in adult cases.[4] FUMHD often starts as classic PLEVA and evolves rapidly to the fulminant widely distributed ulceronecrotic lesions associated with severe constitutional manifestations.[2] Therefore, it has been proposed that patients with PLEVA should be advised to immediately consult their physician if they have fever and if severe ulcerations develop in their lesions to allow early diagnosis and prompt therapy.[2] On the other hand, some patients present with the typical lesions of FUMHD from the onset without previous PLEVA, as was the case in our patient and some other reported cases.[2,3]

Lesions of FUMHD closely simulate those of Stevens-Johnson syndrome, which can also present with rapidly progressing necrotic lesions and mucosal involvement. Moreover, both share many common histopathologic features, including interface dermatitis and dyskeratotic keratinocytes. These features actually occurred in our patient who had Stevens-Johnson syndrome diagnosed at another hospital and received IVIG without any response.

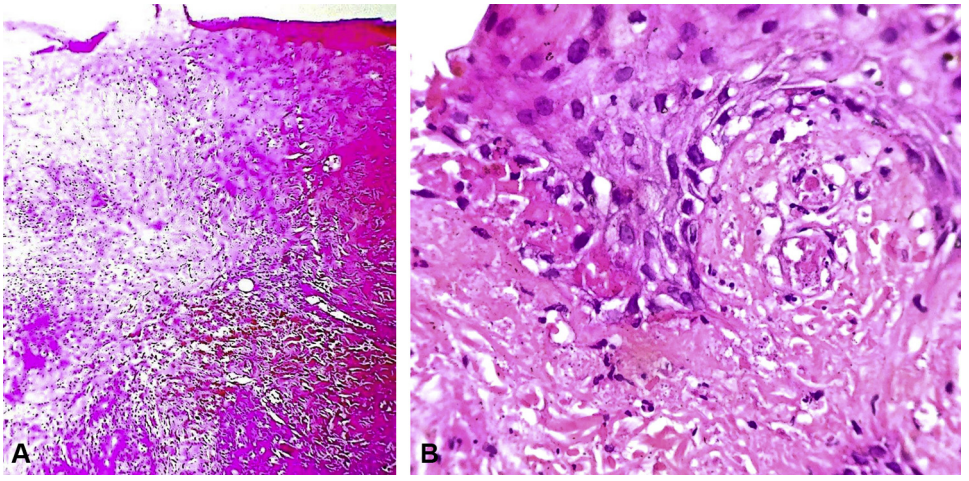

Fig 4. **A**, Histopathologic examination of a necrotic plaque shows full-thickness epidermal necrosis, prominent lymphocytic infiltrate, and focal hemorrhage. **B**, Histopathologic examination of a nonnecrotic lesion shows keratinocytes necrosis, exocytosis, and vacuolar interface dermatitis. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×100; **B**, ×400.)

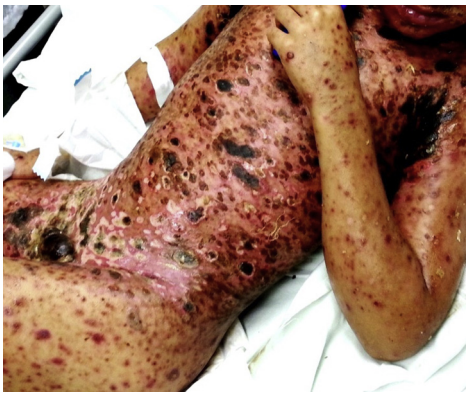

Fig 5. Severe confluent ulceronecrotic plaques covering most of the total body surface area.

Other dermatoses that may exhibit similar clinical features include varicella, papulo-vesicular rosea, leukocytoclastic vasculitis, and lymphomatoid papulosis.[2,3] However, the severe necrotic nature of the lesions, the flexural accentuation, the associated constitutional manifestations, and the clinico-pathologic correlation help to differentiate between FUMHD and these disorders.

The mortality rate of FUMHD is about 13% of the reported cases, and all were in adult patients[5-11] (Table I).The mortality rate increased with the age of the patients, where 7 of the 9 fatal cases were older than 40 years. Therefore, it has been suggested that early intervention in patients of younger ages may result in a favorable outcome.[3] Fatal outcomes in adults have been attributed to pulmonary thromboembolism, pneumonia, sepsis, hypovolemic shock, cardiac arrest and thrombosis of superior mesenteric artery.[4-9]

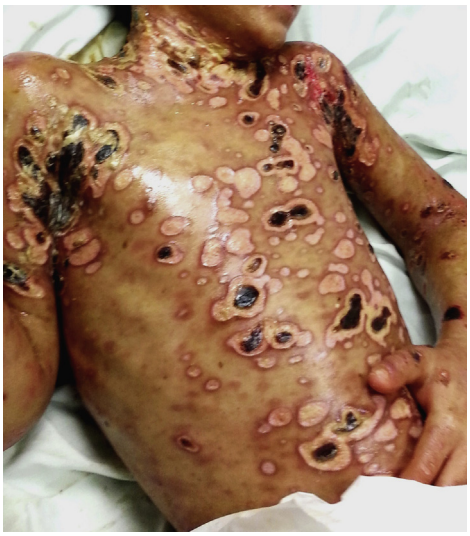

Fig 6. Multiple ecthyma gangrenosum lesions associated with *Pseudomonas* septicemia.

Secondary infection of the lesions is a common finding in FUMHD, and sepsis was the cause of death in our patient as well as in 6 of 9 cases associated with a fatal outcome.[8-11]

Treatment modalities include methotrexate, antibiotics, acyclovir, dapsone, phototherapy, high-dose corticosteroids, IVIG, cyclosporine, and infliximab. However, there is no consensus regarding the most effective therapy because of the uncertain etiology, the few cases reported, the combination therapy often used, and the variable response to the same drug between affected patients.[2,3]

Although systemic steroids, cyclosporine, and IVIG have been previously used with success in the

Table I. Summary of fatal cases of FUMHD

Study	Age/y	Sex	Possible etiology	Clinical features*	Therapy
Hoghton et al, 1989[5]	49	Female	Unknown	MI: Negative SI: SPM, myocarditis, pulmonary embolism	SS, ATB, DDS, MTX, UVR, acyclovir
De Cuyper et al, 1994[6]	82	Female	Unknown	MI: Positive SI: Megaloblastic anemia, pneumonia	SS, ATB, UVB
Gungor et al, 1996[7]	59	Male		MI: Negative SI: Abdominal pain, diarrhea	SS, MTX, ATB
Puddu et al, 1997[8]	43	Female	Unknown	MI: Negative SI: Sepsis	SS, ATB
Miyamoto et al, 2003[9]	76	Male	Monoclonal T cell	MI: Negative SI: Hypovolemic shock, sepsis	ABS
Cozzio et al, 2004[10]	72	Male	Monoclonal T cell	MI: Negative SI: Sepsis, pancytopenia	MTX, IVIG
Cozzio et al, 2004[10]	26	Female	Monoclonal T cell	MI: Negative SI: Sepsis, pancytopenia	SS, MTX, PUVA
Aytekin et al, 2005[11]	27	Female	Unknown	MI: Negative SI: Sepsis	SS, ATB, IVIG, acyclovir
Malnar et al, 2006[12]	60	Male	Unknown	MI: Positive SI: Sepsis, pulmonary thromboembolism, thrombosis of superior mesenteric artery	SS, ATB

ABS, Antibiotics; *DDS*, diamino-diphenyl sulphone; *MI*, mucosal involvement; *MTX*, methotrexate; *SI*, systemic involvement; *SS*, systemic steroids.

Adapted from Nofal A, Assaf M, Alakad R, Amer H, Nofal E, Yosef A. Febrile ulceronecrotic Mucha-Habermann disease: proposed diagnostic criteria and therapeutic evaluation. *Int J Dermatol*. http://dx.doi.org/10.1111/ijd.13195. Published online December 23, 2015.

*Fever and severe generalized, progressive ulceronecrotic papules and plaques were constant clinical features in all patients.

treatment of some cases of FUMHD,[2,3,9] our patient did not respond well to these therapeutic agents. Therefore, we propose that the use of combined aggressive immunosuppressive therapy, in the absence of strong evidence for their efficacy, can lead to impaired immunity and overwhelming infection ending with sepsis, as was the case in our patient. In this respect, methotrexate, which is a less-aggressive immunosuppressive agent, seems to be the most successful therapy in the reported cases.[2,13,14]

The marked severity of the condition, the misdiagnosis, and the combined aggressive therapies represent potential reasons for the fatal outcome in our patient. However, no definite conclusion can be given in this respect, and it seems that no intervention could have prevented this terrible outcome.

We propose that early diagnosis and hospitalization, surveillance for systemic infection, proper skin care for ulceronecrotic lesions, and the prudent use of systemic therapy are among factors that might prevent mortality in FUMHD.

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