Febrile Ulceronecrotic Mucha-Habermann Disease: Treatment with Infliximab and Intravenous Immunoglobulins and Review of the Literature

L. Meziane A. Caudron F. Dhaille M. Jourdan A. Dadban C. Lok G. Chaby

Department of Dermatology, Amiens University Medical Centre, South Hospital, and University Picardie Jules Verne, Amiens, France

Key Words

Febrile ulceronecrotic Mucha-Habermann disease · Intravenous immunoglobulins · Pityriasis lichenoides et varioliformis acuta · Tumor necrosis factor- α inhibitors

Abstract

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) is a rare subtype of pityriasis lichenoides et varioliformis acuta, characterized by an acute onset of ulceronecrotic papules, rapidly coalescing into large ulcers with necrotic crusts, associated with high fever and severe systemic symptoms. We report a case of a 65-year-old woman with a resistant form of FUMHD successfully treated with a tumor necrosis factor- α (TNF α) inhibitor (infliximab). After 1 year of treatment, because of the recurrence of lesions and occurrence of severe sepsis, we decided to change the therapeutic procedure by introducing intravenous immunoglobulin which induced a spectacular improvement. Only few cases of FUMHD treated with intravenous immunoglobulin have been reported to date. In our case, we describe the first utilization of TNF α inhibitors in the treatment of FUMHD: TNF α inhibitors may be useful, particularly in resistant cases. Further reports are required to confirm this potential therapeutic option.

Copyright © 2013 S. Karger AG, Basel

Introduction

Pityriasis lichenoides et varioliformis acuta (PLEVA) is an uncommon, idiopathic, acquired dermatosis characterized by erythematous, scaly papules often accompanied by hemorrhagic and papulonecrotic lesions. A febrile ulceronecrotic severe variant of PLEVA, called febrile ulceronecrotic Mucha-Habermann disease (FUMHD) is more destructive and associated to large coalescent skin necrosis with a rapid progression [1]. 48 cases of PLEVA fulminans have been reported to date in the literature with 9 lethal forms (20%) (table 1) [1–44]. Oral, genital and conjunctival mucosa can be affected [2, 6, 9, 12, 13]. Systemic manifestations are present like high fever, myalgia, arthralgia, gastrointestinal and central nervous system symptoms, interstitial pneumonitis, lymphocytic myocarditis, megaloblastic anemia, pancytopenia, and diffuse intravascular coagulation [1, 3, 4, 8, 9, 12]. FUMHD mainly occurs in children and young adults in the second and third decades of life, with a predominance of male and a mean age of 27 years. Children tend to have more favorable outcomes and no deaths have been reported in children. In adults, the mortality was attributed to pulmonary thromboembolism [8, 34], pneumonia [4, 12, 32], cardiac arrest [3], sepsis [9, 18, 23, 28], hy-

povolemic shock [27], and massive thrombosis of the superior mesenteric artery [34]. The pathogenesis of PLEVA fulminans has not fully been elucidated, although multiple hypotheses exist. Reported treatments include systemic high-dose corticosteroids, methotrexate, ultraviolet, antibiotics, although efficacy is difficult to determine because of the small number of reported cases.

We describe here the first case of FUMHD treated successfully with infliximab, a tumor necrosis factor- α (TNF α) inhibitor, and with intravenous immunoglobulins (IVIG), and completed with a review of cases reported in the literature.

Case Report

A 65-year-old woman was admitted to our department for appearance of disseminated ulceronecrotic lesions and fever to 40°C. Physical examination revealed diffuse erythematous scaly papules with sparse pustules and vesicles that coalesced into confluent ulceronecrotic papules and plaques on the face, the trunk, extremities and flexural areas (fig. 1). The skin lesions involved 90% of the body surface. Oral, genital and conjunctival mucosae were also involved with large and painful ulcerations (fig. 2).

Table 1. Literature review

Reference (first author)	Age	Sex	Triggering factors	Systemic involvement	Therapy	Duration, months	Outcome
Degos, 1966 [1]	36	M	0	CNS involvement, myalgias, lymphadenopathy	SS, ATB	5–6	cure
Degos, 1966 [1]	30	M	0	abdominal pain, lymphadenopathy	ATB	6–8	cure
Burke, 1969 [2]	15	M	0	lymphadenopathy, anemia	ATB, SS	4.5	cure
Burke, 1969 [2]	12	F	0	0	SS	2.5	cure
Lowe, 1975 [3]	32	M	0	cardiomyopathy	UVR	?	cure
Auster, 1979 [4]	7	F	adenovirus	pulmonary involvement	ATB, SS	2.5	cure
Cavalieri, 1982 [5]	13	M	0	0	SS, ATB, IGIV, antivirals	?	cure
Warshauer, 1983 [6]	54	M	0	abdominal pain, megaloblastic anemia, eosinophilia	SS, ATB, MTX, DDS, thiabendazole	18	cure
Nakamura, 1986 [7]	21	M	0	0	ATB, DDS	1	cure
Hoghton, 1989 [8]	49	F	0	SPM, myocarditis, pulmonary embolism	SS, ATB, DDS, MTX, UVR, acyclovir	1	fatal
Luberti, 1991 [9]	12	M	0	arthritis, sepsis	SS, ATB, acyclovir	2	cure
Kasamatsu, 1993 [10]	4	M	0	lymphadenopathy	SS, ATB, DDS	24	cure
Lopez-Estebanz, 1993 [11]	18	M	0	liver dysfunction	SS, ATB, MTX, PUVA	2	cure
De Cuyper, 1994 [12]	82	F	0	megaloblastic anemia	SS, ATB, UVB	7	fatal
Fink-Puches, 1994 [13]	16	M	0	0	SS, ATB, MTX	4	cure
Maekawa, 1994 [14]	16	M	0	eosinophilia	ATB, acyclovir	2	cure
Suarez, 1996 [15]	32	M	0	liver dysfunction, conjunctival ulcer, sepsis	MTX, SS, ATB	6	cure
Gungor, 1996 [16]	59	M	0	abdominal pain	SS, MTX, ATB	?	fatal
Reseghetti, 1996 [17]	27	M	0	bacteremia	SS, ATB, PUVA	?	cure
Puddu, 1997 [18]	43	F	0	sepsis	SS, ATB	?	fatal
Romani, 1998 [19]	12	F	0	0	MTX, PUVA, ATB	?	cure
Tsai, 2001 [20]	45	M	CMV	arthritis	SS, UVB, ATB, acyclovir	?	cure
Hsieh, 2001 [21]	8	F	0	0	ATB, UVB, acyclovir	?	cure
Ricci, 2001 [22]	10	F	EBV	0	acyclovir	?	cure
Yanaba, 2002 [23]	21	M	0	sepsis	SS, DDS, ATB, IVIG, skin grafting	5	cure
Yang, 2003 [24]	14	M	EBV	0	SS, ATB	2	cure
Rivera, 2003 [25]	33	F	0	0	SS, MTX, acetylsalicylic acid	?	cure
Ito, 2003 [26]	12	M	0	anemia, abdominal pain, lymphadenopathy	SS, MTX	?	cure
Miyamoto, 2003 [27]	76	M	infiltrating monoclonal cells	sepsis, hypovolemic shock	ATB	2	fatal
Cozzio, 2004 [28]	72	M	monoclonal T cell population in dermis	sepsis, pancytopenia	MTX, IVIG	4	fatal
Cozzio, 2004 [28]	26	F	monoclonal T cell population	sepsis	SS, MTX, PUVA	?	fatal
Tsianakas, 2005 [29]	9	M	0	0	SS, ATB, MTX	?	cure
Aytekin, 2005 [30]	27	F	0	sepsis	SS, ATB, IVIG, acyclovir	1	fatal
Herron, 2005 [31]	8	F	0	sepsis, DIC, GI hemorrhage, ARDS	MTX, ATB, cyclosporine, SS	2	cure
Aydingöz, 2006 [32]	37	M	0	pulmonary involvement	SS, ATB	?	cure
Helmbold, 2006 [33]	20	M	polyclonal T lymphocyte VZV reactivation	0	ATB, SS, acyclovir	2	cure
Malnar, 2006 [34]	60	M	0	sepsis, pulmonary thromboembolism, thrombosis of superior mesenteric artery	SS, ATB	1.5	fatal
Kim, 2007 [35]	8	M	0	0	ATB, SS, cyclosporine	?	cure
Pyrpasopoulou, 2007 [36]	17	F	0	sepsis, anemia, diarrhea	SS, ATB, MTX, IVIG, acyclovir	?	cure
Sotiriou, 2008 [37]	20	F	0	0	SS, MTX, ATB, acyclovir	7	cure
Kukova, 2007 [38]	21	F	0	0	SS, ATB, UVB	?	cure

Table 1 (continued)

Reference (first author)	Age	Sex	Triggering factors	Systemic involvement	Therapy	Duration, months	Outcome
Smith, 2009 [39]	24	M	genital herpes simplex	0	ATB, acyclovir	1	cure
Cumming, 2009 [40]	21	M	upper airways infection	0	ATB, SS, MTX	4	cure
Marenco, 2010 [41]	23	M	0	0	SS, MTX, IVIG, ECP	1.5	cure
Helbling, 2009 [42]	17	M	recent EBV infection	lymphadenopathy	ATB, MTX	6	cure
Harenberg, 2010 [43]	30	M	0	sepsis	SS, ATB	?	cure
Kaufman, 2012 [44]	1.75	F	0	laryngeal edema	SS, MTX	3	cure
Kaufman, 2012 [44]	1.8	F	0	0	ATB, acyclovir	?	cure

ARDS = Acute respiratory distress syndrome; ATB = antibiotics; CMV = cytomegalovirus; CNS = central nervous system; DDS = 4,4-diaminophenylsulphonate; DIC = diffuse intravascular coagulation; EBV = Epstein-Barr virus; ECP = extracorporeal photochemotherapy; F = female; GI = gastrointestinal; IVIG = intravenous immunoglobulin; M = male; MTX = methotrexate; PUVA = psoralen plus ultraviolet A; SPM = splenomegaly; SS = systemic steroids; UVB = ultraviolet B; UVR = ultraviolet radiation; VZV = varicella zoster virus.

Fig. 1. Diffuse ulceronecrotic lesions on the back, some with central crust.

Routine laboratory tests showed elevated erythrocyte sedimentation rate (120 mm/h), increased level of C-reactive protein (350 mg/l) and a normochromic-normocytic anemia (10 g/dl). Serology for hepatitis B virus, hepatitis C virus, HIV, Epstein-Barr virus (EBV), cytomegalovirus, parvovirus B19, toxoplasma, adenovirus, enterovirus, varicella zoster virus, herpes simplex virus, human herpes virus 6, 7 and 8 were all negative for IgM and IgG. Sampling microbiological tests of the patient's skin, blood and skin cultures also were negative.

Screening for autoimmunity (antinuclear antibodies, lupus anticoagulant, antibodies to cardiolipin, antineutrophil

antibodies), protein electrophoretic, and serum immunoglobulin analysis of peripheral lymphocyte subsets were also normal.

The histopathological exam confirmed the diagnosis of PLEVA and showed acanthosis, focal parakeratosis, with vacuolar and degeneration necrosis of basal layer. Edema of papillary dermis was present, with a perivascular lympho-histiocytic infiltrate and exocytosis. No evidence of vasculitis was present. Immunohistology showed a predominantly CD3+ of lymphocyte infiltrate with an equal number of CD4+ and CD8+ lymphocytes in the epidermal and dermal infiltrate. Staining with CD30 was negative. The research of monoclonal T cell population in the skin and the blood was negative. The diagnosis of FUMHD was made, based on clinicopathologic correlation.

Our patient was initially treated with oral corticosteroids (prednisone, 60 mg/day), without improvement. Despite the intravenous administration of acyclovir (10 mg/kg/day), cutaneous lesions progressed. We started methotrexate (12 mg/week) but it was rapidly discontinued because of the occurrence of a pancytopenia and a renal insufficiency. Because of the severity of the lesions, the resistance to immunosuppressive agents and the progression of PLEVA, TNF α inhibitor was initiated: infliximab 5 mg/kg. The patient received weekly one dose during 4 weeks. The patient became afebrile with a progressive improvement of cutaneous and mucosal lesions. After 4

weeks, injections of infliximab were spaced every 6 weeks with a preservation of complete remission (fig. 3).

One year after the initiation of infliximab, new lesions with painful skin necrosis relapsed. She was septic and hemodynamically unstable. A *Candida* spore grew from fungal cultures in blood and bronchoalveolar lavage, which required introduction of intravenous antifungal treatment. TNF α inhibitor was stopped because of septic complications and that is why the choice of another anti-TNF was not retained. She was ultimately treated with IVIG at 2 mg/kg once a week during 2 weeks and then once monthly. An optimal response was obtained with healing of all cutaneous lesions during several months. The administration of IVIG led to significant clinical stabilization, based on reports in the literature, and the previous episodes of successful administration of IVIG. Unfortunately, 8 months after the introduction of IVIG, the patient was transferred to the intensive care unit because of an acute respiratory disease with severe sepsis, and lymphopenia without any skin lesions. Despite intensified systemic therapy, the patient died.

Discussion

FUMHD involves a sudden, severe flare characterized by coalescent necrotic ulcerations associated with high fever and systemic symptoms, potentially fatal.

Fig. 2. Necrotic papules and erosions on the face with affected conjunctival mucosae.

Fig. 3. Healing of cutaneous lesions after 1 month of infliximab treatment.

FUMHD can occur more frequently in children, adolescents or adults [29]. It exhibits a male predominance (male:female ratio 31:17). The mean age of patients in the reported cases is 27 years (range 1.75–82); 33 of the 48 patients reported were younger than 30 years (table 1).

The reported mortality rate of FUMHD is approximately 20% (9 of 48 patients). There are no child fatalities; fatal outcome has been seen in adult patients. A comparison between adult and pediatric cases shows a more favorable outcome in children. In fact, until 2004 fatal outcomes were confined to persons older than 40 years. Cozzio et al. [28] and Aytekin et al. [30] reported cases in 2005 of 26- and 27-year-old females with fatal outcomes. Fatal outcomes were linked to pulmonary thromboembolism, sepsis, hypovolemic shock and thrombosis of superior mesenteric artery.

The exact pathogenesis of PLEVA fulminans is unknown. Cutaneous immune response with hypersensitivity to infectious agents was suggested, and several pathogens have been proposed to cause PLEVA such as EBV, adenovirus, cytomegalovirus, parvovirus B19, varicella zoster and HIV-1. Reactivated EBV infection in a patient with PLEVA has been reported by Ricci et al. [22], and also reported by Yang et al. [24]. Auster et al. [4] reported positive culture of adenovirus from the urine in a 7-year-old girl with FUMHD and interstitial pneumonitis. Tsai et al. [20] detected cytomegalovirus infection in the skin biopsy specimen from a 45-year-old male. Recently, Smith and Oliver [39] cultured herpes simplex type 2 from genital and a skin biopsy in 24-year-old male presenting a FUMHD. Finally, FUMHD can belong to the concept of paraviral eruptions proposed by Lipsker and Saurat

[45], because viral reactivation is possibly a triggering factor of the disease.

Immunological process might contribute to the pathogenesis of FUMHD. Yanaba et al. [23] observed a predominantly CD8+ lymphocytes infiltrate around the dermis and epidermis which might suggest a cytotoxic attack of lymphocytes to altered epidermal antigens. Some authors have suggested that PLEVA is a benign clonal disorder of activated T cell lymphocytes. Dereure et al. [46] demonstrated that 13 of 20 (65%) PLEVA biopsy specimens had a dominant T cell clone. They concluded that PLEVA exists within a spectrum of clonal T cell cutaneous lymphocytic disorders. Weinberg et al. [47] in a retrospective and prospective analysis of PLEVA tissue samples found that 8 of 14 (57%) specimens demonstrated monoclonal T cell receptor gene rearrangements. These findings lead to the conclusion that PLEVA is a benign clonal T cell disorder. Herron et al. [31] reported the presence of CD30+ T lymphocytes and elevation of soluble IL-2 receptor level in a report of febrile ulceronecrotic PLEVA. Elevated sIL-2R represents systemic T cell activation, seen in cutaneous T cell lymphomas. The clonal nature of FUMHD may represent an aggressive entity of cutaneous T cell lymphomas. Three cases with fatalities had monoclonal disease [27–29]: it has been suggested that T cell clonality may be related to disease severity.

Several treatment modalities have been described in the literature, but it is difficult to evaluate a defined therapy because of the uncertain etiology, the small number of cases and the combination therapy often employed. Immunosuppressive monotherapy with methotrexate [6, 8, 11, 13, 15, 19, 25, 28, 29, 36, 40] or cyclosporine [31, 35] or a combination of one of these with a

high dose of glucocorticoids [6, 8, 11, 13, 25, 28, 29, 36, 41, 43] has been used in several cases. Antibiotics like erythromycin, acyclovir, ultraviolet phototherapy (PUVA) [11, 19], IVIG [5, 28, 36, 41], photochemotherapy [41], 4,4-diaminodiphenyl sulfone [7, 8, 10, 23], and debridement with skin grafting [23] have also been used to treat FUMHD.

Tsianakas and Hoeger [29] reported abnormally high serum levels of TNF α and suggested that anti-TNF α treatment should be considered and might represent a first line option. In our case, a TNF α inhibitor was administered after failure of numerous treatments, which induced a rapidly and complete remission. However, the significant loss of response over time of infliximab, the occurrence of severe sepsis in our patient did not lead to use another TNF α inhibitor. In our case, we decided to treat by IVIG proving to be effective in inducing a spectacular improvement and in arresting the appearance of new lesions. IVIG could play a role as adjunctive therapeutic tool in association with TNF α inhibitors or immunosuppressive therapy.

In conclusion, FUMHD is a rare and severe variant of PLEVA that could lead to death in adults. Because of the disease severity, it is important to make the diagnosis as early as possible to start a treatment. We reported the first case of a resistant form of FUMHD, with an initial favorable response to infliximab, and then to IVIG. We suggested that TNF α inhibitors such as IVIG may represent an appropriate therapeutic solution to maintain remission, in severe cases and should be started rapidly.

Disclosure Statement

The authors declare no conflict of interest.

References

- 1 Degos R, Duperrat B, Daniel F: Hyperthermic ulcero-necrotic parapsoriasis. Subacute form of parapsoriasis guttata. *Ann Dermatol Syphiligr* 1966;93:481–496.
- 2 Burke DP, Adams RM, Arundell FD: Febrile ulceronecrotic Mucha Habermann's disease. *Arch Dermatol* 1969;100:200–206.
- 3 Lowe NJ: Pityriasis lichenoides et varioliformis acuta and suspected cardiomyopathy. *J R Nav Med Serv* 1975;61:85–87.

- 4 Auster BI, Santa Cruz DJ, Eisen AZ: Febrile ulceronecrotic Mucha-Habermann's disease with interstitial pneumonitis. *J Cutan Pathol* 1979;6:66–76.
- 5 Cavalieri R, Didona B, Chinni L: Pitiriasi varioliforme acuta ulcero-necrotica ipertermica. *Chron Derm* 1982;6:617–623.
- 6 Warshawer BL, Maloney ME, Dimond RL: Febrile ulceronecrotic Mucha-Habermann's disease. *Arch Dermatol* 1986;13:381–384.
- 7 Nakamura S, Nishihara K, Nadayama K, Hoshi K: Febrile ulceronecrotic Mucha-Habermann's disease and its successful therapy with DDS. *J Dermatol* 1986;13:381–384.
- 8 Hoghton MA, Ellis JP, Hayes MJ: Febrile ulceronecrotic Mucha-Habermann disease: a fatality. *J R Soc Med* 1989;82:500–501.
- 9 Luberti AA, Rabinowitz LG, Ververeli KO: Severe febrile Mucha-Habermann's disease in children: case report and review of the literature. *Pediatr Dermatol* 1991;8:51–57.
- 10 Kasamatsu M, Yokota K, Morita A: Febrile ulcero-necrotic Mucha-Habermann's disease. *Nishinohon Hifu* 1993;55:665–669.
- 11 Lopez-Estebarez JL, Vanaclocha F, Gil R, García B, Iglesias L: Febrile ulceronecrotic Mucha-Habermann disease. *J Am Acad Dermatol* 1993;29:903–906.
- 12 De Cuyper C, Hindryckx P, Deroo N: Febrile ulceronecrotic pityriasis lichenoides et varioliformis acuta. *Dermatology* 1994;189 (suppl 2):50–53.
- 13 Fink-Puches R, Soyer HP, Kerl H: Febrile ulceronecrotic pityriasis lichenoides et varioliformis acuta. *J Am Acad Dermatol* 1994;30:261–263.
- 14 Maekawa Y, Nakamura T, Nogami R: Febrile ulceronecrotic Mucha-Habermann's disease. *J Dermatol* 1994;21:46–49.
- 15 Suarez J, López B, Villalba R, Perera A: Febrile ulceronecrotic Mucha-Habermann disease: a case report and review of the literature. *Dermatology* 1996;192:277–279.
- 16 Gungor E, Alli N, Artuz F, Lenk N: Febrile ulceronecrotic Mucha-Habermann's disease. *Int J Dermatol* 1996;35:895–896.
- 17 Reseghetti A, Parma A, Rozzoni M: Pitiriasi lichenoides e varioliforme acuta febrile ulceronecrotica. *G Ital Dermatol Venereol* 1996;131:55–58.
- 18 Puddu P, Cianchini G, Colonna L, Girardelli CR, Ferranti G, De Pita O: Febrile ulceronecrotic Mucha-Habermann's disease with fatal outcome. *Int J Dermatol* 1997;36:691–694.
- 19 Romani J, Puig L, Fernandez-Figueras MT, de Moragas JM: Pityriasis lichenoides in children: clinicopathologic review of 22 patients. *Pediatr Dermatol* 1998;15:1–6.
- 20 Tsai KS, Hsieh HJ, Chow KC, Lin TY, Chiang SF, Huang HH: Detection of cytomegalovirus infection in a patient with febrile ulceronecrotic Mucha-Habermann's disease. *Int J Dermatol* 2001;40:694–698.
- 21 Hsieh CC, Chiu YK, Ho JC, Huang SC: Febrile ulceronecrotic Mucha-Habermann's disease: report of a case. *Dermatol Sinica* 2001;19:233–242.
- 22 Ricci G, Patrizi A, Misciali D, Masi M: Pathological case of the month. Febrile Mucha-Habermann disease. *Arch Pediatr Adolesc Med* 2001;155:195–196.
- 23 Yanaba K, Ito M, Sasaki H, Inoue M, Nobeyama Y, Yonemoto H, Ishiji T, Tanaka H, Kamide R, Niimura M: A case of febrile ulceronecrotic Mucha-Habermann disease requiring debridement of necrotic skin and epidermal autograft. *Br J Dermatol* 2002;147:1249–1253.
- 24 Yang CC, Lee JY, Chen W: Febrile ulceronecrotic Mucha-Habermann disease with extensive skin necrosis in intertriginous areas. *Eur J Dermatol* 2003;13:493–496.
- 25 Rivera R, Ortiz P, Rodriguez-Peralto JL, Vanaclocha F, Iglesias L: Febrile ulceronecrotic pityriasis lichenoides et varioliformis acuta with atypical cells. *Int J Dermatol* 2003;42:26–28.
- 26 Ito N, Ohshima A, Hashizume H, Takigawa M, Tokura Y: Febrile ulceronecrotic Mucha-Habermann's disease managed with methylprednisolone semipulse and subsequent methotrexate therapies. *J Am Acad Dermatol* 2003;49:1142–1148.
- 27 Miyamoto T, Takayama N, Kitada S, Hagari Y, Mihara M: Febrile ulceronecrotic Mucha-Habermann disease: a case report and a review of the literature. *J Clin Pathol* 2003;56:795–797.
- 28 Cozzio A, Hafner J, Kempf W, Häffner A, Palmedo G, Michaelis S, Gilliet M, Zimmermann D, Burg G: Febrile ulceronecrotic Mucha-Habermann disease with clonality: a cutaneous T-cell lymphoma entity? *J Am Acad Dermatol* 2004;51:1014–1017.
- 29 Tsianakas A, Hoeger PH: Transition of pityriasis lichenoides et varioliformis acuta to febrile ulceronecrotic Mucha-Habermann disease is associated with elevated serum tumour necrosis factor- α . *Br J Dermatol* 2005;152:794–799.
- 30 Aytekin S, Balci G, Duzgun OY: Febrile ulceronecrotic Mucha-Habermann disease: a case report and a review of the literature. *Dermatol Online J* 2005;11:31.
- 31 Herron MD, Bohnsack JF, Vanderhooft SL: Septic, CD-30 positive febrile ulceronecrotic pityriasis lichenoides et varioliformis acuta. *Pediatr Dermatol* 2005;22:360–365.
- 32 Aydingöz IE, Kocaayan N, Mansur AT, Pekcan Ş, Arman A: A case of ulceronecrotic Mucha-Habermann disease with pulmonary involvement. *Dermatology* 2006;212:388–390.
- 33 Helmbold P, Gaisbauer G, Fiedler E, Stücker M, Wolter M, Marsch W: Self-limited variant of febrile ulceronecrotic Mucha-Habermann disease with polyclonal T-cell receptor rearrangement. *J Am Acad Dermatol* 2006;54:1113–1115.
- 34 Malnar T, Milavec-Puretic V, Rados J, Zarkovic K, Dobric I: Febrile ulceronecrotic pityriasis lichenoides et varioliformis acuta with fatal outcome. *J Eur Acad Dermatol Venereol* 2006;20:303–307.
- 35 Kim HS, Yu DS, Kim JW: A case of febrile ulceronecrotic Mucha-Habermann's disease successfully treated with oral cyclosporine. *J Eur Acad Derm Venereol* 2007;21:272–273.
- 36 Pyrpassopoulou A, Athyros VG, Karagiannis A, Chrysomallis F, Zamboulis C: Intravenous immunoglobulins: a valuable asset in the treatment of a case of septic febrile ulceronecrotic Mucha-Habermann disease. *Dermatology* 2007;215:164–165.
- 37 Sotiriou E, Patsatsi A, Tsorova C: Febrile ulceronecrotic Mucha-Habermann disease: a case report and review of the literature. *Acta Derm Venereol* 2008;88:350–355.
- 38 Kukova G, Gerber PA, Neumann NJ, Bruch-Gerharz D, Homey B: Febrile ulceronecrotic Mucha-Habermann syndrome. *Hautarzt* 2007;58:835–836.
- 39 Smith JJ, Oliver GF: Febrile ulceronecrotic Mucha-Habermann disease associated with herpes simplex virus type 2. *J Am Acad Dermatol* 2009;60:149–152.
- 40 Cumming MM, Salathiel AS, Paino MA, Delort S, Roselino AM: Febrile ulceronecrotic Mucha-Habermann disease with exuberant mucosal involvement: case report. *An Bras Dermatol* 2009;84:655–658.
- 41 Marengo F, Fava P, Fierro MT, Quaglino P, Bernengo MG: High-dose immunoglobulins and extracorporeal photochemotherapy in the treatment of febrile ulceronecrotic Mucha-Habermann disease. *Dermatol Ther* 2010;23:419–422.
- 42 Helbling I, Chalmers RJ, Yates VM: Febrile ulceronecrotic Mucha-Habermann disease: a rare dermatological emergency. *Clin Exp Dermatol* 2009;34:e1006–e1007.
- 43 Harenberg PS, Hrabowski M, Ryssel H, Gazzykan E, Germann G, Engel H, Reichenberger MA: Case report febrile ulceronecrotic Mucha-Habermann disease. *J Plast Surg* 2010;10:433–437.
- 44 Kaufman WS, McNamara EK, Curtis AR, Kosari P, Jorizzo JL, Krowchuk DP: Febrile ulceronecrotic Mucha-Habermann disease (pityriasis lichenoides et varioliformis acuta fulminans) presenting as Stevens-Johnson syndrome. *Pediatr Dermatol* 2012;29:135–140.
- 45 Lipsker D, Saurat JH: A new concept: paraviral eruptions. *Dermatology* 2005;211:309–311.
- 46 Dereure O, Levi E, Kadin ME: T-cell clonality in pityriasis lichenoides et varioliformis acuta: a heteroduplex analysis of 20 cases. *Arch Dermatol* 2000;136:1483–1486.
- 47 Weinberg JM, Kristal L, Chooback L, Honig PJ, Kramer EM, Lessin SR: The clonal nature of pityriasis lichenoides. *Arch Dermatol* 2002;138:1063–1067.