

CASE REPORT

Febrile ulceronecrotic Mucha–Habermann disease: a case report and a review of the literature

T Miyamoto, N Takayama, S Kitada, Y Hagari, M Mihara

J Clin Pathol 2003;56:795–797

This report describes the case of a 76 year old man who suffered from febrile ulceronecrotic Mucha–Habermann disease (FUMHD). Despite this patient's typical clinical and histological findings, the fulminating course led to death. Polymerase chain reaction (PCR) analysis of the skin lesions showed that the infiltrating cells were monoclonal in origin and were from an aberrant clone. FUMHD is a very rare, febrile variant type of pityriasis lichenoides et varioliformis acuta, and is characterised by necrotic cutaneous ulcerations associated with high fever and systemic manifestations. Including this present case, only 18 cases of FUMHD have been reported. FUMHD can occur in both adults and children, although there are several differences between the manifestations of the disease in the two groups. One major difference is prognosis: all cases resulting in fatality are of the adult type, whereas no fatal cases have been reported among children. The aberrant clone detected by PCR may be responsible for host responses, resulting in the severe symptoms observed in this disorder.

Pityriasis lichenoides et varioliformis acuta (PLEVA), which is characterised by erythematous papules with little or no scarring, is most often accompanied by few symptoms other than a low grade fever in a few cases. The patient's general health is usually not affected. It occurs mainly in adolescents and young adults, but it is not uncommon in children.¹ However, there is a very rare variant form of PLEVA called febrile ulceronecrotic Mucha–Habermann disease (FUMHD), which has additional symptoms. FUMHD involves a sudden, severe flare up, characterised by innumerable coalescent necrotic ulcerations associated with high fever. Systemic manifestations include interstitial pneumonitis, abdominal pain, malabsorption, central nervous system involvement, and rheumatological manifestations.²

"Febrile ulceronecrotic Mucha–Habermann disease involves a sudden, severe flare up, characterised by innumerable coalescent necrotic ulcerations associated with high fever"

The aetiology of PLEVA has not been elucidated. Some reports have related the pathogenesis of PLEVA to an infectious agent or the deposition of immune complexes.^{1,2} Furthermore, there are some reports on the relation between PLEVA and T cell clonality.^{3,4}

We report the 18th case of FUMHD, which was analysed by means of the polymerase chain reaction (PCR).

CASE REPORT

On 4 January 2000, a 76 year old man presented to hospital after having experienced a one week history of high fever (ranging from 39°C to 40°C), vomiting, and skin eruptions. Directly

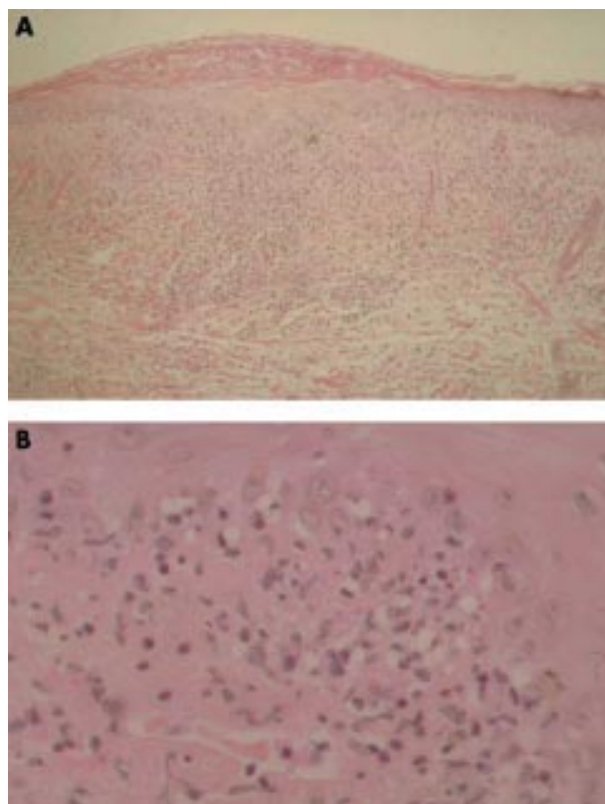


Figure 1 (A) Mild acanthosis and subcorneal small necrotic bullous lesions with pronounced subepidermal lymphocyte infiltrates (haematoxylin and eosin stained; original magnification, $\times 60$). (B) The basal cell layer showed nuclei of various sizes with a pronounced subepidermal infiltrate of lymphocytes (haematoxylin and eosin stained; original magnification, $\times 500$).

before these symptoms occurred, he suffered an unknown fever lasting four weeks. He had been treated for idiopathic thrombocytosis for over three years without symptoms.

A physical cutaneous examination revealed scattered erythematous, purpuric papular, and vesicobullous lesions on his trunk, face, and extremities. The lesions were round and varied from 1 to 2 cm in diameter. Some bulla and pustules were covered with haemorrhagic and necrotic crusts.

The biopsy of a cutaneous lesion on his trunk showed a relatively well demarcated lesion: a mild acanthosis and subcorneal small necrotic lesion with haemosiderin pigmentation (fig 1A). The basal cell layer showed nuclei of

Abbreviations: FUMHD, febrile ulceronecrotic Mucha–Habermann disease; PCR, polymerase chain reaction; PLEVA, pityriasis lichenoides et varioliformis acuta; TCR, T cell receptor

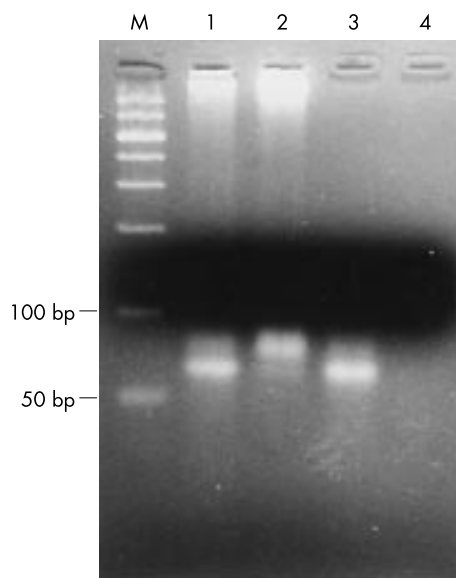


Figure 2 Polymerase chain reaction with the primer pairs D1/J2 shows a discrete amplified band (lane 3). A cutaneous T cell lymphoma shows a single amplified band (lane 1). A broad smear is amplified from granulation tissue (lane 2). No recognisable band is seen when template DNA is omitted from the reaction (lane 4). Lane M is a size marker.

various sizes with a pronounced subepidermal infiltrate of lymphocytes (fig 1B). Immunohistochemical analysis (for CD3, CD20, and CD79a) revealed that the infiltrating lymphocytes were predominantly T cells.

According to McCarthy *et al*,⁵ we assessed the monoclonality of the infiltrating cells by PCR amplification of the rearranged T cell receptor β (TCR β) gene using DNA extracted from formalin fixed, paraffin wax embedded sections as a template. In this method, the rearranged V-D-J portion of the TCR β gene is amplified using several primer pairs selected from three forward primers—V, D1, or D2—and two reverse primers—J1 or J2. Each template was amplified separately with four different primer pairs—V/J1, V/J2, D1/J2, or D2/J2. The PCR conditions and the composition of the reaction mixtures were the same as described previously.⁵ In each experiment, templates from a cutaneous lymphoma and granulation tissue were included as controls for monoclonality and polyclonality, respectively.

The PCR result with the primer pairs D1/J2 and D2/J2 showed a distinct band of the same size (fig 2, lane 3), whereas amplification with V/J1 or V/J2 showed a smear similar to the polyclonal control.

Laboratory studies revealed raised C reactive protein (186 mg/litre) and a mild increase in lactate dehydrogenase. *Treponema pallidum* haemagglutinin test, hepatitis B surface antigen tests, and blood cultures for bacteria and fungi were negative. These clinical and histological findings suggested a diagnosis of FUMHD.

Ten days of treatment with the antibiotics pentocilin and sulperazon resulted in an improvement in the skin lesions and had a slight effect on the patient's general condition by eliminating fever. However, on January 15, the patient suddenly developed hypovolaemic shock. After receiving a transfusion he recovered, but became increasingly weak, with a high fever. However, there were no relapsing skin eruptions. Chest x ray revealed ground glass opacity, and laboratory studies revealed raised white blood cell counts (9800–16 100/mm³) and liver enzymes, including lactate dehydrogenase (762 to 1044 IU/litre). He was treated with sulperazon and minocycline, but died 10 days later. No necropsy was performed.

Take home messages

- We report an adult case of febrile ulceronecrotic Mucha-Habermann disease (FUMHD) with a fatal outcome
- This disease is a rare, febrile variant type of pityriasis lichenoides et varioliformis acuta, characterised by necrotic cutaneous ulcerations associated with high fever and systemic manifestations
- The infiltrating cells of the skin lesions were monoclonal in origin and were from an aberrant clone, which may be responsible for host responses, resulting in the severe symptoms observed in this disorder
- Although FUMHD can occur in both adults and children, all cases resulting in fatality are of the adult type (as in our patient), whereas no fatal cases have been reported among children

DISCUSSION

In this patient, the cutaneous eruptions showed erythematous, purpuric papular, and vesicobullous lesions with haemorrhagic and necrotic crusts. These are all typical histological findings of PLEVA. The cutaneous eruptions were not multiple, but were scattered over the entire body. These eruptions, accompanied by a high fever and vomiting, occurred suddenly. As a result of these clinical and histological findings, we diagnosed the patient as suffering from FUMHD. We treated him with antibiotics, which were effective against the cutaneous eruptions and high fever for the initial 10 days. However, he developed hypovolaemic shock, which worsened and, eventually, led to death.

To our knowledge, only 17 cases of FUMHD have been reported previously.^{2–7} Twelve of the patients were children or young adults (under 40 years). Recently (including our case), cases^{6,7} involving increasingly older patients have been reported. Although FUMHD can occur in both adults and children, there are several differences. One of the major differences is prognosis: a fatal outcome has been seen in adults, but there have been no child fatalities.² Five of 10 adult patients died at some point between eight days and seven months during follow up treatment. In addition, there were six cases involving patients over 40 years old.^{2–6,7} These findings strongly suggest that the adult type of FUMHD has a high malignant potential, and this may be related to PLEVA and T cell clonality.^{1,2}

“This disorder may contain an aberrant clone, which has failed to proceed to V-D-J rearrangement after D-J rearrangement”

Cutaneous lesions of PLEVA are clinically similar to lymphomatoid papulosis, and some authors have suggested that they are part of the same spectrum of lymphoproliferative disorders. Recently, Dereure and colleagues⁴ reported that 13 of 20 PLEVA biopsy specimens revealed the presence of a dominant T cell clone, and they suggested that PLEVA is part of the spectrum of clonal T cell cutaneous lymphoproliferative disorders. Only one FUMHD case has been reported in which a gene rearrangement was not detected.⁸ However, this was a case of child-type FUMHD. In our report, which was of an adult-type FUMHD, monoclonality of the infiltrates was demonstrated by PCR with the primer pairs, D1/J2 and D2/J2, but not with V/J1 and V/J2. These findings appeared to be paradoxical, because monoclonal T cells should have a functional V-D-J rearrangement. However, because the V primer used cannot match some V gene segments, such as V β 2, V β 4, or V β 8,⁵ the monoclonal population may have had a V-D-J rearrangement that could not be detected by the V primer. Alternatively, this disorder may contain an aberrant clone, which has failed to proceed to V-D-J rearrangement after D-J rearrangement. Such an aberrant clone could be

responsible for host responses, resulting in severe symptoms and poor outcome in the adult type of this disorder.

There is a clear distinction between the adult and childhood types of FUMHD. However, because so few FUMHD cases have been reported, further investigation is necessary to confirm whether the two types are completely distinct disorders.

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Accepted for publication 22 April 2003

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J Clin Pathol 2003 56: 795-797
doi: 10.1136/jcp.56.10.795

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