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. 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.

“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. Furthermore, there are some reports on the relation between PLEVA and T cell clonality.

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 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 papules with little or no scarring. 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 bullous lesion with haemosiderin pigmentation (fig 1A). The basal cell layer showed nuclei of various sizes with pronounced subepidermal lymphocyte infiltrates (haematoxylin and eosin stained; original magnification, ×60). (B) The basal cell layer showed nuclei of various sizes with pronounced subepidermal infiltrate of lymphocytes (haematoxylin and eosin stained; original magnification, ×500).

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

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 papules with little or no scarring. 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 bullous lesion with haemosiderin pigmentation (fig 1A). The basal cell layer showed nuclei of various sizes with pronounced subepidermal lymphocyte infiltrates (haematoxylin and eosin stained; original magnification, ×60). (B) The basal cell layer showed nuclei of various sizes with a pronounced subepidermal infiltrate of lymphocytes (haematoxylin and eosin stained; original magnification, ×500).

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

J Clin Pathol 2003;56:795–797

795

www.jclinpath.com
The PCR conditions and the composition of the reaction mixtures were the same as described previously. The PCR result with the primer pairs D1/J2 and D2/J2 showed 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 recognizable band is seen when template DNA is omitted from the reaction (lane 4). Lane M is a size marker.

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 recognizable 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, we assessed the monoclonality of the infiltrating cells by PCR amplification of the rearranged T cell receptor β (TCRβ) 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 TCRβ 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. 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 pentoctin 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.

DISCUSSION

In this patient, the cutaneous eruptions showed erythematous, purpuric papular, and vesiculobullous 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. Eleven of the patients were children or young adults (under 40 years). Recently (including our case), cases 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. 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. 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.

“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 colleagues 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. 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 paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because monoclonal T cells should have a paradoxical, because...
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.

Authors’ affiliations
T Miyamoto, Department of Dermatology, Tsuyama Central Hospital, 1756 Kawasaki, Tsuyama 708–0841, Japan
N Takayama, S Kitada, Department of Internal Medicine, Tsuyama Central Hospital
Y Hagari, M Mihara, Department of Dermatology, Faculty of Medicine, Tottori University, 36 Nishimachi, Yonago 683–8504, Japan

Correspondence to: Dr T Miyamoto, Department of Dermatology, Tsuyama Central Hospital, Kawasaki 1756, Tsuyama 708–0841, Japan; miyamoto@tch.or.jp

Accepted for publication 22 April 2003

REFERENCES


What’s in the next issue

See which articles have just been accepted for publication and preview the table of contents for the next issue a month before it is published

www.jclinpath.com
Febrile ulceronecrotic Mucha–Habermann disease: a case report and a review of the literature

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

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

Updated information and services can be found at:
http://jcp.bmj.com/content/56/10/795

These include:

References
This article cites 7 articles, 0 of which you can access for free at:
http://jcp.bmj.com/content/56/10/795#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Dermatology (222)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/