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Case report

Mucha-Habermann disease☆

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ABSTRACT

A case of Mucha-Habermann disease (MHD), possibly associated with macrophage activation syndrome (MAS), is reported. The purpose of this paper was to describe the rare MHD (also known as pityriasis lichenoides et varioliformis acuta – PLEVA) in a 28-year-old male, who presented with generalized ulceronecrotic lesions on the skin and mucosae, gastrointestinal involvement, and heart andliver failure, associated with continuous high fever. The patient might have progressed to MAS and eventually died. The MHD is rare, potentially fatal and has severe systemic complications. The importance of early diagnosis and aggressive treatment is emphasized.

Doença de Mucha-Habermann

Palavras-chave:
Pitiríase liquenoide
Febre
Síndrome de ativação macrofágica

RESUMO

Os autores descrevem um caso de doença de Mucha-Habermann (DMH), que cursou com quadro sugestivo de síndrome de ativação macrofágica (SAM). O objetivo do trabalho foi descrever um caso de rara vasculite de Mucha-Habermann (pitiríase liquenoide e varioliforme aguda – PLEVA) em paciente de 28 anos que apresentou lesões ulceronecróticas generalizadas em pele e mucosas, acometimento gastrointestinal, cardíaco e hepático, associados a febre alta contínua, com provável evolução para SAM e posterior óbito. Trata-se de doença rara, potencialmente fatal, com graves complicações sistêmicas. Os autores ressaltam a importância de seu diagnóstico e de tratamento agressivo.

Introduction

Mucha-Habermann disease (MHD) was described by Degos et al. in 1966.[1] It is considered a severe variant of pityriasis lichenoides et varioliformis acuta (PLEVA), characterized by polymorphic, ulceronecrotic and crusted lesions on the skin and mucosae, associated with high fever and systemic manifestations. So far, only 40 cases of MHD have been reported, and no treatment is available for that potentially lethal condition.[2] We report the case of a male patient with MHD associated with probable macrophagic activation syn-

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drome (MAS), and highlight the relevance of recognizing this syndrome.

Case report

The patient is a 28-year-old male, previously healthy, admitted to the Hospital Universitário Clementino Fraga Filho, of the Universidade Federal do Rio de Janeiro, due to cutaneous findings initiated after the use of amoxicillin to treat a dental abscess. The patient had ulceronecrotic and crusted cutaneous-mucosal lesions on the limbs and trunk, associated with continuous high fever, emaciation, diarrhea, diffuse facial edema (Fig. 1), and huge hepatomegaly. The patient underwent comprehensive examination during hospitalization, the diagnosis of fever of obscure originbeing established. After improvement with symptomatic drugs, antibiotics and prednisone (1 mg/kg/day), he was followed up on an outpatient basis.

After 15 days, the patient was readmitted with congestive heart failure, whose cause was viral myocarditis. The fever peaks persisted. He showed only residual hypochromic cutaneous lesions. After cardiac compensation and antibiotic therapy (associated pneumonia), clinical improvement was observed.

Thirty days later, the patient was readmitted again with ulceronecrotic skin lesions (Fig. 2), high fever, jaundice, nausea and prostration. Viral and bacterial serologies, cultures, coagulogram and imaging tests resulted unspecific. The skin biopsy showed a lichenoid pattern, necrosis of keratinocytes and typical alterations of pityriasis lichenoides acuta.

Those data in association with high fever and systemic manifestations confirmed the diagnostic hypothesis of MHD. The patient developed liver failure, hyperferritinemia, and bicytopenia (white and megakaryocytic series). His general health status worsened, and he progressed to apathy and coma, being transferred to the intensive care unit with the hypothesis of MAS. Clinical support was instituted along with antibiotic therapy and methylprednisolone pulse therapy (500 mg) for three consecutive days. Myelogram and bone marrow biopsy evidenced no hemophagocytosis on the occasion. Although the skin lesions and fever improved, the patient developed acute pancreatitis, pulmonary sepsis, renal failure and refractory shock, progressing to multiple organ dysfunction and death after 45 days of hospitalization.

Discussion

Mucha[3] and Habermann[4] described in 1916 and in 1925, respectively, a form of pityriasis lichenoides characterized by the sudden onset of papulo-vesicular eruptions, called 'pityriasis lichenoides et varioliformis acuta' (PLEVA).

In 1966, Degos et al.[1] described the MHD in areportof two cases with severe findings titled "*Parapsoriasis ulceronecrotique hyperthermique*".[2,5] It is considered a severe variant of PLEVA, with polymorphic, ulceronecrotic and crusted lesions on the skin and mucosae, associated with high fever and systemic manifestations.[2,6,7] Its etiology remains controversial and unknown, but it is believed to be related to infectious agents or immune complex deposition. The infectious agents most likely involved are as follows: adenovirus; Epstein-Barr virus; *Toxoplasma gondii;* Parvovirus B19; *Staphylococcus aureus; Streptococcus pyogenes;* and *Pseudomonas aeruginosa*.[7] A mechanism related to clonal lymphoproliferative disorder has also been proposed.[8-11] Male patients predominate, the MHD incidence being higher among children, adolescents and young adults. The mean age observed was 27 years, ranging from 4 to 82 years.[12]

The cutaneous manifestations of PLEVA usually precede the acute and severe course of disease.[12-14] The lesions are characteristically polymorphic, ulceronecrotic, crusted and widespread, frequently secondarily infected, and tend to resolve with a hypochromic scar. The oral, genital and conjunctival mucosae might also be affected.[11] The systemic manifestations described include liver and gastrointestinal dysfunction, lymphadenopathy, pancytopenia, cardiopathy, disseminated intravascular coagulation, interstitial pneumonitis, central nervous system impairment and rheumatologic manifestations,[13] similarly to those of our patient.

Fig. 1 – Patient on his first admission, showing diffuse facial edema and ulceronecrotic lesions on the skin and mucosae.

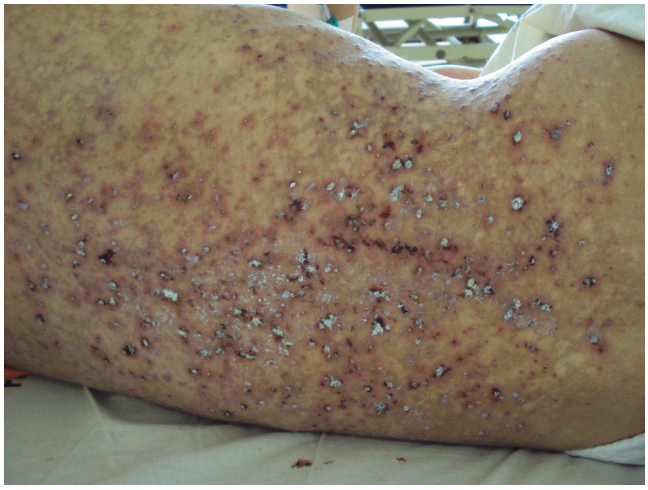

Fig. 2 – Ulceronecrotic lesions on the patient's trunk (the whitish aspect is due to the use of water paste).

The diagnosis is based on the presence of high fever, characteristic clinical findings, typical cutaneous changes, and skin biopsy compatible with PLEVA (perivascular lymphocytic inflammatory infiltrates in the superficial dermis, with epiderma lexocytosis of lymphocytic debris and parakeratotic scales, with accumulation of inflammatory cells between the different layers).[11,14] The following are commonly observed during disease course: leukocytosis; C-reactive protein (CRP) elevation; increased erythrocyte sedimentation rate (ESR); hypergammaglobulinemia; and hypoproteinemia.[13] Our patient's major laboratory findings were as follows: pancytopenia; increased CRP and ESR; hypoalbuminemia; and ferritin over 1,430 ng/dL (reference range: 5–148 ng/dL).

The prognosis is worse in adults, with mortality rate of 33% – there is no report of death in children.[11] Death usually results from pneumonia, sepsis, pulmonary thromboembolism, heart failure, hypovolemic shock, and massive thrombosis of the superior mesenteric artery.[8,11]

Although several therapeutic modalities have been reported, so far there is no definitive treatment recommended for all patients.[11] Most are treated with multiple therapeutic options, such as systemic glucocorticoids, antibiotics, acyclovir, methotrexate, phototherapy, immunoglobulin, cyclosporine[13] and dapsone, reflecting the complexity of the management of those patients.

More recent studies have reported success with the use of methotrexate associated with methylprednisolone pulse therapy.[13] Therapy effectiveness is difficult to measure, because the number of cases reported is small.[11,13] Critical care, supportive therapy and management of superinfections are usually required due to the severity of the pathology. Anti-tumor necrosis factor-α (TNF-α) agents may be first-line therapy in the future, since high TNF-α titers have been observed in those patients. However, further studies are necessary to clarify that observation.[13]

We reported a case initially diagnosed as fever of obscure origin despite extensive investigation. The association of persistent high fever, disseminated ulceronecrotic cutaneous lesions, and typical histopathological findings in the skin biopsy corroborated the diagnosis of MHD. The patient, however, progressed with alterations typical of MAS, such as hyperferritinemia, fever, bicytopenia, apathy, liver and blood dysfunctions. Although there was no evidence of hemophagocytosis in the bone marrow biopsy, that diagnostic hypothesis was not ruled out, because, in the disease's initial phase, bone marrow findings can be unspecific.[14-17] The patient had several complications, such as pulmonary sepsis, acute pancreatitis, liver and renal failures, progressing to death, despite broad spectrum antibiotic therapy, methylprednisolone pulse therapy and supportive therapy at the intensive care unit.[17,18]

We found no association between MHD and MAS reported in the literature. It is worth noting the similarity of the triggers of both pathologies, which may be correlated in the future.

Conclusion

Although rare, the potentially fatal MHD should be considered when assessing patients with high fever, ulceronecrotic skin lesions and systemic manifestations. Skin biopsy is valuable in such cases. The MHD's rarity and difficult management reinforce the importance of exchanging experience about those patients.

Conflicts of interest

The authors declare no conflicts of interest.

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