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Eosinophilia in Pemphigus: Single Center Study in Morocco

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Eosinophils, play major roles in the pathogenesis of various dermatoses (atopic dermatitis, bullous pemphigoid, drug reaction with eosinophilia and systemic symptoms (DRESS)…).
Hypereosinophilia in pemphigus has not been well documented in the literature, hence we initiated this study with the aim of objectivizing this association and studying its characteristics.
Materials & Methods: A retrospective comparative descriptive study was carried out in the dermatology department of Ibn Sina University Hospital, Rabat, between 1990 and 2023, on 391 patients with pemphigus. Data from medical records were analyzed, focusing on variables such as age at diagnosis, gender, duration of disease, medical history, presence of autoimmune conditions, clinical types, eosinophil count in the blood and presence of pruritus. Data entry and analysis were performed using Excel and Statistical Package for the Social Sciences.
Results: In this study, there were no significant age or gender differences. Hypereosinophilia was observed in 13,3% of patients with pemphigus, and for the clinical phenotypes, pemphigus vulgaris was more frequent, followed by pemphigus seborrheic. The majority of these patients had

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associated pruritus. In terms of disease progression, the hypereosinophilia was resolved in the majority of our patients after therapeutic management of pemphigus.
Conclusion: To further understand the implications of eosinophils in the pathogenesis and clinical manifestations of various pemphigus subtypes, additional research is warranted. and for the hypereosinophilia resolved with treatment of pemphigus

Keywords: Pemphigus; eosinophilia; Morocco.

1. INTRODUCTION

Eosinophilic dermatoses are characterized by eosinophilic infiltration of the skin and/or mucous membranes, which may or may not be associated with blood hypereosinophilia (>500 eosinophils/mm^3.

These dermatoses include a group of diseases with different etiologies. Most of these dermatoses can be traced back to allergies, drug allergies, urticaria, allergic contact dermatitis, atopic dermatitis and eczema. Parasitic infestations, arthropod bites and autoimmune vesicular skin diseases such as bullous pemphigoid are also common.

To the best of our knowledge, hypereosinophilia in pemphigus has not been well documented in the literature.

Despite its clinical relevance, the association between hypereosinophilia and pemphigus, has not been extensively explored and documented in existing literature.

Therefore, this study aims to investigate the prevalence, clinical features, and implications of hypereosinophilia in pemphigus patients, with the goal of enhancing our understanding of this potentially significant correlation and providing valuable insights for improved diagnosis and management of this patient population.

2. MATERIALS AND METHODS

We performed a retroprospective descriptive study of 191 patients with pemphigus in the Department of Dermatology at Ibn Sina University Hospital in Rabat between 1990 and 2023. Excel and Statistical Package for the Social Sciences (SPSS Inc, version 15.0 for Windows) were used for data entry and analysis. Our study included all patients with pemphigus with no medical history of atopy or known allergy who underwent a complete blood count (CBC) for eosinophils on admission before starting any treatment. Eosinophilia is defined as greater than 500 eosinophils/mm^3.

In our study, All patients with histologically and immunologically confirmed pemphigus who had an eosinophil assay were included .The eosinophil quantification was performed using the blood cell count (CBC), which is a quantitative indicator of eosinophil concentration in peripheral blood, expressed as eosinophils per cubic millimeter (eos/mm^3).

3. RESULTS

391 cases of pemphigus were collected over 33 years, including 169 P.vulgaris, 113 P.seborrheic , 55 P.foliaceous, 37 P.vegetans, 15 herpetiformis and 2 P.paraneoplasticis. Only 52 patients (13,3%) had a hypereosinophilia >500 eosinophils/mm^3.

The average age of these patients was 52.4 years, with a female predominance (31 women versus 21 men).

Regarding the association with comorbidity, we found that 12 patients had diabetes, 9 had hypertension, and 3 had dysthyroidism.

For the clinical phenotypes, we noticed that pemphigus vulgaris was more frequent (22 cases), followed by pemphigus seborrheic (12 cases), pemphigus foliaceous and vegetans (7 cases each), and finally pemphigus herpetiformis (4 cases).

This suggests that the association between hypereosinophilia and pemphigus may be more pronounced in the vulgar form of the disease, but other forms of pemphigus have also been observed, such as the seborrheic, vegetative and herpetiform forms. Further studies are needed to determine whether specific pathophysiological mechanisms linked to the vulgar form of pemphigus could be responsible for this more frequent association with hypereosinophilia.

Pruritus was found in the majority of patients: 76.9% (N=40 patients).

Eosinophil counts in these patients vary between 530 and 3710, eosinophil counts in these patients ranged from 530 to 3100, of whom 33 patients had mild hypereosinophilia and 19 moderate, but none had severe hypereosinophilia.

The therapeutic protocol used was oral corticosteroids (1 to 2mg/kg/d) associated or not with immunosuppressants (azathioprine, Rituximab, cellcept,Methotrexate,dapsone), and it was noted that the hypereosinophilia normalized once treatment for pemphigus has begun.

4. DISCUSSION

Eosinophils are myeloid cells that were first named by Paul Ehrlich in 1879 due to their bright red staining eosin-fast granules [1,2], they may contribute to pathogen defense, regulate inflammatory responses and induce fibrosis/remodeling [3,4].

A wide range of skin disorders are associated with eosinophil infiltration and the possibility of peripheral blood eosinophilia.

The normal range of blood eosinophils is 0 to 500 cells/mm3 and the typical percentage is less than 5% of WBC. Eosinophilia is defined as greater than 500 eosinophils/mm^3. The degree of eosinophilia can be categorized as mild (500–1500 cells/mm^3), moderate (1500 to 5000 cells/mm^3), or severe (>5000 cells/mm^3) [2].

The majority of eosinophilic dermatoses lie in the allergy- related group, including allergic drug eruption, urticaria, allergic contact dermatitis, atopic dermatitis, and eczema. Parasitic infestations, and arthropod bites [5].

Regarding autoimmune blistering skin diseases, it was well demonstrated that bullous pemphigoid, is a eosinophilic dermatosis. Blood eosinophilia and dermal infiltrates consisting pre-dominantly of eosinophils are observed in the majority of BP patients [6]. In addition, the strict relationship between eosinophils and anti-BP180 IgE autoantibodies, whose pathogenic role in BP has been confirmed in recent years, has been supported [7].

On the other hand, few studies have discussed the association of hypereosinophilia with pemphigus, based mainly on skin eosinophilic infiltration.

After carrying our study, no significant difference was observed between eosinophilia levels and the various comorbidities in these patients, suggesting that the comorbidities studied (diabetes, arterial hypertension and dysthyroidism) do not appear to have a direct impact on eosinophil levels in the context of pemphigus. These results indicate that hypereosinophilia in patients with pemphigus appears to be more closely linked to the pathophysiology of the disease itself, rather than to the comorbidities studied.

Pemphigus vegetans has been associated with eosinophil infiltration in the skin, specifically eosinophil exocytosis and eosinophilic abscesses, as well as elevated blood eosinophil and ECP levels [8]. As well as in patients with pemphigus herpetiformis, cultured keratinocytes showed increased autoantibody-mediated IL-8 secretion as compared with healthy and pemphigus vulgaris controls, with consequent recruitment and stimulation of eosinophils and neutrophils that lead to focal intercellular edema and eosinophilic/ neutrophilic spongiosis with little or no acantholysis [9].

However, the role of eosinophils in terms of epidermal disintegration or hyperproliferation remains unclear.

On the other hand, there are no studies in the literature looking for blood hypereosinophilia in pemphigus patients, and characterize the correlation between hypereosinophilia and the various features of pemphigus, in our study, hypereosinophilia was observed in 13,3% of patients with pemphigus, and for the clinical phenotypes, pemphigus vulgaris was more frequent, followed by pemphigus seborrheic. The majority of these patients had associated pruritus, and for the hypereosinophilia resolved with treatment of pemphigus.

5. CONCLUSION

in bullous dermatoses, hypereosinophilia has been reported in pemphigoid patients, but not in pemphigus. That’s why further studies are needed to clarify the role and association of eosinophils in the different types of pemphigus.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of the Ibn Sina University Hospital in Rabat.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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