Case study

Comment [DNS1]: Justify the text

Eosinophilia in pemphigus: single center study in Morocco

Abstract:
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.
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
Key words: Pemphigus, eosinophilia, Morocco

UNDER PEER REVIEW

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(>500eosinophils/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, hence we initiated this study with the aim of objectivizing this association and studying its characteristics.

Material and methods:

We performed a retroprospectivedescriptive study of 191 patient 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

Comment [DNS2]: How many prescriptions werestudied total

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

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).

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

Comment [DNS3]: Add the missingtext

Discussion :

Eosinophils are myeloid cells that were first named by Paul Ehrlich in 1879 due to their bright red staining eosin-fast granules (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.

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 hypereosinophiliain 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.

Comment [DNS4]: Use statistical Tools

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.

UNDER PEER REVIEW

Reference:

1-De Graauw, E., Beltraminelli, H., Simon, H.-U., & Simon, D. (2015). *Eosinophilia in Dermatologic Disorders. Immunology and Allergy Clinics of North America, 35(3), 545–560.*doi:10.1016/j.iac.2015.05.005
2- Kuang FL. Approach to Patients with Eosinophilia. Med Clin North Am. 2020 Jan;104(1):1-14. doi: 10.1016/j.mcna.2019.08.005. PMID: 31757229; PMCID: PMC7089574.
3- Simon D, Simon HU, Yousefi S. Extracellular DNA traps in allergic, infectious, and autoimmune diseases. Allergy 2013;68:409–16.
4- Yousefi S, Simon D, Simon HU. Eosinophil extracellular DNA traps: molecular mechanisms and potential roles in disease. CurrOpin Immunol 2012;24:736–9.
5- Long, H., Zhang, G., Wang, L., & Lu, Q. (2015). *Eosinophilic Skin Diseases: A Comprehensive Review. Clinical Reviews in Allergy & Immunology, 50(2), 189–213.*doi:10.1007/s12016-015-8485-8

Comment [DNS5]: Maintainuniformity in references

6- Rüdrich, U., Gehring, M., Papakonstantinou, E., Rabenhorst, A., Engmann, J., Kapp, A., … Raap, U. (2018). *Eosinophils are a Major Source of Interleukin-31 in Bullous Pemphigoid. Acta DermatoVenereologica, 0.*doi:10.2340/00015555-2951
7- Cozzani E, Gasparini G, Di Zenzo G, Parodi A. Immunoglobulin E and bullous pemphigoid. Eur J Dermatol. 2018;28:440–8.
8-Zaraa I, Sellami A, Bouguerra C, Sellami MK, Chelly I, Zitouna M, Makni S, Hmida AB, Mokni M, Osman AB (2011) Pemphigus vegetans: a clinical, histological, immunopathological and prognostic study. J Eur Acad Dermatol Venereol 25:1160–1167. https://doi.org/10.1111/j.1468-3083.2010.03939.x
9. O'Toole EA, Mak LL, Guitart J, Woodley DT, Hashimoto T, Amagai M, et al. Induction of keratinocyte IL-8 expression and secretion by IgG autoantibodies as a novel mechanism of epi- dermal neutrophil recruitment in a pemphigus variant. Clin ExpImmunol. 2000;119:217–24.

UNDER REVIEW