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Role of peripheral eosinophilia in adverse cutaneous drug reactions

F. DRAGO, L. COGORNO, A.F. AGNOLETTI, A. PARODI

DISSAL Section of Dermatology, IRCCS University-Hospital San Martino-IST, Genoa, Italy

Abstract. – OBJECTIVE: The objective of this retrospective study was to verify whether peripheral eosinophilia (PE) may be a marker of severity for adverse cutaneous drug reactions (ACDR).

PATIENTS AND METHODS: We investigated sixty-three patients diagnosed as adverse cutaneous drug reactions for PE. All the patients underwent blood tests at baseline visit. Only patients that showed a very likely connection between ACDR and the suspected causative drug were enrolled in the study.

RESULTS: We found that 11 out of 63 patients (17%) presented PE for values ≥ 0.6 x 10^9 cells/l or for a percentage of total leukocytes ≥ 6%. These patients with PE showed a longer recovery time, more severe cutaneous reactions and needed a systemic therapy.

CONCLUSIONS: These outcomes prompt us to believe that peripheral eosinophilia may be an index of severity for adverse cutaneous drug reactions.

Therefore, we suggest physicians to always detect the presence of peripheral eosinophilia in order to not underestimate the reaction and to promptly start an appropriate therapy.

Key Words:
Peripheral eosinophilia, Adverse cutaneous drug reactions, Prognosis, Severity index, Eosinophils.

Introduction

Cutaneous drug reactions are the most common adverse reactions attributed to drugs ranging from mild to severe forms that may also lead to death. Therefore, the identification of markers that characterize the most severe reactions can be crucial to choose whether and when to start a treatment.

It is widely accepted that peripheral eosinophilia (PE), for values > 2.0 × 10^9 cells/L, has a diagnostic relevance in drug reactions with eosinophilia and systemic symptoms (DRESS) where it can be detected in the 30% of cases[1]. On the contrary, PE may be also found in adverse cutaneous drug reactions (ACDR) with no systemic involvement (18% when the cut off is set at 0,69 × 10^9 cells/l and approximately 22% when the cut off was set at more than 7% of total leukocytes)[2] but, in this this context, its presence or absence is usually considered of little value in excluding or confirming the diagnosis. In order to verify whether PE may be a marker of severity for ACDR we performed a retrospective study of sixty-three patients with ACDR.

Patients and Methods

The patients were enrolled from the Department of Dermatology of the University of Genoa from 2003 to 2012. All the patients underwent blood tests at baseline visit to search for peripheral eosinophilia. The diagnosis was based on history, on clinical manifestations, and if possible and when life-saving drugs were suspected to have induced the reaction, *in vivo* tests were performed[3]. Specifically, every patient who was diagnosed an ACDR had no alternative explanation for the clinical manifestation, had plausible time relationship between the introduction of the drug and the onset of the reaction and promptly improved after withdrawal of the culprit drug. Eighteen patients also underwent histological examination.

Results

We found that 11 out of 63 patients (17%) presented PE for values ≥ 0.6 × 10^9 cells/l or for a percentage of total leukocytes ≥ 6%. Histological examination was performed on lesional skin of all patients with PE revealing the presence of eosinophils in the 36% of cases.

Corresponding Author: Ludovica Cogorno, MD; e-mail: lucogorno@yahoo.it

Table I. Clinical types of ACDR in our series of patients with PE.

Types of ACDR	Number of cases
DRESS	1
Polymorphous erythema	2
Diffuse orticaria	3
Morbilliform exanthema	2
Vasculitis	2
Diffuse lichenoid reaction	1

All patients discontinued the culprit drug and the 44% of these followed a therapy consisting of oral corticosteroids and oral antihistamines.

Among the 11 patients with PE, 10 had a favorable outcome. One patient with DRESS induced by strontium ranelate died for of a multiorgan failure. Among the 52 patients without PE, 44 had a favorable outcome and 8 dropped out.

Discussion

Tissue eosinophilia resulted present in less than a half of the patients with PE, confirming that usually peripheral eosinophilia is not predictive for the presence of eosinophils in the tissue[2,4].

Nevertheless, several outcomes of our study may indicate eosinophilia as a severity index. First of all, we realized that patients with PE had a longer recovery time (mean time 84 days). On the contrary, patients without PE showed complete remission after an average of 24 days (this value was greatly affected by one case of metformin-induced lichenoid reaction that took nearly 4 months to heal).

We also realized that PE was mostly associated to diffuse severe cutaneous reactions (Table I) even though not necessarily associated with systemic involvement (only one case of DRESS).

Lastly, all patients with PE needed a systemic therapy compared to the 41% of patients without PE.

Conclusions

We suggest physicians to always detect the presence of PE, since it is often associated to more severe ACDR, in order to not underestimate the reaction and to promptly start an appropriate therapy.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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