Nasal eosinophils associated with rheumatoid arthritis: description of some clinical cases and review of the literature

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Case Report

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Abstract

In this review we describe the relation between nasal eosinophilia and rheumatoid arthritis (RA). Moreover we was performed a literature revision that valued the relation between eosinophilia in respiratory system with arthritis. We have examined, through nasal cytology, 7 patients (5 men and 2 women) aged between 7 and 60 years old, with a middle age of 38,5 years; this patients are affected by RA, members of UO of Diagnostic ORL and nasal cytology of the AIAS (Italian Association of Disadvantages assistance) of Afragola.

Between them we put in evidence only a case of youth RA. All patients was not allergic and affected by recurrent rhinitis in maintenance therapy and not related with pollen calendar. The withdrawal documented the presence of rare eosinophils in nasal mucosa. This evidence could induce us to use this practice not only as follow up of patients but also as means of early diagnosis.

Introduction

The rheumatoid arthritis (RA) is an inflammatory sistemi disease that shot at first the sinovial joints with a progressive, erosive and chronic sinovitis which bring at distruction as the bone as the cartilage. Could be envolved also other organs, with extra-articular manifestations that shot cardiovascular system, respiratory system, skin and eye for most cases. The respiratory system manifestation could be envolved in a complessive mortality between 10% and 20%. Recent pathogenetic discoveries provide some relations between pneumopaties and development of RA [1,2]. Some Authors [3,4] have documented a serum ipereosinophilia in the 40% of RA affected during the active phase of desease. Other Authors [5-8] substain the hypothesis that activation of eosinophils could be related at the presence of rheumatoid factor (RF), as it was found a higher incidence of infiltration by eosinophils in patient with higher serum eosinophilia and RF. Although the RA it's a rare clinical entity, the eosinophilic riniti in relationship with RA it's never been documented.

Case Presentation

We have been observed 7 patients (five men and 2 women) aged between 7 and 60 years old, with a middle age of 38,5 years; this patients are affected by RA, members of UO of Diagnostic ORL and nasal cytology of the AIAS (Italian Association of Disadvantages assistance) of Afragola. Between them we put in evidence only a case of youth RA. The family history of negative for allergic diseases and are reported riniti nad recurrent sneezing, indipendent form pollen calendar. We find only a smoker. All patients are treated with maintenance therapy with NSAIDs (children), just prednisone 5mg/die (two cases), Methotrexate and prednisone association (two cases) and just one case in treatment with Tocilizumab. After completing privacy and informed forms, all patients underwent a physical examination that

included rhinofiberscope with a rhino-fiberscope (Xion Amplaid, Milan, Italy) 4 mm in diameter using disposable sheaths for protection, which objectively documented a pink nasal mucosa with hypertrophic and pale nasal turbinate, nonché presenza di muco abbondante muco. Nasal septum basically in axis. Normally the remaining districts observed. During the diagnostic procedure, a cytological nasal fetch was performed.

The cytological was carried out crawling 2-3 times a respond (Nasal-scraping®) on the mucosal surface of the central zone the inferior turbinate. The nasal mucosal cells were placed on an electrostatically charged cytology slide (Super Frost Plus Menzel - Gläser, Thermo Scientific, Milan, Italy). The cells were then stained according to the panoptic Pappenheim method (3 min in pure May-Grunwald dye [Carlo Erba, Milan, Italy], 6 min in 50% May- Grunwald, 1 min in bidistilled water [Carlo Erba, Milan, Italy] and 30 min in Giemsa solution [Carlo Erba, Milan, Italy] diluted 1:10 v / v). Images with 24 x 50 mm and observed, on fifty observational fields, under an optical microscope (Nikon Eclipse 50i at 100 x enlargement in oil-immersion, the images were acquired using software D - Elements of the Nikon.

The microscopic observation of nasal mucosa (viewed in summary table), in all examined subjects, documented the presence of widespread epithelial pain with a low prevalence of mucipar cells, rare eosinophils, someones with eosine granules. We not put in evidence bacterial or fungal infection. (fig.1)

Nr	Age	Sex	Objective exam	Smoke	Treatment	Citological Observation
1	7	W	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	NSAIDs	ciliated Cells SIS negative. Prevalence of mucipar cells. 1 eosinophils, rare eosina granules
2	35	M	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	PREDNISONE	ciliated Cells SIS negative. Prevalence of mucipar cells. 3 eosinophils.
3	40	M	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	PREDNISONE	ciliated Cells SIS negative. Prevalence of mucipar cells. 1 eosinophil.
4	45	M	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	METHOTREXATE PREDNISONE	ciliated Cells SIS negative. Prevalence of mucipar cells. 3 eosinophils
5	41	M	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	METHOTREXATE PREDNISONE	ciliated Cells SIS negative. Prevalence of mucipar cells. 3 eosinophils
6	42	M	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	No	METHOTREXATE PREDNISONE	ciliated Cells SIS negative. Prevalence of mucipar cells. 4 eosinophils and rare granules of eosina
7	60	W	Mucosal edema hypertrophy of the inferior turbinates. Abundant mucus	Yes	TOCILIZUMAB	ciliated Cells SIS negative. Prevalence of mucipar cells. 5 eosinophils and rare granules of eosina.

Discussion

All patients were not allergic and show as at objective exam as at citologic observation an inflammatory distress with widespread epithelial pain, with prevalence of mucipar cells and eosinophils, classifiable as not allergic eosinophilic rhinitis (9). The last ones are the expression of eterogeneous pathologies, whose cause it is not well defined. However, Armone Caruso et coll. Associates them with colon adenocarcinoma (10) and Younis, associates them with squamous carcinoma of mouth (11).

Clinical cases of eosinophilia of respiratory system and RA are rare in literature, but the possibility of this associations and rheumatological disease it was discuss by most authors (12-15). But cases of eosinophilia and RA are never been describes. At the first time we report this correlation.

The relation between nose and pulmons is given obviously from their streight embryological derivation and from the same immunological behavior of both anatomical structures. The first description of Eosinophilia of respiratory system associated at RA was maden by Payne et al [16], which tried to demonstrate the same origin not related with immunity. *Yousem et al.* [3]in the 1985 analized 40 casual

patients with RA and pulmonary pathologies and one of them present eosinophilia of respiratory system. *Van Esch et al.* [17] in the 2001 described as iperactivation of T-cells, through the reticulation of B-cells mediated by CD40, it is at the same time responsible of the sistemyc chemotaxis of eosinophils and production of RF. Most recently, it is demonstrated that the role of some interleukines (IL6,IL1,IL10; IL5,IL4 and IL12 in mouse model CIA)(24) and Chemokines (eotaxin 1 and 2) induce the recruitment of eosinophils by macrophages and limphocytes T and inhibit apoptosis of eosinophilic infiltrates in tissues.

As we put in evidence in studies about animals (18), the mechanisms that induce the eosinophilic recruitment are mainly lead from a TH2-limphocitary way.

However the RA is a desease mainly lead by TH1/TH17, the switch purpose by a regulation of the flogistic way (use of drugs like Tocilizumab, prednisone, methotrexate), suggest an improvement of the desease towards an allergic inflammatory stimulation. *Sandhya et al.* [19] suggest that the switch from Th1/Th17 way to Th2 could be a mecchanism that causes remission by RA, with a massive release of eosinophils in blood with consequent infiltration in target organs. [20-22].

In Our study we demonstrate that simptoms of RA are inactivated in the moment of the nasal withdrawal [23]. Actually there aren't studies that make a correlation between nasal cytology and RA; However even if the number of the patients it is slender, we can hipothize that the presence of eosinophils is a prognostic indicator of the evolution of the desease or could have a predictive role, in consequence of the sthright relations between RA and respiratory system.

Conclusion

The study of nasal mucosa it's undoubtedly a simple and not invasive method that consent to study the inflammatory condition of nasal mucosa. In particular way, the present study could be a starter pointfor implementation of protocols, whose end is not monitoring the disease but making early diagnosis.

Declarations

Funding: No funding was received for this study.

Conflict of Interest declaration.

Conflict of Interest: Del Prete Salvatore; Marasco Daniela; Rosalaura Sabetta; Caruso Armone Arturo; Grumetto Lucia and Del Prete Antonio, declare that they have no conflict of interest.

Compliance with Ethical Standards:

This study did not receive funding.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The patient consented to participate and have their clinical data published as a case report.

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Figures

Figure 1

Cytological nasal scraping,(MMG staining 100x magnification in oil immersion). A red arrow eosinophil and green arrow eosin granules are observed