Interstitial Lung Disease, Eosinophilia and Rheumatoid Arthritis

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Interstitial lung disease (ILD) can cause mortality and morbidity in rheumatoid arthritis (RA). However, there is no definite risk factor, guide or marker to obtain before examining lung with high resolution computerized tomography (HRCT). We studied eosinophil in RA patients if there is a relation with inflammation and ILD. We could not find any relation between eosinophil and inflammation. However, there was eosinophilia in all patients with ILD findings of HRCT. Increased numbers of eosinophil can be a risk factor for ILD in patients with RA. Nevertheless, it is still needed further studies to make such a conclusion.

Keywords: Interstitial lung disease, Rheumatoid Arthritis, Eosinophil

INTRODUCTION

Interstitial lung disease is one of the reason of the morbidity and mortality in RA; however, the prevalence and natural history are undefined (Kelly et al., 2014). On the other hand, early diagnosis of the ILD is very important to treat. HRCT is the most important tool for the early diagnosis and the management of ILD. However, both exposed to radiation and undetermined time interval for HRCT are the definite controversies for diagnosis of ILD in RA. Eosinophils can cause fibrosis such as in chronic hypereosinophilic syndrome (Flavia et al., 2008; Jaimes-Hernández et al., 2012; Sandhya et al., 2012; Cancelliere et al., 2011). In this study, it is aimed if eosinophilia can be related with ILD in RA to estimate the risk of ILD early.

MATERIAL AND METHODS

Patients with RA according to the American College of Rheumatology ’87 criteria were included to the study retrospectively (between 2011-2013) from the medical records of Medical Faculty of University of Maltepe-Istanbul. Patients were specifically questioned from their medical records reviewed for demographic and clinical data including the following: age, gender, disease duration, previous and current medical history emphasizing those that might be related to eosinophilia, such as diarrhea, inflammatory bowel disease, anal pruritus, allergic rhinitis, bronchial asthma, history of atopy, neoplasias, chronic renal failure, peritoneal dialysis, and splenectomy. Those patients with other previous or concomitant connective tissue diseases and current medical history emphasizing any disease that might be related to eosinophilia, were all excluded.

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The presence of respiratory manifestations as well as findings of the High Resolution Computerized Tomography (HRCT), previous and current treatment for RA were also evaluated. Patients were asked about eosinophilia-inducing drug intake (penicillin, cephalosporin, gold, allopurinol, nitrofurantoin, sulfas, dantrolene, bleomycin, methotrexate, phenothiazine, tolbutamide, phenytoin, and aspirin).

Laboratory records of the patients including rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), White Blood Cell Count (WBC), Monocyte Count (MC), Eosinophile Count (EC) were included the study from only the records of the Laboratory of University of Maltepe-Istanbul. All WBC, EC, MC were done by an automatic cell count.

Eosinophile counts of 5% or greater and monocyte counts 10% or greater were accepted as high levels of these cell counts.

The statistical analysis was performed by SPSS, descriptive statistics was analyzed and differences between categorical variables of patients with and without eosinophilia, were compared by continuous variables by Mann-Whitney U test.

RESULTS

One hundred and sixty six patients were included, 103 female (62.2%) and 63 male (37.8%); mean age was 56.8 ±16.2 years and mean disease duration 9.8±5.6 years. The demographic and medical characteristics of patients were detailed in Table 1. Twelve (7.2 %) and twenty four (24.4%) patients showed mild eosinophilia and monocytosis respectively.

Forty two patients (25%) with RA were examined with HRCT. Eight of them were obtained ILD. Seven of those patients with ILD have also high eosinophile counts interestingly.

All of the patients were given methotraxate in the past or in the current. Number of steroid using patients was 111 (%67). All eight patients with ILD were also using steroid.

There was no correlation between EC and ESR, CRP, MC. However, seven of eight patients with radiological ILD findings had high EC interestingly.

DISCUSSION

Eosinophils can cause fibrosis in some clinical problems (Flavia et al., 2008; Jaffe, 1996; Bruyn et al., 1995; Cuesta et al., 1993; Dawes et al., 1986; Lutalo, 1983). So, we assumed that they may correlate with the inflammation in RA to cause interstitial lung disease at the end. However, it was found that eosinophilia is not correlated with inflammatory response in RA in this study. So, it may be considered that result of this study was negative. However, there were eosinophilia in most of the patients with radiological findings of the interstitial lung disease of RA.

Recent research on the role of cytokines in RA development indicates that they may have pro- or anti-inflammatory effect. Type Th1 (INFγ, TNFα, IL-2) and type Th2 (IL-10, IL-6, IL-4) cytokine levels in sera of RA patients. The levels of all cytokines studied were significantly increased in RA patients; the highest increase relative to healthy controls (7-fold) was observed for IL-6 (Flavia et al., 2008; Edelman et al.,

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### Table 1. Demographic and medical records of RA Patients (n:166)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male n</th>
<th>Female n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>56.8±16.2</td>
<td></td>
</tr>
<tr>
<td>Disease duration (year)</td>
<td>9.8±5.6</td>
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<tr>
<td>Eosinophil Counts, n (%)</td>
<td>2.7±1.1</td>
<td></td>
</tr>
<tr>
<td>Eosinophilia &gt; 5%, n</td>
<td>12 (7.2%)</td>
<td></td>
</tr>
<tr>
<td>Monocyte Counts, n (%)</td>
<td>7.7±3.6</td>
<td></td>
</tr>
<tr>
<td>Monocyte &gt; 10%, n</td>
<td>24 (14.4%)</td>
<td></td>
</tr>
<tr>
<td>White Cell Count</td>
<td>7.6±3.5</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Factor (IU/L)</td>
<td>31.4±24.4</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/ hour)</td>
<td>29.9±24.04</td>
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<tr>
<td>CRP (mg/dL)</td>
<td>2.3±2.1</td>
<td></td>
</tr>
<tr>
<td>Number of HRCT patients</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Number of HRCT patients with radiologic ILD findings</td>
<td>8</td>
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</tbody>
</table>
1983; Winchester et al., 1971; Panush et al., 1971; Sylvester and Pinals, 1970).

IL-5, produced by TH2, induces eosinophilia. Eosinophilia can be secondary to different disorders; even though the most common causes arise from parasite and allergic reactions. However, it is also observed in connective tissue diseases such as RA, polyarteritis nodosa, Wegener granulomatosis, eosinophilic fascitis, gastroenteric diseases, neoplasias, certain cutaneous disorders, and other diseases such as sarcoidosis, Addison disease, brucellosis, liver cirrhosis, and radiation exposure. So, it may be speculated that during the development of RA, balance between the TH1 and TH2 cytokines may shift to the TH2 and IL5 production (Flavia et al., 2008).

On the other hand, there are some reports that related eosinophilia to gold salts and methotrexate treatment (Flavia et al., 2008). However, all of the patients in this study were given methotrexate and glucocorticoids. Even though glucocorticoids are the most effective agents to reduce eosinophilia by transcription suppression of different inflammatory mediators genes (IL-3, IL-4, IL-5, etc). So, it may be expected that these to drugs balance each other (Flavia et al., 2008; Rosenstein et al., 2014).

Probably, eosinophils do not make the RA worse. So, there is no relation between inflammation and numbers of eosinophils. If eosinophilia occurs then interstitial lung disease may occur or the reasons to outcome interstitial lung cause eosinophilia. However, we have some limitations to make such an assertive comment. First of all numbers of our study cases are very small. Second our population is not homogeneous. Third eosinophil count has been done automatically. So, further studies are still needed to explain the relation between eosinophil and RA. However, RA patients with eosinophilia may be examined more detailed for interstitial lung disease according to this study.

REFERENCES


