Eosinophilia in rheumatoid arthritis patients and its relation to disease activity: A single center experience from Kashmir, India

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1. Introduction

Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults [1]. It has prevalence of slightly less than 1% in adults [2]. It is a chronic systemic inflammatory disease of unknown etiology which primarily targets synovial joints and protean clinical features. RA not only affects health related quality of life, but also increases mortality [2–4]. Synovial tissues proliferate in an uncontrolled fashion, resulting in excess fluid production, destruction of cartilage, erosion of marginal bone, and stretching and damage of the tendons and ligaments [2].

It is clear that cytokines play a fundamental role in various inflammatory processes, articular destruction, and RA-associated comorbidities [5]. The balance between the activities proinflammatory and anti-inflammatory cytokines RA patients determines disease severity [6]. The cytokine imbalance favors the induction of autoimmunity, chronic inflammation, and thereby joint damage [7]. Many cytokines were detected as the important biomarkers for RA patients [8–10].

Traditionally, the monitoring of RA in treat to target strategies has been based on indices such as the Disease Activity Score with 28-Joint Counts (DAS28) involving formal joint counts performed by trained professionals [11]. Formal joint counts, though valued for their information, have been criticized for their use in daily practice because of their time-consuming nature [12].

Almost all RA patients exhibit some systemic features such as fatigue, low-grade fevers, anemia and elevations of acute phase reactants as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). This systemic inflammation is believed to be responsible for vascular endothelial damage and a marked increased risk for coronary artery disease and congestive heart failure in RA patients [2]. Certain blood picture parameters as mean platelet volume (MPV) and red blood cell distribution width (RDW) were sig-
Eosinophilia, elevated peripheral blood eosinophilic count (>6% or absolute count >400/mm³) is not uncommon in arthritis patients especially when they have associated drug reactions, allergies or helminthic infection [14,15]. Peripheral and tissue eosinophilia can be a prominent feature of several unique rheumatologic and vascular diseases [16]. Even though eosinophilia is rare in recent-onset arthritis suggestive of RA, it is usually directly related to the rheumatic disease and patients with mild eosinophilia at diagnosis could respond worse to treatment [17]. The risk of developing eosinophilia appears to be significantly associated with the presence of rheumatoid factor (RF) auto-antibodies [18]. Eosinophilia in RA has been reported to range from 11% to 63% with an absolute eosinophilic count of 0.69 to 7.08 × 10⁶ cells/l and has been considered as a marker of disease activity [19,20].

The aim of this study was to detect the frequency of eosinophilia in a cohort of RA patients from Kashmir, India and to study its relation to disease activity.

2. Patients and methods

This study was conducted on 134 RA patients attending the Rheumatology outpatient clinic, Sher-i-Kashmir Institute of Medical Sciences (SKIMS) Medical Institute, Srinagar, Jammu and Kashmir, India. The patients fulfilled the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria for RA [21]. The disease activity score in 28 joints (DAS-28) was measured for the RA patients [22]. The study was approved by the local college ethics committee and the study conforms to the provisions of the Declaration of Helsinki in 1995. All patients gave their informed consent prior to their inclusion in the study.

Patients with known cause associated with eosinophilia such as drug reaction, allergies or helminthic infection were excluded. The patients were clinical examined and routine laboratory investigations assessed. The eosinophilic count of the white blood cell (WBC) differential count was recorded. Eosinophilia was considered when the absolute count was >400 mm³ or >6% of the differential WBC count.

2.1. Statistical analysis

The statistics was done using software SPSS 21 describing the frequency and mean ± SD. Correlation was done using Pearson’s correlation test. Results were statistically significant at p < 0.05.

3. Results

The study included 134 RA patients with a mean age of 36.6 ± 11.5 years and disease duration of 6.8 ± 5.3 years (range 0.2 and 27 years). They were 103 (76.9%) females and 31 (23.1%) males with a female-to-male ratio of 3.2:1. All the patients were rheumatoid factor (RF) positive. The age of the patients ranged from 17 to 73 years with only one patient of juvenile onset. The mean DAS28 was 4.53 ± 0.96 (range: 2.9–7.1). 42 (31.3%) had high disease activity (DAS28 ≥ 5.1) while the rest of the patients (n = 92; 68.7%) had mild to moderate disease activity (DAS28 < 5.1).

The mean eosinophilic count was 4.53 ± 3.12% with a range of 1.1% to 16.4% and eosinophilia was found in 29 (21.6%) patients. The mean eosinophilic count in those 29 patients was 9.4 ± 2.6% (range 6.3–16.4%). The rest of the 105 patients had normal eosinophilic count. The mean eosinophil count was lower in RA patients with high disease activity (4.14 ± 2.62%). Those RA patients with eosinophilia had a mean DAS28 of 4.4 ± 0.74. A non-significant negative correlation was present between the eosinophilic count and the DAS28 (r = −0.038, p = 0.66) (Fig. 1). None of the eosinophilic patients had any associated pneumonia.

4. Discussion

The role of eosinophilia in connective tissue diseases and the relationship with symptoms of rheumatic disease have not been clearly established. Eosinophilia can be seen in various rheumatologic conditions but, as corticosteroids are one of the most common medications used in collagen tissue diseases, the eosinophil numbers found may be lower than expected and eosinophilia may be more frequent than reported [23]. Short et al. in 1957 [24] noted a mild eosinophilia in a large number of RA patients. An increase in the circulating levels of eosinophil cationic protein, an eosinophil specific granule protein in RA patients has also been reported [15].

From the Results of the present study it is clear that although mild eosinophilia is fairly common in RA patients, which was present in 29/134 patients (21.6%) there was no correlation between the eosinophil count and disease activity as assessed by DAS28. In spite that the presence of eosinophilia in peripheral blood has been considered as an indicator of bad prognosis in RA patients, in the study of Chiardola et al. [25] it has been reported that the frequency of eosinophilia in Argentinean RA patients was 73.3% and was not an indicator of disease severity of the disease as in all cases there was evidence for parasitic infection. However our patients did not have any kind of helminthic infection.

In a retrospective study of 45 RA patients selected for their severity or elevated RF titer, unexplained eosinophilic counts of 5% or greater were encountered in 40% pointing to a possible relation to the immune events occurring in the course of RA [26]. Eosinophilia is considered as a poor prognostic factor and associated with poor response to disease modifying drugs. In a French study, eosinophilia has been reported to occur in only 3.2% of patients with new onset arthritis and was associated with poor prognosis [17] however no such relation was seen in the current study possibly as a higher level of eosinophilic count, >500/mm³, was considered as eosinophilia in their study, in addition to the fact that only new arthritis patient were included and may be also due to ethnic variation. RA cases with massive eosinophilia have also been reported [27]. Eosinophilic pneumonia has also been described in...
RA patients [28] however none of the present study patients had any similar condition. Eosinophilia has also been observed in RA patients with extra-articular manifestations as subcutaneous nodules, vasculitis, pleural/pericardial involvement or pulmonary fibrosis [29]. In addition, eosinophilia has been observed as a side effect of methotrexate in patients with chronic arthritis and may or may not be accompanied by pancytopenia [26].

Among the limitations of the study is the lack of control subjects and depending on the universal normal value for eosinophilic count. Involving a larger number of patients in a longitudinal study and considering the other clinical and laboratory variables as well as the impact of medications used could add more in-depth to the reached results. To conclude eosinophilia is quite common in RA patients but does not have any relation with disease activity.

Conflict of interest

None.

References