Relationship between Rheumatoid arthritis and anemia of chronic disease of patient in province Diwaniya

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Abstract

Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults. Rheumatoid arthritis is also a chronic destructive inflammatory disease characterized by the accumulation and of an inflammatory infiltrate in the synovial membrane that leads to sinusitis and the destruction of the joint architecture resulting in impaired function. The anemia of chronic disease (ACD) is a result of Body response to inflammation or system disease. ACD, usually a mild to moderate anemia, is the most prevalent anemia after iron deficiency anemia and also the most prevalent anemia in hospitalized patients. This anemia, first described in chronic infections, may be found in subjects with diseases involving acute or chronic immune activation and thus could be seen in a variety of inflammatory conditions, acute or chronic Infections, rheumatologic disorders, autoimmune disorders and cancer. The study includes thirteen (20 female and 10 male) patient with RA and (10 male and 20 female ) as the control. In the present study, significantly increased ($p < 0.05$) At ferretin , and significant decrease ($p < 0.05$). In Hb, iron, transferitin, transferin saturated.

These results suggest Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease, primarily located in the synovial joints, Anemia of chronic disease is anemia connected with inflammation or system disease. It is mediated by inflammatory cytokines TNF, IL-1, IL-6 and IFN that engulf iron than iron metabolism dysregulation, decreased RBC production in bone marrow, shortening the RBC lifespan, and decreased erythropoietin secretion.

Key word : anemia of chronic disease , Rheumatoid arthritis , transferin , ferretin

Introduction

Rheumatoid arthritis is a chronic progressive disease associated with systemic inflammation. The disease directly affects physical function and mobility and results in substantial short-term and long-term morbidity. Furthermore, individuals with rheumatoid arthritis have a substantially shorter life expectancy than does the general population. Deaths from cardiovascular disease, infection, and cancer are increased among individuals with rheumatoid arthritis. The anemia of chronic disease (ACD) is the most prevalent anemia after iron deficiency anemia. It is associated with infectious, inflammatory and neoplastic disease. ACD is a medical condition caused by the release of cytokines, which mediate inflammatory and immune response (tumor necrosis factor, interleukins 1 and 6, and interferon). Abnormal iron metabolism with iron trapping in reticuloendothelial cells is primarily the cause of this condition, making iron unavailable for erythropoiesis although iron tissue reserves are elevated. This anemia, first described in chronic infections, may be found in subjects with diseases involving acute or chronic immune activation and thus, could be seen in a variety of inflammatory conditions, acute or chronic infections, rheumatologic disorders, autoimmune disorders and cancer. Most chronic inflammatory rheumatic diseases are complicated by hematologic abnormalities, including anemia; disorders of leukocytes, platelets, and the coagulation system; and hematologic malignancies. Patients with rheumatoid arthritis (RA) may suffer from a variety of hematologic disorders, particularly anemia, leukopenia, and thrombocytosis.
Methods, Material

Patients

Thirty patients (15 female and 15 male) and thirty normal (15 male and 15 female) as control (non-RA group) attendants of Rheumatologic unit in Al-Diwaniya Teaching hospital of period between January 2015 to December 2016 aged 18 to 74 years (median, 48.5 years) who fulfilled the criteria of the American Rheumatism Association for classic rheumatoid arthritis. The examination by specialist and their routine laboratory investigations. Blood was drawn from both patients and controls. The blood collection in EDTA tube to measure blood parameter that includes reticulocyte count, Hb. Serum levels of iron were estimated using the frozen calorimetric method. Total Iron Binding Capacity (TIBC) was estimated colorimetrically by the following procedure: An excess of iron is added to the serum iron to saturate the transferrin. The unbound iron is precipitated with basic magnesium carbonate. After centrifugation, the iron in the supernatant was determined. Unsaturated iron-binding capacity (UIBC), the amount of protein (apotransferrin) still available to bind iron, can be estimated from the formula: UIBC = TIBC – Serum iron. The ferritin quantitative kit based on a solid phase enzyme-linked immunosorbent assay (ELISA) was supplied by Monobind® Inc. USA. The assay system utilizes one rabbit anti-ferritin antibody for solid phase (microtitre wells) immobilization and a mouse monoclonal anti-ferritin antibody in the antibody enzyme horseradish peroxidase (HRP) conjugate solution. Estimated Total Iron Body Stores (ETIBS) were calculated using the following formula: ETIBS (in μmol) = (serum ferritin in μg/L) * 143. Transferrin saturation percentage (TS%) was calculated from the following equation: TS% = (Serum Iron/TIBC) *100%

Results

The result was shown in table significant decrease (p< 0.05) in Hemoglobin (Hb), packed cell volume (PCV), Unsatuated iron-binding capacity (UIBC), total Iron Binding Capacity (TIBC), Estimated Total Iron Body Stores (ETIBS), Transferrin saturation percentage (TS%), Transferrin concentration while The result was shown in table significant increase (p< 0.05) in a concentration of Ferritin.
The table showed Iron indices in patients with RA and control

<table>
<thead>
<tr>
<th>Iron indices</th>
<th>Patients Group with RA</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>11.33 ±2.11*</td>
<td>12.65 ±1.13</td>
</tr>
<tr>
<td>PCV %</td>
<td>39.5±2.5 *</td>
<td>41.94 ±3.39</td>
</tr>
<tr>
<td>S.Ferritin (pmol/L)</td>
<td>168±3.4*</td>
<td>164.34 ±115.49</td>
</tr>
<tr>
<td>EIBS (mmol/L)</td>
<td>9.2±2.4*</td>
<td>10.46±7.35</td>
</tr>
<tr>
<td>S.Iron (umol/L)</td>
<td>15.8±4*</td>
<td>17.85 ±6.52</td>
</tr>
<tr>
<td>TIBC (umol/l)</td>
<td>51±4.3*</td>
<td>56.19 ± 10.76</td>
</tr>
<tr>
<td>TS%</td>
<td>30±4.5*</td>
<td>32.91±11.11</td>
</tr>
<tr>
<td>Transferrin Conc.  (g/L)</td>
<td>0.13±0.55*</td>
<td>0.15 ± 0.03</td>
</tr>
<tr>
<td>UIBC (umol/l)</td>
<td>37±5.1*</td>
<td>38.56 ± 11.34</td>
</tr>
</tbody>
</table>

Discussion

The Rheumatoid arthritis is a chronic destructive inflammatory disease characterized by accumulation and persistence of an inflammatory infiltrate in the synovial membrane that leads to synovitis and the destruction of the joint architecture resulting in an impaired function that results response immunity. Most chronic inflammatory rheumatic diseases are complicated by hematologic abnormalities, including anemia, disorders of leukocytes, platelets, the coagulation system, and hematologic malignancies and agree with study condition. Patients with rheumatoid arthritis (RA) may suffer from a variety of hematologic disorders, particularly anemia, leukopenia, and thrombocytosis [14], agree with study condition. The pathogenesis of the anemia of chronic inflammatory disease as in RA are incompletely understood. Two major factors appear to be important: trapping of iron in macrophages, making it relatively unavailable for new hemoglobin synthesis; and inability of the morphologically normal marrow to increase erythropoiesis in response to the anemia where inflammatory mediators, particularly tumor necrosis factor-alpha (TNFa), interleukin-1, interleukin-6, interleukin-10, and interferon gamma, have been shown to contribute to these changes that explains low of plasma iron [15]. This type of anemia is usually mild and non-progressive, characterized by decreased plasma iron, decreased total iron-binding capacity, decreased iron saturation of transferrin, decreased bone marrow sideroblast, and normal or increased reticulo-endothelial iron [16], that agrees we study the condition. The Cytokine activity on disturbance in iron metabolism is the main feature of ACD, The iron plasma level is decreased, while the level of iron in the reticuloendothelial system is increased, Reduced availability of iron leads to restricted iron in erythropoiesis, Additionally inflammatory cytokines stimulate iron storage into macrophages in multiple ways: stimulating receptors for erythrophagocytosis, stimulating the expression of the protein divalent metal transporter (DMT-1) through which the transmembrane import of non-transferrin iron and inducing transferrin receptor (TfR) iron uptake in macrophages occur. The increased iron storage in macrophages and hepatocytes leads to increased ferritin expression these agree with result condition [17]. In ACD, the RBC production in bone marrow is impaired due to the inhibitory effects of TNF-alpha, beta and IL-1, which is indirectly mediated by IFN alpha, beta and gamma. The most potent inhibitory effect appears to be the one of
IFN gamma, The mechanism involves induction of apoptosis or down regulation of the expression of erythropoietin receptors or other hematopoietic growth factors, Acute phase proteins efficiently inhibit TfR and TfR mediated 18.  

Conclusion

The result in the study explained that rheumatoid arthritis causes an increase in inflammatory body than engulf iron by macrophage where low concentrations of iron in plasma. Also decrease in some parameter of iron and increase Ferritin (it acts as a buffer against iron deficiency and iron overload). The low in iron causes anemia deficiency of iron in rheumatoid arthritis Evidence suggests that increased production of inflammatory cytokines (tumor necrosis factor-α) is linked to a decrease erythropoietin response in the bone marrow, thereby leading to inadequate erythropoiesis.

