Revista Colombiana de
REUMATOLOGÍA
www.elsevier.es/rcreuma

Editorial

Anemia and lupus☆

Anemia y Lupus

Juan C Rueda[a], *John Londoño*[a,b,*]

[a] *Unidad de Reumatología e Inmunología. Campus Biomédico, Universidad de La Sabana, Chía, Cundinamarca, Colombia*
[b] *Grupo de Investigación Espondiloartropatías, Universidad de La Sabana – Hospital Militar Central, Bogotá D.C., Colombia*

In this issue of the Journal is published the article «Pathogenic role of erythropoietin in Egyptian SLE anemic patients: Prevalence of different types of anemia in systemic lupus erythematosus». This article raises a dissertation to which we are frequently exposed in the process of diagnosis or follow-up of patients with rheumatic diseases of autoimmune origin. It is sometimes difficult to identify the cause of the anemic syndrome that accompanies these patients. The explanations of the phenomenon can be multiple and it requires an individualized approach in which it is necessary to establish whether it obeys to a manifestation proper of the entity we are facing; if it is a manifestation of the chronic inflammatory state; if it is related to a nutritional deprivation in which the iron deficit occupies the first place; if it is secondary to some comorbidity such as gastrointestinal bleeding or renal failure, or if, as is common, it has a multicausal origin in which the mechanisms outlined above are combined.[1]

It is not a matter of little concern, nor should it be seen as a common issue or of minimal importance given the implications that an anemic syndrome can have on a patient with a complex disease, in whom this condition may end up compromising the cardiovascular status or deepening the intensity of the «constitutional» symptoms, sometimes poorly weighted by being framed within the group of manifestations identified as «fibromyalgia» that accompanies the majority of these patients.[2] It is the case of fatigue, a cardinal symptom of the patient with chronic rheumatic disease, that we are obliged to consider as an inflammatory activity of the disease and rethink, if necessary, the therapeutic approach that allows to reduce the impact that this manifestation produces in the quality of life of these patients.[3]

The anemia that accompanies the chronic inflammatory diseases is usually mild or moderate, and rarely the level of hemoglobin is below 10 g per liter.[4] Approximately 50% of patients with systemic lupus erythematosus (SLE) have this type of anemia prior to starting the treatment of the disease.[5] Finding lower values of hemoglobin obliges us to consider a different cause, especially those related to pathophysiological mechanisms altered by the chronic autoimmune disease. The anemia of systemic inflammatory disease is essentially an immune disorder with multiple alterations, in which iron homeostasis, proliferation of erythroid progenitors, reduced erythropoietin activity, and decreased erythrocyte half-life stand out.[6]

We cannot forget, in the context of patients with chronic rheumatic diseases of autoimmune origin, the anemia related to iron deficiency. In the case of SLE and its relationship with the female gender, the menstruation is an important condition that must be taken into account in the diagnosis and treatment,[7] without underestimating situations related to gastrointestinal disorders associated with chronic consumption of non-steroidal anti-inflammatory drugs and glucocorticoids, which favor the decrease in serum iron levels secondary to bleeding from the digestive tract.[8] It becomes necessary to rule out in every rheumatic patient in whom the use of these drugs for a long time is contemplated, the

PII of original article: S0121-8123(19)30057-X
☆ Please cite this article as: Rueda JC and Londoño J. Anemia y Lupus. Rev Colomb Reumatol. 2019;26:149–150.
* *Corresponding author*.
E-mail address: john.londono@unisabana.edu.co (J. Londoño).

presence of an active acid-peptic disease that favors this condition. The age of the patient is another determining circumstance in the onset of the anemia.[9] In general, few patients have anemia related to poor iron intake, and its origin is multicausal.[10]

It is important to take into account the effect of immunosuppressive medications in patients with diseases such as SLE or rheumatoid arthritis (RA). Immunosuppressants such as methotrexate, cyclosporine, azathioprine, leflunomide and mycophenolate exert a direct effect on the bone marrow, they reduce erythropoiesis and the half-life of erythrocytes.[11] New drugs, such as the inhibitors of JAK kinases (inhibitors of Janus kinases), have an intrinsic effect on the bone marrow and, to a greater of lesser extent, they have an impact on the regulatory mechanisms of the formation of the formed elements of the blood that oblige to their frequent monitoring in the patients who receive them.[12]

The article of Dr. Ahmed et al. studies the frequency of the 3 most common causes of anemic syndrome in an important group of Egyptian patients with an established diagnosis of SLE. The anemia related to chronic inflammatory status was the most frequent (41.3%), followed by the anemia secondary to iron deficiency (33.3%), and finally by the anemia of autoimmune etiology (25.3%). The authors complement the results with the relationship that anemia could have with serum erythropoietin (EPO) levels, and although in all three conditions the serum level of this hormone was higher than that found in the controls, the levels in the patients classified with anemia related to autoimmune mechanisms of the disease were significantly lower than the levels in patients with anemia due to chronic inflammation and iron deficiency.

The results obtained by Dr. Ahmed are in concordance with what was reported by other researchers. Serum levels of EPO in patients with SLE appear to be inadequate to respond properly to the degree of anemia, or the response of the bone marrow to the hormone would be diminished compared with healthy individuals.

Whatever the explanation, the reduced biological activity of EPO in patients with SLE could be a consequence of the effects of increased levels of TNF, IL-1 and toxic radicals on EPO producing cells in the kidney, as well as of the infiltration of the renal peritubular region by macrophages and T cells.[13,14]

In conclusion, the anemia in patients with chronic rheumatic diseases of autoimmune origin, such as SLE and RA, should be considered as an important issue to take into account in the diagnosis, treatment and prognosis of these patients. No effort should be spared to find the origin of the condition. The recovery of serum hemoglobin levels will result in the well-being of patients and will favor the appropriate response to other therapeutic measures implemented.

REFERENCES

1. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005;352:1011–23.
2. Nissenson AR, Goodnough LT, Dubois RW. Anemia: not just an innocent bystander? Arch Intern Med. 2003;163:1400–4.
3. Margiotta DPE, Fasano S, Basta F, Pierro L, Riccardi A, Navarini L, et al. Clinical features of patients with systemic lupus erythematosus according to health-related quality of life, entity of pain, fatigue and depression: a cluster analysis. Clin Exp Rheumatol. 2019;37:535–9.
4. Wolfe F, Michaud K. Anemia and renal function in patients with rheumatoid arthritis. J Rheumatol. 2006;33:1516–22.
5. Tzioufas AG, Kokori SI, Petrovas CI, Moutsopoulos HM. Autoantibodies to human recombinant erythropoietin in patients with systemic lupus erythematosus: correlation with anemia. Arthritis Rheum. 1997;40:2212–6.
6. Weiss G, Schett G. Anaemia in inflammatory rheumatic diseases. Nat Rev Rheumatol. 2013;9:205–15.
7. Gordeuk VR, Brittenham GM, Bravo J, Hughes MA, Keating LJ. Prevention of iron deficiency with carbonyl iron in female blood donors. Transfusion. 1990;30:239–45.
8. Moore RA, Derry S, McQuay HJ. Faecal blood loss with aspirin, nonsteroidal anti-inflammatory drugs and cyclo-oxygenase-2 selective inhibitors: systematic review of randomized trials using autologous chromium-labelled erythrocytes. Arthritis Res Ther. 2008;10:R7.
9. Dallman PR, Yip R, Johnson C. Prevalence and causes of anemia in the United States, 1976 to 1980. Am J Clin Nutr. 1984;(39):437–45.
10. Behiry ME, Salem MR, Alnaggar AR. Assessment of nutritional status and disease activity level in systemic lupus erythematosus patients at a tertiary care hospital. Rev.Colomb.Reumatol. 2019;26:97–104.
11. Levine AB, Erkan D. Clinical assessment and management of cytopenias in lupus patients. Curr Rheumatol Rep. 2011;13:291–9.
12. Vélez P, Jaller JJ, Otero Escalante WJ, García EG, Rojo R, Chapman D, et al. Tofacitinib, an oral Janus kinase inhibitor, in patients from Colombia with rheumatoid arthritis: Pooled efficacy and safety analyses of data from phase III studies. Rev Colomb Reumatol. 2018;25:233–44.
13. Bertero MT, Caligaris-Cappio F. Anemia of chronic disorders in systemic autoimmune diseases. Haematologica. 1997;82:375–81.
14. Jelkmann W. Proinflammatory cytokines lowering erythropoietin production. J Interferon Cytokine Res. 1998;18:555–9.