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BRIEF REVIEW ABOUT NEUROLOGICAL, HEMATOLOGICAL, GASTROINTESTINAL, CARDIOVASCULAR AND PULMONAR MANIFESTATIONS OF SYSTEMIC ERYTHEMATOSUS LUPUS

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ABSTRACT

Systemic Lupus Erythematosus is an autoimmune multisystem pathology, characterized by being more prevalent in women, especially African women. One of the most frequent pathologies is usually the presence of Lupus Nephritis (1). The prevalence is higher in women in relation to men in a ratio of 9:1, with an age onset between 15 and 44 years of age (2).

***Objective**: to detail the current information related to cardiovascular, neurological, hematological manifestations of systemic erythematosus lupus, analyzing which pathologies are present in this disease.*

***Methodology**: a total of 32 articles were analyzed in this review, including review and original articles, resulting in the election of 15 bibliographies due to the relevance of them. The sources of information were PubMed, Google Scholar and UpToDate; the terms used to search for information in English was: Systemic Erythematosus Lupus and its manifestations.*

***Results**: The most frequent gastrointestinal manifestations are regurgitation, peptic ulceration, protein-losing enteropathy, pseudo-obstruction and mesenteric vasculitis; neurological manifestations include seizures, stroke, optic neuritis, altered mental status, aseptic meningitis, chorea, psychosis or depression. At the hematologic level, anemia, thrombocytopenia, leukopenia, thrombotic thrombocytopenic purpura is usually manifested, so the patient's clinical manifestations should be analyzed and any other etiology of the patient that is not related to systemic lupus erythematosus should be ruled out. Pulmonary manifestations usually include pleuritic pain, lupus pneumonitis, interstitial pulmonary alterations and pulmonary hypertension. Cardiovascular manifestations should be ruled out considering that patients with lupus have an increased risk of cardiovascular disease.*

***Conclusions**: This bibliographic review sought to show the symptoms of patients diagnosed with systemic lupus erythematosus, and which are related to the most important organs; in this case, at the neurological, cardiovascular, pulmonary, hematological and gastrointestinal levels. This review shows us that we must consider several pathologies in patients with Lupus; however, we must remember that the diagnosis of these entities is a rule-out diagnosis, which means that if we have a symptomatology of a certain apparatus or system, we must rule it out with the most frequent, and then consider the less frequent pathology, related to lupus.*

KEYWORDS: *Systemic lupus erythematous; Protein-losing enteropathy; Treatment.*

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INTRODUCTION

Genetic studies have identified more than 80 loci that are associated with increased susceptibility to systemic lupus erythematosus, among which the most important is the signal transducer and activator of transcription (STAT). It is responsible for producing an inflammatory response, continuing with receptor stimulation and INF-I receptor non-signaling. A recent study has determined that IL-12 mediated co-activation of STAT1 and STAT4 alters histone modification, with altered expansion of Tfh-Th1 sequencing. This leads to the induction of pathogenic Tfh cells, which may be useful in the case of studying the effect on these specific cells (3).

There are several endotypes and dominant organs that systemic lupus erythematosus affects; an example is childhood-onset systemic lupus erythematosus (they have high activity and tend to be more severe and need more aggressive therapy), organ-dominant lupus erythematosus, lupus with antiphospholipid syndrome. Patients who manifest idiopathic thrombocytopenic purpura, hemolytic anemia, serositis are those patients who have to be well evaluated and well controlled (4).

Although the pathophysiology of lupus is not known in depth, it has been determined that the manifestations of lupus are associated with the formation of antibodies and the creation of immune complexes. The fact of immune complex deposition and subsequent complement activation in the kidney produces tissue damage, characteristic of lupus nephritis. The pathogenic potential of immune complexes depends on the characteristics of the antibody and the capacity of mediators to produce inflammation, the nature of the antigen and the capacity of the immune complex to be solubilized by complement and bind to the receptor (5).

GASTROINTESTINAL DISORDERS

Dysphagia is usually the most frequent manifestation and is associated with the presence of heartburn, retrosternal pain, odynophagia or regurgitation. The cause of this pathology is usually due to a motility disorder gastroesophageal reflux disease or pill esophagitis. In addition, patients may manifest peptic ulcer, manifested as epigastric pain, early satiety, and nausea. However, it is necessary to rule out any pathology that may produce this symptomatology and to consider at that time the possibility that it may be generated by Lupus itself. Intestinal pseudo-obstruction is characterized by symptoms related to mechanical obstruction of the small or large intestine. Normally, patients usually present abdominal distension and abdominal pain. There is a pathology called protein-losing enteropathy, which is characterized by the appearance of hypoalbuminemia in the absence of proteinuria of nephrotic range and deep edema. Another variant present in these patients is mesenteric vasculitis, which usually manifests as postprandial abdominal pain, food aversion, nausea, vomiting, diarrhea and weight loss. Treatment of this variant is usually with high-dose corticosteroids to control the disease. When symptoms are recurrent or do not respond to glucocorticoid therapy, Cyclophosphamide is initiated; surgery is only for patients who present advanced ischemia or do not respond to medical therapy. Primary peritonitis secondary to lupus presents as abdominal pain with surgical features, although symptoms may be masked by the use of corticosteroids. Chronic peritonitis manifests with gradual painless ascites (6)(7).

NEUROLOGICAL MANIFESTATIONS

Strokes occur 1.5 to 3 times more often in patients with systemic lupus erythematosus, with a 3 times higher risk of ischemic stroke and a 3 times higher risk of hemorrhagic stroke; the pathogenesis is thought to be caused by arterial thrombosis in situ, or by cardiogenic embolisms. These cardioembolic accidents are usually generated due to valvular diseases or due to atrial fibrillation. A pathology called non-inflammatory microangiopathy is defined as a hyalinization of small vessels, which is associated with microinfarcts. In these patients, management is performed with tombolytic therapy and mechanical thrombectomy; to continue the management of lupus, it should be maintained with hydroxychloroquine or chloroquine since it reduces thrombotic events.

Another event that usually occurs is seizures; these occur in 4 to 12% of patients. The risk of presenting seizures increases when the patient has positive antiphospholipid antibodies and is being treated with corticosteroids. Usually, the patient presents with focal seizures and altered consciousness, which may progress to generalized seizures.

The altered mental status is usually characterized by delirium or psychosis. Moreover, the latter is often also called lupus psychosis, most frequently occurring in young people and with males. In these patients, immunomodulatory therapy has to be used; it is suggested to start high doses of glucocorticoids added with cyclophosphamide or mycophenolate; in refractory cases, rituximab or intravenous immunoglobulins can be used.

Optic neuritis is usually a pathology present in 1% of patients, characterized by acute loss of vision, with the presence of scotomas and pain on eye movement. On physical examination it may manifest with afferent pupillary defect. For this pathology, glucocorticoid pulses (1 gram of methylprednisolone) should be administered for 3 to 5 days; in these patients, it is necessary to escalate immunosuppression with the use of cyclophosphamide, and continue its use for 3 to 6 months; mycophenolate, azathioprine or rituximab can be used as an alternative for the control of the pathology.
Aseptic meningitis is a rare manifestation presenting with headache, nuchal rigidity, and lymphocytic pleocytosis with elevated cerebrospinal fluid protein; it is treated with a course of glucocorticoids once infectious causes have been excluded.

Chorea is characterized by movement disturbance, manifested as involuntary, stereotyped and brief movements, unilateral or bilateral; it may be associated with cognitive disturbances or stroke; infarcts at the basal ganglia level are usually present. On some occasions, this condition usually resolves in a few weeks, with or without treatment; although

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hydroxychloroquine and glucocorticoids are usually added; and if not effective, rituximab or intravenous immunoglobulins are administered.

Depression and anxiety are common in these patients; 24% of patients present depression and 37% of patients present anxiety. It is necessary to diagnose this pathology and treat it in a timely manner (8)(9).

HEMATOLOGIC MANIFESTATIONS

Anemia affects more than half of the patients with Lupus; it can be produced by multiple causes, among which are: chronic inflammation, iron deficiency, medication, autoimmune hemolysis, vitamin B12 deficiency, and thrombotic microangiopathies, such as thrombotic thrombocytopenic purpura. The evaluation of these patients should be directed towards a blood count, accompanied by reticulocytes and red blood cell index. The presence of leukopenia is common in patients with Lupus, and is related to disease activity; neutropenia may be caused by immunosuppressive medication or hypersplenism. Lymphopenia can even be caused by autoantibodies; in these cases, immunosuppressive medication or lupus therapy is usually necessary. Mild thrombocytopenia is common in these patients (less than 100,000), but platelet counts less than 50,000 are not very common. An important point is that thrombocytopenic purpura can occur prior to the development of lupus, as a chronic complication or acutely at disease activation. In these patients it may include splenomegaly, thrombotic microangiopathy or antiphospholipid syndrome. Pancytopenia is less common than individual cytopenias, but may occur in patients with Lupus. In these patients, it is necessary to rule out hematophagocytic lymphohistiocytosis, sepsis, thrombotic microangiopathy or vitamin B12 or folate deficiencies. Antiphospholipid syndrome is detected in 30 to 40% of patients with Lupus. Antibodies can prolong the partial thromboplastin time and, less frequently, the prothrombin time (10) (11).

When speaking of pulmonary disorders, it may involve pathology at the level of the lung, its vasculature, diaphragm or pleura. Cough or dyspnea are the most important points to investigate in these patients, especially in order to rule out infections. In cases of chest pain at the pleuritic level, with or without evidence of pleural effusion, it may be caused by lupus. In cases of pleural pathology, they have a good response to non-steroidal anti-inflammatory drugs, and those who do not respond should be treated with glucocorticoids. Chest pain usually has several sites of involvement: muscles, connective tissues or costochondral joints. Another pathology that can be evidenced is acute lupus pneumonitis, which is characterized by an abrupt onset of fever, cough, dyspnea, radiographic pulmonary opacities, hypoxemia and basal crackles. The diagnosis of these is based on clinical and serological evidence; however, it is necessary to mention that heart failure, infections, pulmonary embolism, diffuse alveolar hemorrhage and malignancy should be excluded. Another important entity to consider is pulmonary hemorrhage, which usually appears abruptly, manifested with dyspnea, cough and hemoptysis; bleeding is sufficient to produce anemia. On chest X-ray and CT scan it usually manifests as patchy opacities or diffuse bilateral opacities. For diagnosis, flexible bronchoscopy with bronchoalveolar lavage should be performed; treatment includes high-dose glucocorticoids in combination with immunosuppressive agents. Interstitial lung disease is an entity that produces non-productive cough, dyspnea and decreased exercise tolerance; a restrictive pattern is usually evidenced, with decreased diffusion capacity; high resolution chest CT is the radiological imaging of choice; when there are doubts about the diagnosis, lung biopsy can be performed. In these patients, management should be with glucocorticoids and immunomodulators. Pulmonary hypertension is a rare complication that usually manifests with palpitations, fatigue and exercise intolerance (12) (13).

CARDIOVASCULAR MANIFESTATIONS

The risk of coronary heart disease is highly increased in these patients compared to patients without lupus. Lupus patients have an increased prevalence, both due to glucocorticoid treatment and disease activation. For the detection of their symptomatology, it is always necessary to evaluate any atypical symptoms. Now, it is clear that cardiovascular pathology due to systemic lupus erythematosus is performed after ruling out pleuritis, pericarditis, pulmonary emboli, pneumonia, interstitial lung pathology and even gastroesophageal reflux. In general, prevention and treatment of cardiovascular disease is based on not smoking, regular exercise, optimization of lipid levels, controlling blood pressure, with prophylactic use of aspirin and minimizing the use of glucocorticoids; hydroxychloroquine, which is widely used in lupus, has been shown to have an additional antithrombotic and anti-atherogenic benefit (14) (15).

CONCLUSIONS

This bibliographic review sought to show the symptoms of patients diagnosed with systemic lupus erythematosus, and which are related to the most important organs; in this case, at the neurological, cardiovascular, pulmonary, hematological and gastrointestinal levels. This review shows us that we must consider several pathologies in patients with Lupus; however, we must remember that the diagnosis of these entities is a rule-out diagnosis, which means that if we have a symptomatology of a certain apparatus or system, we must rule it out with the most frequent, and then consider the less frequent pathology, related to lupus.

BIBLIOGRAPHY

1. *Kiriakidou M, Ching CL. Systemic Lupus Erythematosus. Ann Intern Med. 2020;172(11):ITC81-ITC96. doi:10.7326/AITC202006020*
2. *Zucchi D, Elefante E, Schilirò D, et al. One year in review 2022: systemic lupus erythematosus. Clin Exp Rheumatol. 2022;40(1):4-14. doi:10.55563/clinexprheumatol/nolysy*
3. *Zucchi D, Elefante E, Calabresi E, Signorini V, Bortoluzzi A, Tani C. One year in review 2019: systemic lupus erythematosus. Clin Exp Rheumatol. 2019;37(5):715-722.*
4. *Fanouriakis A, Tziolos N, Bertsias G, Boumpas DT. Update on the diagnosis and management of systemic lupus*

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erythematosus. Ann Rheum Dis. 2021;80(1):14-25. doi:10.1136/annrheumdis-2020-218272

5. *Schur, Peter H., and Bevra H. Hahn. "Epidemiology and pathogenesis of systemic lupus erythematosus." UpToDate. Waltham, MA (US) (2011).*
6. *Massarotti, Elena M., et al. "Gastrointestinal manifestations of systemic lupus*
7. *erythematosus." UpToDate, Post, TW (Ed), UpToDate, Waltham, MA (2020).*
8. *Li Z, Xu D, Wang Z, et al. Gastrointestinal system involvement in systemic lupus erythematosus. Lupus. 2017;26(11):1127-1138. doi:10.1177/0961203317707825*
9. *Gelfand, J. M., Yazdany, J., Pisetsky, D. S., Tung, G. A., Silver, J. M., & Curtis, M. R. Neurologic and neuropsychiatric manifestations of systemic lupus erythematosus. (2021). UpToDate, Post, TW (Ed), UpToDate*
10. *Shaban A, Leira EC. Neurological Complications in Patients with Systemic Lupus Erythematosus. Curr Neurol Neurosci Rep. 2019;19(12):97. Published 2019 Nov 26. doi:10.1007/s11910-019-1012-1*
11. *Schur, Peter H., Nancy Berliner, and Jennifer S. Tirnauer. "Hematologic manifestations of systemic lupus erythematosus." UpToDate. UpToDate (2020).*
12. *Meyer A, Guffroy A, Blaison G, et al. Systemic lupus erythematosus and neutropaenia: a hallmark of haematological manifestations. Lupus Sci Med. 2020;7(1):e000399. doi:10.1136/lupus-2020-000399*
13. *Wallace, Daniel J., and Dafna D. Gladman. "Clinical manifestations and diagnosis of systemic lupus erythematosus in adults." UpToDate. Waltham (2020).*
14. *Tani C, Elefante E, Arnaud L, et al. Rare clinical manifestations in systemic lupus erythematosus: a review on frequency and clinical presentation. Clin Exp Rheumatol. 2022;40 Suppl 134(5):93-102. doi:10.55563/clinexprheumatol/jrz47c*
15. *COSTENBADER, Karen H.; PISETSKY, D. S.; CURTIS, M. R. Non-coronary cardiac manifestation of systemic lupus erythematosus in adults. Up to Date (2022).[Internet].[Cited in 2023 jan. 16]. Available from: http://www.uptodate.com.*
16. *Miner JJ, Kim AH. Cardiac manifestations of systemic lupus erythematosus. Rheum Dis Clin North Am. 2014;40(1):51-60. doi:10.1016/j.rdc.2013.10.003*