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Literature Review

Clinical and therapeutical features of patients with systemic lupus erythematosus associated with gastroparesis: A systematic review

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Abstract

This paper aims to analyze the clinical, therapeutic, and evolutionary characteristics of patients with systemic lupus erythematosus (SLE) that is associated with gastroparesis. We have systematically researched articles published in Pubmed, MEDLINE, LILACS, and Scielo dating from 1966 to April 2020. All the researched articles are based on gastroparesis and SLE in the following literature: English, Chinese, and Japanese. We obtained five cases of SLE associated with gastroparesis. There are three case reports included and two retrospective epidemiological studies where the clinical data are not detailed. Of the case reports, all of them were females aged between 27 and 58 years. All of them showed symptoms of nausea and vomiting. Abdominal pain and weight loss were reported in the only two-third of the cases. Only one case showed early satiety. All the cases were tested positive for antinuclear antibodies and anti-dsDNA antibodies at the time of gastroparesis. In all the cases, scintigraphy was performed to check gastric emptying. This is the gold standard for diagnosing gastroparesis. Concerning therapy used, three-third of the cases received glucocorticoids 1 mg/kg daily. In two-third of the cases, azathioprine was used. Before starting the corticosteroids therapy, all the cases received antibiotics and motility stimulants with poor outcomes. The early diagnosis of gastroparesis with SLE must be rapid so that the therapy can be initiated promptly. Due to the severity of the condition that may result in nausea, abdominal pains, and satiety, using endoscopy and gastric emptying scintigraphy is fundamental.

Keywords: Systemic lupus erythematosus, gastroparesis, gastric outlet obstruction

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune condition that is characterized by periods of activity and remission. It involves several bodily systems and organs. The reported prevalence of SLE is 14.6-50.8 per 100,000 people, and its incidence is 1.8-7.6 per 100,000.[1] The organs affected the most include the skin, joints, central nervous system, kidneys, serous organs, and rarely, the gastrointestinal tract.

Gastrointestinal involvement in patients with SLE is reported to be up to 50%. Among the most common manifestations included nausea, anorexia, and vomiting.[2] Severe manifestations of the digestive tract include mesenteric vasculitis and pancreatitis. The occurrence of gastroparesis in patients with SLE is considered to be unusual. The condition is largely characterized by delayed gastric emptying in the absence of any mechanical obstruction factor. Gastroparesis affects up to 4% of the American population.[3] This shows that it is not a very unusual condition after all. However, it is slightly underdiagnosed due to the unavailability of the golden method of diagnosis, the gastric emptying scintigraphy.

Gastroparesis is very commonly associated with diabetes, only secondary to diabetic neuropathy. Gastroparesis is described in case reports of lupus. Additionally, it has also been described in two gastroenterological studies where lupus was the causative agent for the respective conditions.[4,5]

This study aims to describe the clinical, therapeutic, and evolutionary characteristics of gastroparesis associated with patients of SLE. Furthermore, this study adds a new case of this rare association.

Methods

Patient selection

This research is characterized as a descriptive and transversal study with a retrospective analysis of the medical report of a patient diagnosed with both SLE[6] and gastroparesis.

Literature review

We have systematically researched articles published in Pubmed/MEDLINE, LILACS, and Scielo dating from 1966 to April 2020. All the researched articles are based on gastroparesis and SLE in the following literature: English, Chinese, and Japanese. Furthermore, we give a detailed case report on a patient of SLE who was diagnosed with gastroparesis as well. We reviewed the articles concerning demographic characteristics (gender and age), clinical characteristics (clinical presentation of gastroparesis, SLE antibodies detection, the onset of symptoms, and progression), therapy provided, and response to said therapy. We used the keywords "systemic lupus erythematosus," "gastroparesis," and "gastric outlet obstruction."

Case report

A female patient (41 years old) was diagnosed with SLE for over 20 years and presented with the following signs and symptoms: serositis, low complement hematological disorders, positive for antinuclear antibody, anti-dsDNA, anti-Sm, and anti-Ro. She was treated with corticosteroids, hydroxychloroquine, and azathioprine. The therapy kept her condition in control. In 2013, she presented with nausea, vomiting, abdominal pains, diarrhea, and a weight loss of 17 kg in 2 months. During this period, she was only using hydroxychloroquine (HCQ) and prednisolone 5 mg/daily. She did not respond to therapy with omeprazole and antiemetics. After being admitted, her test results showed positive for anti-dsDNA with C3 50 mg/dL, C4 11 mg/dL, lymphopenia 500 cel/mL, erythrocyte sedimentation rate (ESR) 16 mm/h, C-reactive protein (CRP) 1.6 mg/dL, and normal amylase. Abdominal ultrasound was normal. Abdominal radiography revealed distension of intestinal loops. Upper gastrointestinal endoscopy revealed mild pangastritis and esophagitis, with biopsy compatible with gastritis. Colonoscopy was normal, and colon biopsies were compatible with mild and nonspecific retinitis, colitis, and enteritis. The hypothesis of gastroparesis was suggested, and gastric scintigraphy was requested. The scintigraphy revealed a marked reduction in the speed of gastric emptying (retention: first hour: 100%, second hour: 90%, third hour: 90%, and normal: 50% in 20-40 min) (Figure 1). She received treatment with omeprazole, ondansetron, metoclopramide, domperidone, and mebeverine. Abdominal tomography revealed thickening of the peritoneal wall, gastric wall, bowel, bladder, ureters, and pleural basal thickening (pleuritis). Treatment with methylprednisolone 1 mg/kg/day was decided until improvement followed by oral prednisone. Within 5 days of starting corticosteroids, there was a marked reduction in nausea, vomiting, and diarrhea, with subsequent normalization. Gastric motility medications, antiemetics, omeprazole, and azathioprine 100 mg/day were suspended. After 1 month, she was asymptomatic and a new abdominal CT scan was performed, which was normal. Furthermore, a new gastric emptying scintigraphy was also performed, which showed marked improvement (retention: first hour: 74%, second hour: 45%, and third hour: 0.5%). Currently, outpatient follow-ups, she was found completely asymptomatic, using only HCQ 400 mg/day and azathioprine 50 mg/day.

Main Points

- Gastroparesis is an uncommon manifestation in systemic lupus erythematosus.
- The presence of nausea, vomiting, and early satiety, with minimal or normal endoscopy, rule out an obstructive cause.
- A positive gastric emptying scintigraphy is the gold standard to diagnosis gastroparesis.
- The main therapy is glucocorticoids which is essential and providing an effective response.

Results

The demographic, clinical, and laboratory characteristics of our patient with SLE and gastroparesis, as well as the other cases described in the literature reviews are summarized in Table 1.

In the international literature from 1966 to 2020, only four studies of SLE associated with gastroparesis were reported.[4,5,7,8] We have associated our case report with the analysis.

There are three case reports[7,8] and two retrospective epidemiological studies[4,5] where clinical data are not detailed. The reports showed that all cases were females with ages ranging from 27 to 34 years old[7,8]

Regarding the clinical manifestations in the case reports, all presented with nausea and vomiting. Abdominal pain and weight loss were reported in only two-third of the cases. Only one case showed early satiety. Regarding autoantibodies, all had antinuclear antibody and were positive for anti-dsDNA antibody (three-third) at the time of gastroparesis. One of the cases (one-third) required parenteral nutrition until receiving corticosteroid therapy.[7] Scintigraphy, the gold standard for diagnosis, was performed in all cases for checking the gastric emptying.[7,8]

Regarding therapy, all the cases (three-third) received glucocorticoids 1 mg/kg/day, and one of the cases (one-third) received intravenous methylprednisolone until the clinical picture improved. Azathioprine was used in two-third of the cases, and antiemetic medications (metoclopramide and ondansetron), proton pump inhibitors, and motility stimulants were used in all the cases before corticosteroid therapy was initiated, with poor results.[7,8]

Discussion

This paper adds a new case of gastroparesis associated with SLE to patients previously described.

Gastroparesis can be acute when it occurs in situations such as decompensated hypothyroidism, acute gastroenterocolitis, and disorders of hydroelectrolytic balance due to the use of drugs such as opiates and levodopa. Chronic cases are mainly associated with diabetes, but other diseases are also associated with this condition, such as Parkinson's disease, postgastric surgery, and neoplasms.[9] Rheumatic diseases such as systemic sclerosis may be associated with gastroparesis due to infiltration of collagen in the myenteric structure, followed by polymyositis and eventually leading to SLE.

In a large epidemiological study that evaluated data from the healthcare cost and utilization project: nationwide inpatient sample between the years 2013 and 2014, the authors screened nondiabetic patients diagnosed with gastroparesis.[5] A total of 27,543 patients with nondiabetic gastroparesis were found. The major risk factors were concluded to be the female sex and the standard American diet. Several other conditions were considered risk factors as well, including chronic pancreatitis, end-stage renal disease, irritable bowel syndrome, fibromyalgia, and venous thromboembolism. Regarding lupus, the authors detected 824 lupus patients with gastroparesis. The odds ratio was 2.06 to present this gastroenterological condition.[5] A few limitations to this study are the following: did all patients have the gastric emptying scintigraphy, the gold standard, to diagnose gastroparesis? This is highly unlikely. This study was done by crossing ICDs in a database. The diagnosis of gastroparesis must have been based on the gastrointestinal clinical manifestations that are although sensitive, but very little spe-

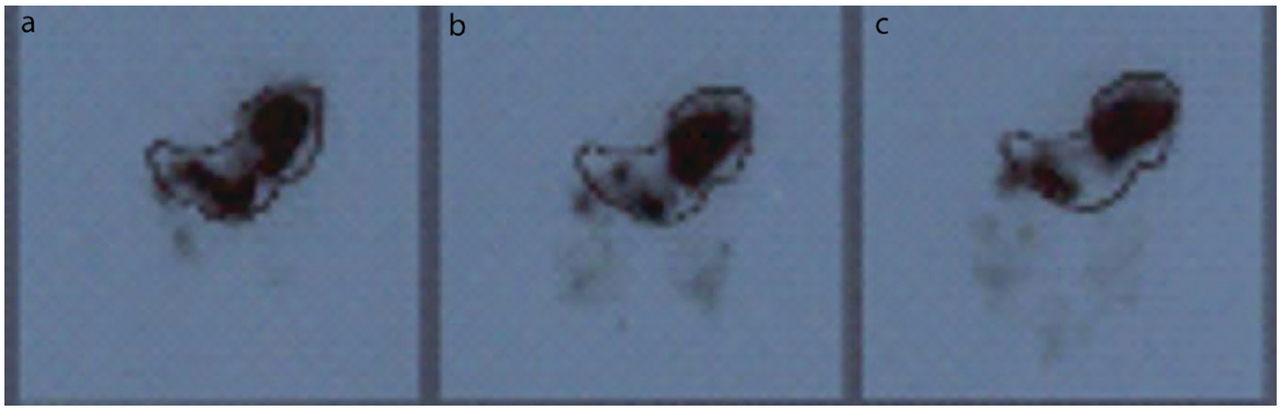

Figure 1. Scintigraphy showing marked reduction in the speed of gastric emptying: (a) 1 hour: 100%, (b) 2 hours: 90%, (c) 3 hours: 90%. Normal: ≤50% in 20-30 minutes.

Table 1. Clinical, demographical, and treatment features of the five studies regarding the association between systemic lúpus erythematosus and gastroparesis.

Author, year	N, gender	Age (years)	Clinical symptoms	Treatment	Improvement after therapy	Time to achieve clinical response
Posthuma et al,[7] 1994	1, female	27	Nausea, vomiting, abdominal cramps, weight loss ANA, LE cell pos., low complement, anti-DNA neg., parenteral nutrition	Prednisolone 60 mg/day	Yes, complete recovery	It was quick, but the authors did not write the exact time
Soykan et al,[4] 1998	1, female	58	Nausea vomiting	N/A	N/A	N/A
Chou et al,[8] 2013	1, female	29	Nausea, vomiting, anti-dsDNA, anti-Sm	Prednisolone, azathioprine, rituximab, pantoprazole, metoclopramide, erythromycin	Yes, but the patient was not adherent to therapy	It was quick, but the authors did not write the exact time
Nassar et al,[5] 2018	832, probably more females	N/A	N/A	N/A	N/A	N/A
Carvalho et al., 2021*	1, female	34	Nausea, vomiting, abdominal cramp, weight loss, early satiety ANA, anti-dsDNA, anti-Sm, anti-Ro, low complement	Methylprednisolone 50 mg IV A, prednisolone 40 mgHCQ, AZA	Yes	5 days to 1 month (complete recovery)

ANA, antinuclear antibodies; AZA, azathioprine; HCQ, hydroxychloroquine; IV, intravenous; N/A, not available; pos., positive.
*Present study.

cific for gastroparesis. The second hypothesis is that rheumatologists are not reporting clinical studies in the field of rheumatology, which are mild in the start but can progress to having severe manifestations.

Another limitation regarding SLE criteria is the lack of current data, since they need to be externally validated in various other cohorts besides the one that it was originated.[10]

The clinical manifestations resulting from gastroparesis can vary from asymptomatic or oligosymptomatic cases to severe ones. Patients complain of nausea, vomiting, abdominal pain, and early satiety. This is possibly a symptom that can aid the diagnosis.[9] In the evaluation, an upper gastrointestinal endoscopy should be performed to avoid structural lesions of this organ. Generally, this test will not, however, reveal the diagnosis of gastroparesis. The gastric emptying scintigraphy is the gold standard.

The image of the digestive tract is mandatory to rule out tumor lesions and other differential diagnoses. Similarly, an intestinal biopsy is also mandatory in all cases so other diseases such as amyloidosis and lymphangiectasia can be ruled out.

The treatment of gastroparesis in SLE must include glucocorticoids.[7,8] In fact, in all studies in which steroids are used, a quick and adequate response was observed in the treated patients. Moreover, the adding of azathioprine to the therapeutic scheme is very reasonable, since this drug may reduce the time of steroid use and also may have an additional role in controlling the lupus disease activity. Symptomatic patients can be treated with proton pump inhibitors and motility stimulants like domperidone as well. However, the response is poor according to case reports. In our patient, tomography showed a diffuse serous thickening in the abdomen, including intestines, bladder, ureter, and also pleuritis. This can be undoubtedly explained by the lupus activity of the disease in conjunction with reduced complement and

positive anti-dsDNA, and therefore corticosteroid therapy in these individuals is imperative.

Finally, certain questions that remain to be fully answered include the following:

- What is the best mode of treatment for gastroparesis associated with SLE? Oral or parenteral?
- Can immunosuppressants and rituximab, for instance, play a therapeutic role comparable to that of glucocorticoids?

Studies involving other patient samples are needed to answer these questions.

In summary, this article systematically reviewed the literature for all published cases of the rare association gastroparesis with SLE and described an additional case. The presence of nausea, vomiting, and early satiety, with minimal or normal endoscopy, rule out an obstructive cause. A positive gastric emptying scintigraphy should lead the doctor to the diagnosis of gastroparesis. In these cases, the early use of glucocorticoids is essential, providing an effective response.

Informed Consent: Informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

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References

1. Nusbaum JS, Mirza I, Shum J, et al. Sex differences in systemic lupus erythematosus: Epidemiology, clinical considerations, and disease pathogenesis. *Mayo Clin Proc*. 2020;95(2):384-394. [Crossref]
2. Sultan SM, Ioannou Y, Isenberg A. A review of gastrointestinal manifestations of systemic lupus erythematosus. *Rheumatology*. 1999;38:917–932. [Crossref]
3. Hasler WL. Gastroparesis—Current concepts and considerations. *Medscape J Med*. 2008; 10(1):16.
4. Soykan I, Sivri B, Sarosiek I, Kiernan B, McCallum RW. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. *Dig Dis Sci*. 1998;43(11):2398–2404. [Crossref]
5. Nassar Y, Richter S. Gastroparesis in nondiabetics: associated conditions and possible risk factors. *Gastroenterol Res*. 2018;11(5):340–345. [Crossref]
6. Petri M, Orban AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum*. 2012;64(8):2677–2686. [Crossref]
7. Posthuma EF, Warmerdam P, Chandie Shaw MP, et al. Gastric outlet obstruction as a presenting manifestation of systemic lupus erythematosus. *Gut*. 1994;35(6):841–843. [Crossref]
8. Chou J, Zheng H, Bertkenb R. Gastroparesis in systemic lupus erythematosus: a case report. *J Med Cases*. 2013;4(5):314–315. [Crossref]
9. Tack J, Carbone F, Rotondo A. Gastroparesis. *Curr Opin Gastroenterol*. 2015;31(6):499-505.
10. Aringer M. EULAR/ACR classification criteria for SLE. *Semin Arthritis Rheum*. 2019;49(3S): S14–S17. [Crossref]