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CASE BASED REVIEWS

Necrotizing mesenteric vasculitis in systemic lupus erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disorder which may affect the gastrointestinal system. Half of patients with SLE experience gastrointestinal symptoms, with the most common being nausea, vomiting, anorexia, and abdominal pain. Mesenteric vasculitis is a severe and rare complication of SLE and one of the most frequent causes of severe acute abdominal pain. The authors present the case of a 57-year-old woman with SLE who was diagnosed with necrotizing mesenteric vasculitis following a urinary septic shock. The patient was treated with high-dose corticosteroid therapy and cyclophosphamide, with resolution of the clinical picture.

Keywords: Systemic lupus erythematosus and autoimmunity; Vasculitis; Mesenteric; Necrosis; Shock.

INTRODUCTION

Systemic lupus erythematosus (SLE), a multisystemic autoimmune disorder, can be potentially severe and life threatening. It may affect any system or organ, although there is a predilection for the musculoskeletal, cutaneous, renal, and haematological systems. Even though not being seen as a commonly involved system, about 50% of patients with SLE experience gastrointestinal symptoms (mainly related to medication or infection), with the most common being nausea, vomiting, anorexia, and abdominal pain[1].

Vasculitis in SLE is relatively common, with most studies reporting a prevalence between 11% and 36%, and usually being present within a flare of the disease with other severe manifestations[2,3]. It may adopt various forms, depending on the size and type of the affected vessels, and it can be associated with some antibodies, namely antiphospholipid antibodies, causing thrombosis phnomena[1,4].

Mesenteric vasculitis, also known as lupus enteritis, is a severe and rare complication of SLE, with an estimated prevalence of 0.2-9.7%[2]. It is one of the most potentially severe manifestations of SLE, with a high mortality rate. This type of vasculitis mostly affects the superior mesenteric artery, and therefore the small bowel[2,4]. Computed tomography (CT) is considered the gold standard for diagnosis and a prompt diagnosis is essential to the prognosis of the patient.

CASE REPORT

A 57-year-old Colombian female with a 20-year history of SLE (positive anti-double stranded DNA antibodies [anti-dsDNA], antinuclear antibodies 1/1280 (homogenous pattern), positive anti-Ro(SSA), anti-La(SSB), antinuclear ribonucleoprotein (anti-RNP), anti-Ku and anti-Mi-2 antibodies, negative antiphospholipid antibodies, low levels of complement fraction [C] 3 and 4, normocytic and normochromic anaemia, malar rash, polyarthralgia, Raynaud phenomena, pleurisy, chronic kidney disease - stage III of the Kidney Disease: Improving Global Outcomes [KDIGO] classification - and peripheral nervous system involvement, with distal sensorial symmetric polyneuropathy) was admitted to the Rheumatology inward department, due to a vascular and articular flare of the disease (Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] 2K of 28 – motor neuropathy, vasculitis, arthritis, oral ulcers, malar rash, low complement, thrombocytopenia and leukopenia with lymphopenia). This followed a 1-week stay in the intensive care unit (ICU) secondary to a septic shock with origin in a urinary tract infection due to *Escherichia coli* (treated withpiperacillin/tazobactam), worsened by a hypovolemic shock as a result of dehydration. Before hospitalization, the patient had a

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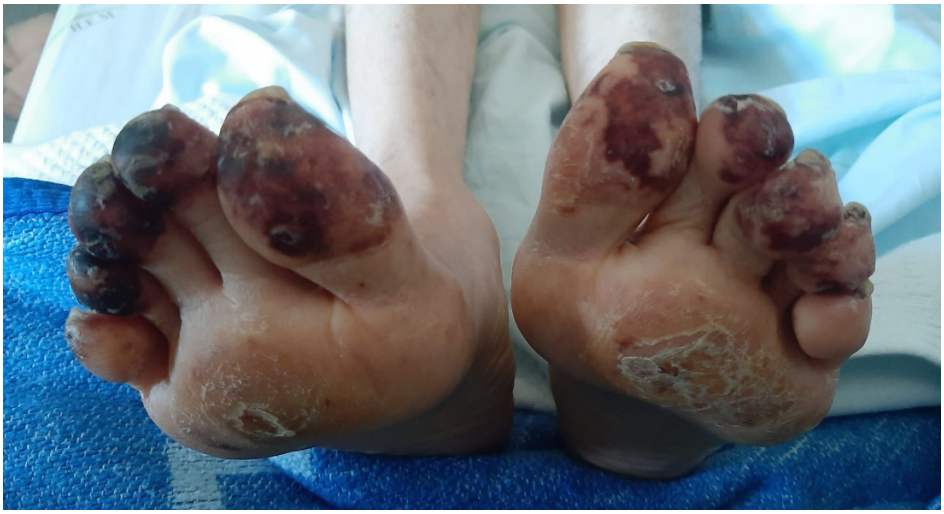

Figure 1. Plantar view of the toes of the patient – necrotic areas are seen in all toes, except the 4th, worse in the right foot (left side of the picture). Peeling of the skin is also observed.

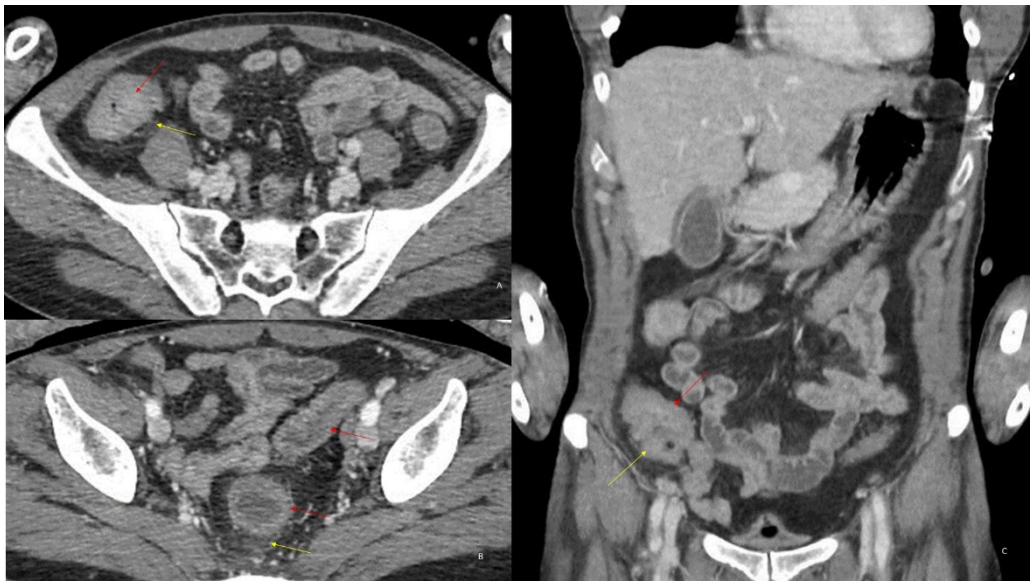

Figure 2. Axial (A and B) and coronal (C) contrast-enhanced abdominal and pelvic computed tomography images demonstrate regular concentric wall thickening involving the colon and the rectosigmoid junction (red arrows) with slightly increased attenuation of mesenteric fat (yellow arrows). Low-grade mural hyperenhancement of the sigmoid colon and rectosigmoid junction is also noted.

SLEDAI of 12 (articular and vascular complaints with Raynaud phenomena) and was medicated with prednisolone (PDN) 15mg/day, acetylsalicylic acid 100mg/day, nifedipine 30mg/day, hand topical nitroglycerin 5mg/24h, pentoxifylline 400mg twice a day, chlorthalidone 50mg/day, ramipril 10mg/day and bisoprolol 10mg/day. There was a history of intolerance to multiple drugs, including azathioprine, mycophenolate mofetil, chloroquine and hydroxychloroquine (visual complaints). The patient had no history of prior pregnancy.

At admission, she presented bloody diarrhoea and diffuse abdominal pain, digital ulcers of both feet and hands, with necrosis of several toes (Figure 1), but palpable arterial pulses (worsened by Raynaud phenomena and vasopressor therapy administered in the ICU), and polyarthralgia without arthritis. Blood analysis showed low levels of both C3 and C4 (C3 27mg/dL; C4 4mg/dL) and undetectable CH50, high titres of anti-dsDNA (387.5 UI/mL), anaemia (haemoglobin 8.8 g/dL, mean corpuscular volume 89.4 fL, mean corpuscular haemoglobin concentration 338 g/dL), leukopenia (3 390/uL)

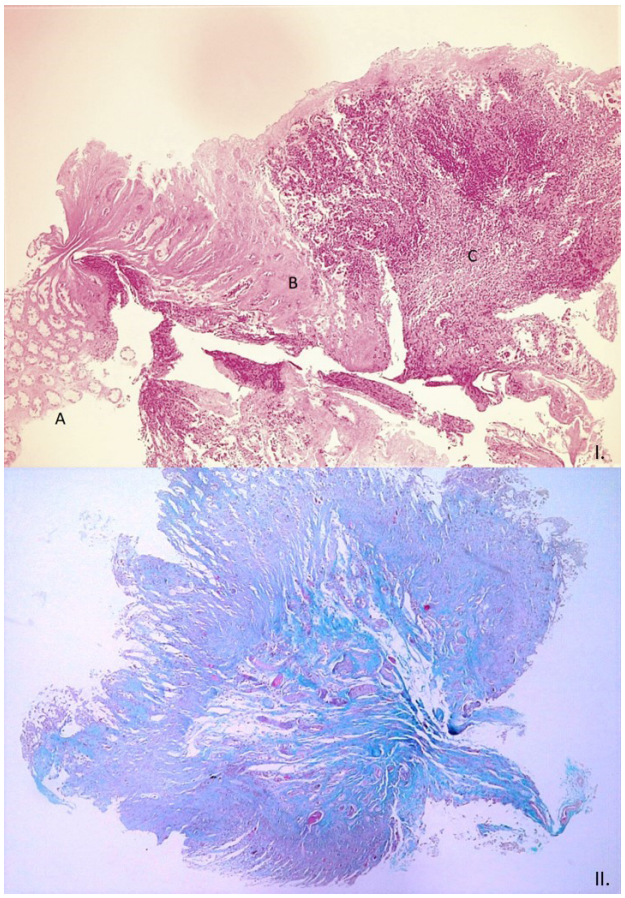

Figure 3. Fragments of the mucosa of the colon observed with haematoxylin and eosin (I) and Masson's trichrome staining (II), both with amplification 10X. A necrotizing inflammatory process with large ulceration, fibrinous-granulocyte exudate and blood vessel hyalinization is seen in the images (A – "Ghost" crypts; B – Necrosis; C – Inflammatory cells and debris). In II., Masson staining highlights the smooth muscle fibers (in blue) and the necrotic mucosa. Posterior staining with Congo red was negative for amyloid deposits and the immunochemistry for both cytomegalovirus and herpes simplex 1 and 2 was also negative.

and thrombocytopenia (25 000/uL); antiphospholipid antibodies were absent. Urinalysis showed haematuria and pyuria, with an *Enteroccocus faecium* isolated (for which vancomycin was administered).

Due to the GI symptoms, a contrast-enhanced abdominal CT scan was performed and revealed wall thickening involving the colon and the rectosigmoid junction, with slightly increased attenuation of mesenteric fat (Figure 2). Small bowel segments were spared in the images. Colonoscopy showed ulcerate areas mainly located in the sigmoid and rectum; local biopsies presented a necrotizing inflammatory process with large ulceration and fibrinous-granulocyte exudate (Figure 3) and the immunochemistry was negative for both cytomegalovirus and herpes simplex infection.

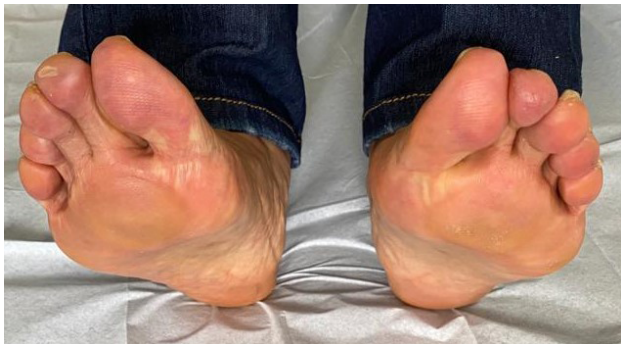

Figure 4. Plantar view of the toes of the patient six months after the pictures presented in Figure 1 – note the total resolution of the necrosis, with residual telangiectasias observed.

Stool sample culture tests were negative.

The case was discussed with the gastroenterology team. Considering the exclusion of an active infection and the resolution of the septic and hypovolemic shock, and the high disease activity of SLE, the conclusion was in favour of a necrotizing mesenteric vasculitis due to SLE. Pulses of methylprednisolone were administered (1000mg/day; 3 days), followed by PDN 1mg/kg/day and hydroxychloroquine 400mg/day (ophthalmological evaluation was negative for maculopathy related with the drug). Cyclophosphamide was also started according to the NIH regimen[5]. CT scan was repeated after the first cycle of cyclophosphamide, with complete resolution of the colonic wall thickening. Digital ulcers and necrosis of the toes also improved with therapy. Considering her clinical stability, the patient was discharged and followed in the outpatient clinic with a scheduled cyclophosphamide scheme. After completing it, rituximab was adopted as maintenance therapy (1000mg biweekly in a six-month interval) and, during a 24-month period of follow-up, there was no recurrence of the GI symptoms and there was a complete resolution of the digital ulcers and necrosis (Figure 4). Antiphospholipid antibodies remained undetectable in a follow-up study.

DISCUSSION

Lupus mesenteric vasculitis is a rare and severe manifestation of SLE. The British Isles Lupus Assessment Group's disease activity index (BILAG) -2004 includes lupus enteritis or colitis as one of the items to assess, defining it as a vasculitis or inflammation of small or large bowel (alongside imaging and/or histopathological findings)[6]. Its pathophysiology is complex but usually involves one of two mechanisms: inflammation,

due to immunocomplex deposition or thrombosis, frequently associated with antiphospholipid antibodies[7]. All of the intestinal layers may be affected, with several degrees of involvement, ranging within segmental oedema, ulcers, perforation and haemorrhage, eventually leading to death[3,7]. Endoscopic exams have a high risk of complications due to the frailty of the intestinal wall, and should be carefully performed. They do not always convey a definitive diagnosis as the deeper layers may not be biopsied[7]. Abdominal CT scan with contrast is considered the gold standard for the diagnosis, showing, as it was observed in this patient, dilatation of intestinal segments and increased attenuation of mesenteric fat, as well as wall oedema and prominence of mesenteric vessels[4]. Reports show a predominance of small bowel rather than large bowel involvement, with Wang et al. revealing a prevalence of 82% of jejunum/ileum involvement in a cohort of 50 SLE patients[1,4,8,9]. This predominance explains the common use of the term lupus enteritis. Notably, the patient described in this case report presented with an exclusive involvement of colon and rectosigmoid junction, without images suggesting small bowel implication, which emphasizes the rarity and relevance of this description.

Treatment varies considering the severity of manifestations and the hemodynamic state of the patient. High dose corticosteroid therapy is the primary approach, although cyclophosphamide may be needed. If there is no positive response to the immunosuppressive treatment, surgery may be required. Although necrosis is a possible complication of the disease, with some studies reporting a prevalence around 8%, this is one of the few cases published reporting a necrotizing form of mesenteric vasculitis[9–12].

This severe manifestation followed a urinary septic shock. One may wonder if the urinary abnormalities were part of an already onset of SLE flare or the trigger for this episode. An Escherichia coli was isolated from the urine prior to the administration of cyclophosphamide; furthermore, with appropriate antibiotic therapy, a sterile urine was obtained, and haematuria and pyuria resolved, which suggest the possible role of infection as a trigger for flares of autoimmune diseases such as SLE.

CONCLUSION

Mesenteric vasculitis is a rare and potentially fatal manifestation of SLE. A fast diagnosis is essential to change the prognosis of the patient. This case enhances the rarity of some SLE manifestations and the importance of a holistic approach in SLE patients.

REFERENCES

1. Brewer BN, Kamen DL. Gastrointestinal and Hepatic Disease in Systemic Lupus Erythematosus. Rheumatic Disease Clinics of North America 2018; 44: 165-175. https://doi.org/10.1016/j.rdc.2017.09.011
2. Barile-Fabris L, Hernández-Cabrera MF, Barragan-Garfias JA. Vasculitis in Systemic Lupus Erythematosus. Curr Rheumatol Rep 2014; 16: 440. https://doi.org/10.1007/s11926-014-0440-9
3. Ebert EC, Hagspiel KD. Gastrointestinal and Hepatic Manifestations of Systemic Lupus Erythematosus. J Clin Gastroenterol 2011; 45: 436-441. https://doi.org/10.1097/MCG.0b013e31820f81b8
4. Leone P, Prete M, Malerba E, et al. Lupus Vasculitis: An Overview. Biomedicines 2021; 9: 1626. https://doi.org/10.3390/biomedicines9111626
5. Austin HA, Klippel JH, Balow JE, et al. Therapy of Lupus Nephritis. New England Journal of Medicine 1986; 314: 614-619. https://doi.org/10.1056/NEJM198603063141004
6. Isenberg DA, Rahman A, Allen E, et al. BILAG 2004. Development and initial validation of an updated version of the British Isles Lupus Assessment Group's disease activity index for patients with systemic lupus erythematosus. Rheumatology 2005; 44: 902-906. https://doi.org/10.1093/rheumatology/keh624
7. Ju JH, Min JK, Jung CK, et al. Lupus mesenteric vasculitis can cause acute abdominal pain in patients with SLE. Nat Rev Rheumatol 2009; 5: 273-281. https://doi.org/10.1038/nrrheum.2009.53
8. Wang H, Gao Q, Liao G, et al. Clinico-Laboratory Features and Associated Factors of Lupus Mesenteric Vasculitis. Rheumatol Ther 2021; 8: 1031-1042. https://doi.org/10.1007/s40744-021-00323-x
9. Janssens P, Arnaud L, Galicier L, et al. Lupus enteritis: from clinical findings to therapeutic management. Orphanet J Rare Dis 2013; 8: 67. https://doi.org/10.1186/1750-1172-8-67
10. Wang Z, Wu C, Ruan F, et al. A case of systemic lupus erythematosus with rectal necrosis. Lupus 2020; 29: 334-339. https://doi.org/10.1177/0961203319897130
11. Ch R, Vaithiyam VS, Manchanda S, et al. A 23-Year-Old Woman With a Rare Presentation of Systemic Lupus Erythematosus and Its Complication. Chest 2021; 160: e661-e664. https://doi.org/10.1016/j.chest.2021.02.079
12. Zh Moskova, G Mikhaĭlov, A Donkova. Sluchaĭ na nekrotizirasht enterit kato pŭrva iziava na sistemen lupus eritematodes [Case of necrotizing enteritis as the first symptom of systemic lupus erythematosus]. Vutr Boles.