Case report

*Salmonella enteritidis* infection in patients with systemic lupus erythematosus

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**A B S T R A C T**

*Salmonella enteritidis* infection (SEI) is rare in systemic lupus erythematosus (SLE) patients, and it is often mistaken with SLE flares. SEI in SLE patients has been associated with a poor outcome. A description is presented of the clinical features and outcomes of five patients with an SEI from a cohort of 325 patients with SLE (1.53%). All patients were women, with a mean age of 28.2 years (14 to 37 years). Mean duration of SLE before clinical SEI was 3.2 years (1 to 7 years). There was no evidence of recurrent infection. The patients were treated with ciprofloxacin and/or ceftriaxone, with resolution of clinical manifestations in four of them. One patient died due to multisystem organ failure. Our report highlights the unspecific clinical manifestations of SEI that resembles lupus flare-up. An accurate diagnosis and early antibiotic treatment are essential to improve their outcomes.

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**Infección por Salmonella enteritidis en pacientes con lupus eritematoso sistémico**

**R E S U M E N**

La infección por *Salmonella enteritidis* (ISE) es rara en pacientes con lupus eritematoso sistémico (LES), y comúnmente se confunde con exacerbaciones del LES. ISE en pacientes con LES se ha relacionado con malos desenlaces. Este artículo describe los hallazgos clínicos y desenlaces de 5 pacientes con LES y diagnóstico de ISE, en una cohorte de 325 pacientes (1.53%), Todos los pacientes fueron mujeres, con una edad promedio de 28.2 (14 a 37 años). La duración promedio del LES antes de la ISE clínica fue de 3.2 años (1 a 7 años). No hubo evidencia de infección recurrente. Los pacientes fueron tratados con ciprofloxacino o ceftriaxona, con resolución de las manifestaciones clínicas en 4 pacientes.

**Palabras clave:**

Salmonella enteritidis
Lupus eritematoso sistémico
Tratamientos inmunosupresores
Tratamiento antibiótico

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Un paciente murió debido a falla orgánica multisistémica. Nuestro reporte remarca las manifestaciones clínicas inespecíficas de la ISE que asemeja actividad lupica. Un adecuado diagnóstico y una terapia antibiótica temprana son esenciales para mejorar los desenlaces de estos pacientes.

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**Introduction**

Patients with systemic lupus erythematosus (SLE) are highly susceptible to infections, either due to immune dysfunction associated with the pathology or secondary to immunosuppressive treatments. Infections are a cause of higher morbidity and mortality in these patients, added to the neurological and renal commitment of lupus activity by itself. Salmonella enteritidis – S. enteritidis infection (SEI) is a rare but recognized complication in patients with SLE, it is associated with non-specific clinical manifestations, and it is often mistaken with lupus flares. Several cases of SEI have been described, most of them have common risk factors such as treatments with steroids and immunosuppressants, renal involvement, vasculitis and low complement levels. A high mortality has been described in these patients (around 20%). Here, we report 5 new cases of SEI in patients with SLE and their particular form of presentation.

**Methods**

A retrospective analysis of patients with SLE and positive cultures for S. enteritidis was conducted in order to describe their clinical characteristics. These patients were evaluated between August 2001 and June 2015 in the Valle del Lili Foundation, a fourth level institution in Cali (Colombia). We identified 5 female patients with SEI from a cohort of 235 patients with SLE (1.53%). At the time of the SEI all patients had active lupus and were receiving steroids and immunosuppressive treatment.

**Patient number 1**

A 48-year-old female patient with a diagnosis of SLE and initial manifestations consisting of pleuritis, pericarditis, severe Raynaud’s phenomenon with digital necrosis of the distal phalanx of the fourth finger of the right hand, cutaneous (discoïd rash), and hematological (leukopenia, hemolytic anemia) commitment, complement consumption, class III lupus glomerulonephritis and high positive antibody titers (ANA, anti-DNA, anti-Sm and anti-Ro), with requirement for induction with pulses of methylprednisolone and cyclophosphamide until completing 6 cycles with clinical improvement and on maintenance treatment with prednisolone (10 mg/kg/day) and azathioprine (2 mg/kg/day). The patient consulted for a clinical picture of 6 days of evolution consisting of general malaise, fever, headache, asthenia, emesis and erythematous rash. On physical examination with evidence of tachycardia (HR: 116 beats per minute), arterial hypotension (84/48 mmHg), fever (39.2 °C) and generalized rash. No other clinical findings suggestive of lupus activity were found. The laboratories showed mild anemia (Hb: 10.8 g/dl), leukocytes 10,450/mm³, neutrophils 72%, complement (C3: 55 mg/dl and C4: 8 mg/dl), creatinine 1.6 mg/dl, 24-h proteinuria of 750 mg. The acute phase reactants were elevated (ESR: 66 mm/h, C-reactive protein: 16 mg/dl), and the blood cultures were positive for S. enteritidis confirming active infection, so treatment was initiated with intravenous ciprofloxacin 200 mg/every 8 h for 14 days, with which the patient presented a favorable evolution and total resolution of the clinical picture.

**Patient number 2**

A 37-year-old woman with a long-standing diagnosis of SLE, with class III lupus glomerulonephritis, polyarthritis, Jaccoud’s arthropathy, discoïd rash, Libman-Sacks endocarditis, complement consumption, positive ANA 1:640 speckled pattern, positive anti-DNA, anti-Sm, and ant cardioliopin antibodies. Currently managed with prednisolone 7.5 mg/day, azathio- prine 50 mg/day, and warfarin, and who had required the use of rituximab 2 years before due to severe articular and cutaneous involvement refractory to the initial management. The patient consulted to the emergency department for a clinical picture of 7 days of evolution, consisting in fever, adynamia, myalgias, headache, abdominal pain predominantly in the mesogastrium and diarrhea. The physical examination evidenced bradycardia (HR: 47 beats per minute), blood pressure 114/66 mmHg, respiratory rate: 18 breaths per minute, fever (T: 38.9 °C) and signs of moderate dehydration. The laboratories showed anemia (Hb: 11.2 g/dl), leukopenia (leukocytes: 3900/µl), neutrophils: 2700 µl, lymphopenia: 850 µl, mild thrombocytopenia (platelets: 127,000 µl), complement (C3: 90 mg/dl and C4: 22 mg/dl), creatinine 1.3 mg/dl. The stool culture was positive for S. enteritidis for which the infectology service started treatment with ciprofloxacin 1000 mg daily, for 14 days, with a complete improvement of the clinical picture.

**Patient number 3**

A 14-year-old female patient, who was diagnosed with SLE one year before admission, with cutaneous and hematological (lymphopenia and thrombocytopenia) manifestations and class III lupus glomerulonephritis (focal glomerulonephritis) treated with steroids and cyclophosphamide in the induction phase with subsequent maintenance management with
prednisolone and azathioprine. She consulted the emergency department for a clinical picture of 10 days of evolution consisting of marked deterioration of her general condition, fever, asthenia, joint pain and generalized erythematous rash. When performing the physical examination, she had bradycardia (HR: 40 beats per minute), arterial hypotension (86/50 mmHg), fever (T: 39.6 °C) and eruptive rash. The laboratories showed a marked elevation of ESR 120 mm/h and CRP 22 mg/dl, low complement (C3: 40 mg/dl and C4: 9 mg/dl), renal function within normal ranges (0.7 mg/dl), and the blood cultures were positive for *S. enteritidis* at 9 h, for which she received antibiotic coverage with ceftriaxone 1000 mg/day, during 14 days, with a complete improvement of the clinical picture and without clinical signs of relapse of the autoimmune disease.

**Patient number 4**

A 14-year old adolescent girl with a diagnosis of antiphospholipid syndrome and SLE of 3 years of evolution with multisystemic compromise given by articular component, maculopapular rash, class IV lupus nephritis, lymphopenia, thrombocytopenia, psychosis related to involvement of the central nervous system, and an antecedent of mechanical prosthetic mitral valve due to Libman-Sacks endocarditis. The patient consulted for a clinical picture of 4 days of evolution consisting of myalgias, asthenia and fever. The physical examination showed tachycardia (105 beats per minute), fever (39 °C), without the presence of heart murmurs, with signs of moderate dehydration. The laboratory tests showed anemia (Hb: 9.6 g/dl), creatinine: 1.4 mg/dl, complement consumption (C3: 35 mg/dl and C4: 6 mg/dl). A transesophageal echocardiogram was performed, ruling out endocarditis. Blood cultures were taken, which were positive for *S. enteritidis* at 14 h of incubation. Management was started with ceftriaxone 1000 mg/day for 2 weeks. The patient presented a satisfactory response to the antibiotic treatment with complete resolution of the symptomatology.

**Patient number 5**

A 28-year old female patient with a diagnosis of SLE given by central nervous system vasculitis, arthritis, hemolytic anemia, class IV lupus nephritis, complement consumption, positive ANA, anti-DNA and anti-Sm antibodies; was admitted to the institution for a clinical picture of 2 days of evolution consisting of fever, adynamia, diarrhea, chest pain, cough and progressive dyspnea. On physical examination the patient presented tachycardia (120 beats per minute), arterial hypotension (76/40 mmHg) and fever (39.4 °C). The paraclinical tests on admission evidenced CRP: 90 mg/dl, ESR: 70/h, creatinine: 2.1 mg/dl, leukocytes: 23,000/mL (lymphocytes: 800/mL, neutrophils: 21,900/mL), and lactic acid 3 mEq/l. It was considered that the patient had a severe sepsis which required management in the intensive care unit and empiric broad-spectrum antibiotic coverage with cefepime and vasopressor support. The blood cultures were positive for *S. enteritidis* at 12 h of incubation. Coverage was adjusted with intravenous ceftriaxone and ciprofloxacin; however, the patient developed multi-organ dysfunction and died.

**Discussion**

Two forms of clinical presentation of SEI are relevant: (1) with intestinal manifestations: gastroenteritis or enteric fever and (2) with extraintestinal manifestations. This last form of clinical presentation in the patient with SLE can be difficult to detect, since it can be mistaken with symptoms related to SLE such as lymphopenia, thrombocytopenia, fever, arthralgia or pulmonary involvement. The findings in the laboratory tests most commonly found in the SEI, in patients with SLE, include the presence of anemia and lymphopenia (90%), leukocytosis (50%), thrombocytopenia (20%) and increased PCR (96%). All these findings were seen in our patients. The definitive diagnosis is based on positive cultures in blood or other fluids or tissues. The initial diagnosis in our patients was a SLE flare or infection.

The diagnosis of the SEI was established rapidly thanks to the positive culture. All patients were treated with antibiotics (ciprofloxacin or ceftriaxone) with resolution in all except one; one patient died due to a severe lung affection. The conditions that resemble lupus are not rare and are associated with a wide range of etiologies, including infections and malignant and benign neoplasms. A high index of suspicion of SEI in patients with SLE, with systemic symptoms is necessary to establish an early diagnosis and an opportune treatment.

**Ethical disclosures**

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

**Conflict of interest**

The authors declare they do not have any conflict of interest.

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