LETTERS TO THE EDITOR

Juvenile systemic lupus erythematosus triggered by Lamotrigine

Barbosa Rodrigues A[1], Oliveira-Ramos F[1], Costa-Reis P[1]

Dear Editor,

Drugs can participate in systemic lupus erythematosus (SLE) pathogenesis and reveal clinically silent SLE, induce flares in patients with known SLE diagnosis or cause lupus-like syndromes. The most frequent drugs are hydralazine, procainamide, quinidine, isoniazid, minocycline, phenytoin, carbamazepine, diltiazem and TNFα inhibitors[1]. It is estimated that 10% of SLE cases are drug-induced[3]. Symptoms normally occur weeks to months after drug initiation[1]. Most patients have one or more criteria for SLE, but they don't necessarily meet the 2019 EULAR/ACR classification criteria.

Discontinuation of medication is recommended. If symptoms are severe, immunosuppressive drugs should be given. Generally, there is resolution of symptoms and gradual normalization of serologic abnormalities[1,3,4,6], however, some patients may maintain lupus-like symptoms, while others may develop SLE.

Lamotrigine is an anticonvulsant drug and it is also effective in the treatment of bipolar disorder.[5] Between 5 to 10% of the patients treated with lamotrigine develop skin reactions, which can be life threatening, including Stevens–Johnson syndrome, drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) and toxic epidermal necrolysis. Drug induced lupus erythematosus associated with lamotrigine has been very rarely described[3,4,6,9].

We would like to report a 17-year-old female, with panic and generalized anxiety disorders, who was being treated with quetiapine and propranolol for more than one year and who started lamotrigine one month before being admitted to the hospital.

The patient presented with a three-week history of daily fever, fatigue, odynofagia, arthralgias and myalgias. There were no manifestations of serositis or neurological involvement. On physical exam it was identified a diffuse erythematous maculopapular rash, a vasculitic rash of the fingers, and lips and vulvar edema. Alopecia, oral and nasal ulcers, organomegalies and arthritis were not detected. On the blood tests, it was found leukopenia (3920/µL), lymphopenia (880/µL) and a slightly elevated C-reactive protein (2.9mg/dL). Renal function and urine analysis were normal. Serologies were negative for cytomegalovirus, Epstein Barr, parvovirus, coxsackie, echovirus, herpes virus, *Mycoplasma pneumoniae* and Chlamydia. It was detected low serum C3 (59 mg/dL; [90-180 mg/dL]) and C4 levels (9 mg/dL [10-40 mg/dL]) and antinuclear (1:320), anti-double stranded DNA (anti-dsDNA) (50.5 UI/mL [<27 UI/mL]) and anti-Ro (SSA) antibodies (163.2 UQ [< 20 UQ]).

Lamotrigine was stopped and an immediate clinical improvement occurred. The patient became afebrile and there was a regression of the maculopapular rash in less than 24 hours. No anti-histone antibodies were found 3 months after lamotrigine withdrawal. C3 and C4 levels remained below normal ranges and anti-dsDNA antibodies persisted elevated (maximum value 148.9 UI/mL). Treatment with hydroxychloroquine was started. The patient remained asymptomatic for two years. Recently, she developed photosensitivity and had a new vasculitic rash on the fingers, which improved with a short course of steroids.

In conclusion, we describe a rare case of juvenile SLE triggered by lamotrigine, who presented with diffuse erythematous rash, leukopenia, low C3 and C4 levels, antinuclear, anti-dsDNA and anti-Ro antibodies. The patient met the 2019 EULAR/ACR SLE criteria. Four patients have been described with lamotrigine-induced lupus[3,4,6,9], none with anti-histone antibodies identified (not reported[4,6,9] or described as negative[3]). There are no case reports known in pediatrics.

The symptoms began after the initiation of lamotrigine and the withdrawal of the drug was essential for initial clinical improvement. Nevertheless, autoantibodies remained positive, with consumption of C3 and C4. The patient relapsed after two years, which supports the hypothesis that lamotrigine might have been the trigger for juvenile SLE in a genetically predisposed individual. A thorough clinical history, including previous medications, should be performed in all patients with lupus like symptoms, in order to identify possible triggers and, when feasible, eliminate the exposure and improve the outcome of the patients.

[1] Pediatric Rheumatology Unit, Hospital de Santa Maria, Lisbon, Portugal / CHULN

Submitted: 07/12/2021
Accepted: 27/02/2022

Correspondence to: Ana Barbosa Rodrigues
E-mail: acatbrodrigues@gmail.com

REFERENCES

1. Vaglio A, Grayson PC, Fenaroli P, Gianfreda D, Boccaletti V, Ghiggeri GM et al. Drug-induced lupus: traditional and new concepts. Autrev 2018; 17(9):912-918
2. Vedove CD, Giglio M, Schena D, Girolomoni G. Drug-induced lupus erythematosus. Arch Dermatol Res 2009; 301:99-105
3. Ravindran V. Lamotrigine-induced lupus: a case report. Int J Rheum Dis 2011; 14: e47-48
4. Batra J, Kaur S, Kaushal S, Singh A. Lamotrigine-induced Systemic Lupus Erythematosus: A Diagnostic Dilemma. Indian DermatolOnline J 2018; 9(6):445-447
5. Prabhavalkar KS, Poovanpallil NB, Bhatt LK. Management of bipolar depression with lamotrigine: an antiepileptic mood stabilizer. Front Pharmacol 2015; 6:242
6. Chang RS, Cole AJ. Lamotrigine-Induced Lupus-Like Syndrome: A Case Report and Literature Review. Am J Ther 2014; 21(3):e85-7
7. Tsokos GC, Lo MS, Reis PC, Sullivan KE. New insights into the immunopathogenesis of systemic lupus erythematosus. Nat Rev Rheumatol 2016;12(12):716-730
8. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortinn PR et al. Derivation and Validation of Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheum. 2012; 64(8):2677-2686
9. Sarzi-Puttini P, Panni B, Cazzola M, Muzzupappa S, Turiel M. Lamotrigine-induced lupus. Lupus 2000; 9:555-557
10. He Y, Sawalha A. Drug-induced lupus erythematosus: an update on drugs and mechanisms. Co-rheumatology 2018; 1040-8711