Age and Ageing 2015; **44:** 1062–1063
doi: 10.1093/ageing/afv123
Published electronically 28 September 2015

CASE REPORT

Drug-induced lupus erythematosus associated with donepezil: a case report

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Abstract

The possibility that drug-induced lupus erythematosus (DILE) can be induced by donepezil is presented in this clinical case. Donepezil is an inhibitor of acetylcholinesterase used for the treatment of Alzheimer's disease. It is the first time that donepezil causes DILE.

Keywords: *donepezil, Alzheimer's disease, drug-induced lupus erythematosus, older people*

The occurrence of systemic lupus erythematosus (SLE) as a result of pharmacological treatments is a condition named drug-related lupus (DRL) or drug-induced lupus erythematosus (DILE). This disorder has been described for the first time in 1945 by Hoffman [1]. We report the clinical case of an 80-year-old woman in which a framework of DILE was induced by donepezil. On November 2012, this woman came to our attention for the skin rash on her face (Figure 1), widespread arthromyalgia mainly in the lower limbs, dyspnoea and positive antinuclear antibodies (ANA) (1:640, homogeneous pattern on HEp-2 cells). For >20 years, she was on therapy with antihypertensive, nitroderivative patch 5 mg, aspirin 100 mg, 300 mg allopurinol and omeprazole 10 mg. Two months earlier, after an examination at the Alzheimer Evaluation Unit (AEU) located in her district, she had started a therapy with donepezil (10 mg) for primary dementia of the Alzheimer type. After evaluation (Table 1), the replacement of donepezil with memantine 20 mg/day (according to International titolation) was suggested. The replacement of donepezil was necessary for the elongation of the QTc, whereas the introduction of memantine was justified by the absence of cardiac side-effects associated with this drug. After this change, we observed complete disappearance of polyarthralgias and myalgias, the resorption of pericardial effusion, the normalisation of CRP and of QTc with progressive reduction of ESR (32), ANA (1:160) and antihistone antibodies until their clearance (Table 1). On July 2013, the patient autonomously decided to take some tablets of donepezil that she still had at home (she had finished the memantine and neither the primary care physician nor the AEU specialist was available). After a week of this occasional reintroduction, polyarthralgias with marked functional limitation, widespread myalgia and petechiae in the legs associated with other manifestations reappeared. In Table 1, we display all the results on the drug, after drug withdrawal and after its occasional new intake. She was advised to give back the residual donepezil to her geriatrician. We gave prednisone 25 mg/day in the first week, followed by gradual dose reduction. Currently, she continues the treatment with memantine. She has no longer presented any manifestation compatible for SLE. The study on her HLA type did not provide any significant information; for example HLA-DR2, DR3 and B8 (usually present in patients affected by LES) were absent. In the elderly subjects, frequently treated

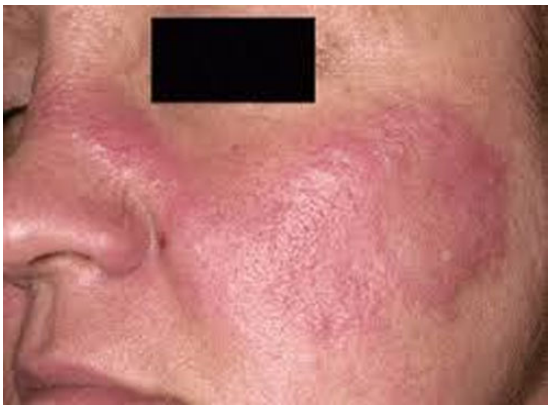

Figure 1. Malar rash appeared in our patient during therapy with donepezil.

Table 1. Clinical, laboratory and instrumental data in our patient

On the first assumption of donepezil (2 months earlier)
Clinical manifestation
Skin rash on her face (Figure 1)
Dyspnoea
Widespread arthromyalgia mainly in the lower limbs
Laboratory data
ESR = 48 mm/h
CRP = 18 mg/l versus <6
ANA = 1:640, homogeneous pattern on HEp-2 cells
Absence of anti-ENA and of anti-dsDNA antibodies
High anti-histone antibodies (+++)
BUN = 67 mg/dl (<50); creatinine = 1.57 mg/dl (<1.10 mg/dl)
The presence of red blood cells (RBC) and RBC casts in the urine
Normal values of complement factors 3 and 4 (C3, C4)
Normal liver and thyroid indices
Instrumental data
Echocardiogram: pericarditis with minimum circumferential pericardial effusion on
ECG: elongation of QTc (0.51 s, reference values <0.48)
After donepezil withdrawal
Progressive disappearance of the rash
Complete disappearance of polyarthralgias and myalgias
Resorption of pericardial effusion
Normalisation of CRP and QTc
Reduction of ESR (=32 mm/h), ANA (1:160, homogeneous pattern)
Anti-histone antibodies progressively decreasing until clearance
Progressive normalisation of urinary sediment
After donepezil re-introduction (a week)
Polyarthralgias with marked functional limitation, widespread myalgia
Petechiae in the legs
Gross haematuria and RBC casts at microscopic examination of the urine sample
ESR = 47 mm/h; PCR = 6 mg/l; RBC = 2,450,000 mmc/l with Hb = 8.8 g/dl; platelets = 25,000 mmc/l; normal white blood cells and values of C3; C4 = 8 g/dl (>20)
ANA = 1:1,320 (homogeneous pattern); absence of anti-ENA and anti-dsDNA antibodies; recurrence of anti-histone antibodies (++)
Normal liver and thyroid indices; creatinine = 1.87 mg/dl versus <1.10 mg/dl
Pericarditis was excluded by a control echocardiography. An ECG control revealed QTc elongation (0.50 s versus <0.48)

with many drugs, determining what is (or may be) the responsible one for DILE is problematic. Besides, some manifestations of DILE are comparable with those of late-onset idiopathic SLE [2]. Donepezil is an inhibitor of acetylcholinesterase used for the treatment of Alzheimer's disease. Our patient presented a DILE induced by donepezil. The drug withdrawal caused the spontaneous regression and its occasional reintroduction caused the re-appearance of a frame compatible with SLE. The slight discordance in the manifestations after the first and the second cycles of donepezil does not exclude the diagnosis of DILE, because it is known that the same drug can induce different frameworks even in the same patient [3, 4]. After the second episode, no manifestations compatible with SLE appeared. No additional reports about donepezil-induced DILE are present in the literature [5].

Key points

- Drug-induced lupus erythematosus induced by donepezil.
- Donepezil in Alzheimer's disease.
- Cardiotoxicity by donepezil.

Conflicts of interest

None declared.

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Received 22 March 2015; accepted in revised form 17 June 2015