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C) BRIEF CASE REPORT

Hepatitis C virus infection, interferon α and lupus; a curious combination

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To the Editor,

Drug-induced lupus is a syndrome that shares clinical and analytical characteristics with idiopathic systemic lupus erythematosus and which appears after exposure to certain drugs that induce autoantibody formation.

In 1945, Hoffman described the first case of drug-induced lupus, which involved the antibiotic sulfadiazine as the agent responsible for the condition. Eight years later, in 1953, Morrow et al. published a new case relating to the use of hydralazine¹. Since then, the list of associated drugs has continued to increase and in recent years, biological therapies, such as tumour necrosis factors (TNF) and interferons (IFN), have joined with classic agents, such as procainamide, the aforementioned hydralazine, isoniazid or minocycline^{2,3,4}.

The mechanism causing this condition has not been fully defined; immunogenetic (certain HLA alleles) and pharmacogenetic (slow acetylator phenotype) factors appear to play an important role in its aetiopathogeny^{1,5}.

In terms of clinical presentation, the most common symptoms are fever, general malaise, muscle pain, joints pain, arthritis, rash and serositis. Unlike idiopathic lupus, kidney, haematologic and nervous system disorders are uncommon⁶. Antihistone antibodies are typical laboratory findings. Hypocomplementaemia and anti-double-stranded DNA, characteristics of idiopathic lupus, tend to be absent, although the latter can test positive in cases of anti-TNF- or IFN-induced lupus (Table 2).

The interval of time between starting the drug and the condition appearing is highly variable, being between 2 weeks and 7 years in the case of IFN- α ; a case developing two months after the drug's suspension has been described⁷.

This condition's prognosis is favourable, such that discontinuation of the

responsible drug is followed by recovery in the majority of cases, in a time frame that can stretch from weeks to months. Until then, non-steroidal anti-inflammatory drugs (NSAID), hydroxychloroquine and low-dose systemic corticosteroids can be used temporarily to control symptoms.

CASE

We present a 51-year-old male, with chronic kidney failure secondary to IgA glomerulonephritis, on a periodic haemodialysis programme, hypertensive, an ex-user of cocaine by inhalation and with chronic hepatitis C virus (HCV) disease, for which reason he was treated with ribavirin and pegylated IFN- α (180 μ g per week) for 49 weeks, obtaining a sustained viral response. Two weeks after finishing this treatment, he sought consultation due to asthenia and generalised joint pain of 10-15 days evolution, also experiencing in the last 48 hours 38 °C fever and increased right hip pain. In the physical examination he presented pain on moving the aforementioned joint, with neither functional weak-

Table 1. Medicines associated with drug-induced lupus⁴

Medicines definitively associated with drug-induced lupus		
Chlorpromazine	Methyl dopa	Procainamide
Isoniazid	Minocycline	Quinidine
Hydralazine		
Medicines possibly associated with drug-induced lupus		
Acebutolol	Phenylbutazone	Para-aminosalicylic
Acecaide	Phenytoin	Penicillamine
Nalidixic acid	Phenopyrazone	Penicillin
Adalimumab	Fluvastatin	Perazine
Allopurinol	Griseofulvin	Perphenazine
Aminoglutethimide	Guanoxan	Pyrazinamide
Amoprofan	Ibuprofen	Pyridoxine
Anthiomaline	Infliximab	Practolol
Atenolol	Interferon- α	Promethazine
Atorvastatin	Interferon- γ	Propafenone
Benoxaprofen	Interleukin-2	Propylthiouracil
Captopril	Labetalol	Propranolol
Carbamazepine	Leuprolide	Psoralen
Chlorprothixene	Levodopa	Quinidine
Chlorthalidone	Levomepromazine	Reserpine
Cimetidine	Lithium	Simvastatin
Cinnarazine	Lovastatin	Sulindac
Clonidine	Mephyton	Sulfadimethoxine
Danazol	Mesalazine	Sulfamethoxy-pyridazine
Diclofenac	Methimazole	Sulfasalazine
Diphenylhydantoin	Methysergide	Tetracyclines
Disopyramide	Methylthiouracil	Tetracin
Enalapril	Metoprolol	Thioamide
Spiroolactone	Metrizamide	Thioridazine
Streptomycin	Minoxidil	Timolol
Oestrogens	Nitrofurantoin	Tolazamide
Etanercept	Nomifensine	Tolmetin
Ethosuximide	Oxyphenisatin	Trimethadione
Ethylphenacemide	Oxprenolol	

Table 2. Characteristics of spontaneous and drug-induced lupus⁶

Clinical characteristics	Spontaneous lupus	Drug-induced lupus
Constitutional symptoms	83%	50%
Arthralgia and arthritis	90%	95%
Pleuropericarditis	50%	50%
Hepatomegaly	25%	25%
Rash	74%	10-20%
Kidney disease	53%	5%
Central nervous system disorder	32%	0%
Haematological abnormalities	Common	Uncommon
Immunological abnormalities		
- ANA	95%	95%
- Anti-RNP	40-50%	20%
- Anti-Sm	20-30%	Rare
- Anti-dsDNA	80%	Rare
- Antihistone	60-80%	90-95%
- Complement	Bajo	Normal

ness nor inflammatory signs at this level nor in other joints. The increase of acute-phase reactants (C reactive protein was 9, ESR 120 and neutrophilia) stood out in the laboratory analysis. Blood cultures were taken (which were sterile) and, in order to rule out septic arthritis, an ultrasound of the joint was requested, which did not show signs of arthritis nor joint fluid on being drained and analysed. An echocardiogram ruled out endocarditis. In the study undertaken to rule out tumours/inflammation (bone scan, body gallium scan and chest/abdominal/pelvic CT scan), degenerative changes were only observed in the scapulohumeral, glenohumeral and coxofemoral joints, with no other significant findings. The autoimmunity test was positive for ANA (IIF) at titres of 1:80 and anti-chromatin (antihistone), with negative anti-dsDNA and normal complement levels. Other findings were rheumatoid factor 29 and positive cryoglobulins (but with only 0.33% cryocrit). It must be mentioned that one year before, prior to starting treatment with pegylated IFN, autoimmunity was negative and by contrast, cryoglobulins were positive with 4.4% cryocrit. Given these results suggesting drug-induced lupus (related to the pegylated IFN- α that the patient had been receiving until two weeks before due to his HCV), treatment with NSAID, low dose corticosteroids and hydroxychloroquine was started, with significant improvement of symptoms.

Lymphocyte populations were also counted before and during IFN- α therapy, showing significant lymphopenia, with a decrease of both T cells (CD4+ and CD8+) and B cells during treatment (Figure 1).

DISCUSSION

Drug-induced lupus is a condition without established diagnostic criteria. It should be considered in those patients who have received one of the implied drugs for longer than one month and who have compatible symp-

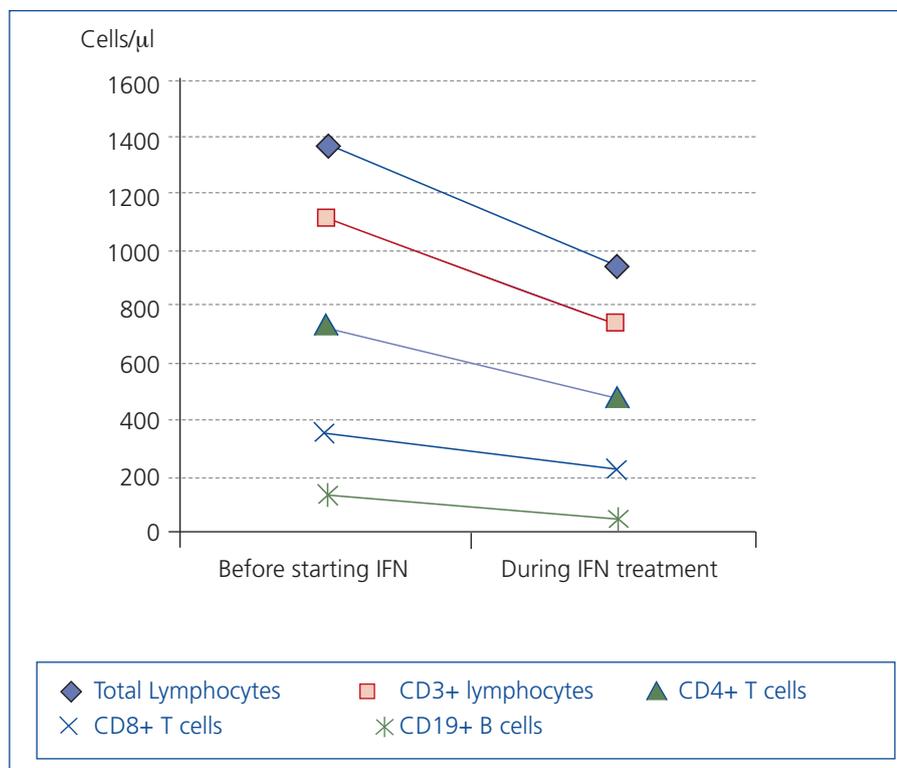


Figure 1. Evolution of lymphocyte populations following treatment with interferon α . IFN: interferon.

toms and autoimmunity test. The growing appearance of new pharmacological therapies, as well as the important pharmacosurveillance of their adverse effects, make the list of agents associated with this condition increasingly comprehensive. For this reason, high clinical suspicion is key, and therefore timing is of great importance.

For our patient, significant lymphocyte depletion induced by IFN- α should also be noted. Although T cell lymphopenia is an effect already described with the use of IFN- α due to thymus' function alteration, this situation, together with the patient's significant B lymphopenia, would mean a dysregulation of the immune response which could be involved in autoimmunity.

Conflict of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Baclofen neurotoxicity in a patient with end-stage chronic renal failure

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To the Editor,

Baclofen (4-beta-chlorophenyl-gamma-aminobutyric acid) is a muscle relaxant, used as an antispasmodic in diseases such as multiple sclerosis, medullary trauma and hiccups^{1,2}.

It is mainly excreted through the kidneys (69%-85%) and has a 2 to 6 hr. half life in healthy people. There is a high risk of neurotoxicity in patients with renal failure, especially if administered with <30ml/min glomerular filtration rate, causing episodes of unconsciousness^{3,4}.

Baclofen intoxication in dialysis patients is rare, with very diverse forms of clinical presentation⁵⁻⁹.

We present the clinical case of a patient with baclofen-induced encephalopathy, with atypical clinical evolution; symptoms did not improve with haemodialysis and the patient went into complete remission following the drug's discontinuation.