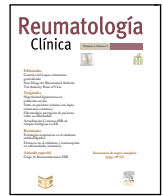




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Letter to the Editor

Pleuroperitoneal serositis as a manifestation of pyrazolone (metamizole) induced lupus

Serositis pleuroperitoneal como manifestación de un lupus inducido por pirazolonas (metamizol)

To the Editor:

In 1945, Hoffman described the first case of lupus-like disease that appeared after treatment with sulfadiazine. Since then, more than 70 drugs have been implicated in the induction of this disease. Of these, hydralazine, procainamide, chlorpromazine, isoniazide, methyl dopa, quinidine, and penicillamine are the most common.

Patients affected by drug-induced lupus may have all the manifestations of lupus erythematosus, however, in general, and joint involvement is the most common, serositis, renal and central nervous system involvement are rare. Symptoms are mild in most patients, few cases have a severe presentation and clinical multisystem involvement usually subsides after removal of the drug.¹

We report the case of a young man who, after receiving analgesic treatment with metamizole developed a case of pleuroperitoneal serositis, which disappeared after drug withdrawal.

The patient, an 18 year old male, healthy and with no known drug allergies, was operated a week before admission to hospital due to a left internal meniscal tear, with surgery being uneventful. He was treated with low molecular weight heparin (LMWH) and metamizole (Nolotil R). This last drug he took for five days, continuing the administration of LMWH. On subsequent days, he presented abdominal pain and right upper quadrant abdominal fullness, leading to the patient attending the ER. Analytical evidence showed only slight leukocytosis with neutrophilia, inflammatory pancreatic involvement was not found and chest and abdomen radiographs were normal. Pain was treated with butylscopolamine bromide (Buscopan Compositum R) and metamizole with clinical worsening leading to the performance of an abdominal ultrasound that showed moderate abdominal distension of the gallbladder, without stones, and a collection of perivesicular and subhepatic fluid. With the suspected diagnosis of acalculous cholecystitis, he entered the General Surgery Department and was prescribed metamizole and antibiotics every 8 hours for pain control. At 48h after admission he presented progressive deterioration with increasing pain, fever and abdominal distension.

The hemogram showed slight leukocytosis with eosinophilia (13%), coagulation was normal, the sedimentation rate was 4 mm in the 1st hour and C reactive protein was 11 mg/dl. Some biochemical alterations were seen transaminase (GOT: 60 u/l, ALT: 193 U/l, GGT: 131 U/l), with the remainder being normal. Protein electrophoresis, immunoglobulins, complement, rheumatoid factor, antimitochondrial antibodies and serology tests for *Salmonella*, *Brucella*, hepatitis A, B and C, citomegalovirus, Epstein-Barr virus, rubella, toxoplasma, *Coxiella*, *Mycoplasma*, chlamydia and herpes, did not show any remarkable change. There were no ECG abnormalities. An abdominopelvic CT showed evidence of bilateral pleural effusion, abundant amount of ascites in all locations, homogeneous hepatosplenomegaly and retroperitoneal intrabdominal adenopathy, with the largest being of 1.3 cm. Diagnostic paracentesis was performed showing a lymphocytic exudate with no evidence of malignant cells, and conventional and mycobacterial cultures were negative (glucose: 82 mg/dl, protein: 3.1 g/dl, LDH: 65U/l, 520 cells/ul with lymphocytic predominance). Antinuclear antibodies (ANA) (IgG, indirect immunofluorescence [IFI] HEp-2, Manufacturer: INOVA) were weakly positive (1/80) with a homogeneous pattern and anti-histone antibodies (IgG Line-blot technique INNO-LIA ANA, manufacturer: Innogenetics, qualitative method) were strongly positive.

Suspecting drug-induced serositis, we suspended metamizole treatment, both in its presentations as a single agent and in combination with other active ingredients. Symptoms gradually decreased and the patient progressed to being asymptomatic. On further review, after 12 weeks, there were no analytical alterations, control abdominal CT was normal and anti-histone antibodies were negative.

Anti-histone antibodies are common in drug-induced lupus (over 95%) and systemic lupus erythematosus (50%-70%), but can occur in other rheumatic diseases (rheumatoid arthritis, mixed connective tissue disease, scleroderma, etc.) and in up to 5% of healthy individuals. They may remain positive for years after clinical remission.^{2,3}

It is not often that a clear positive anti-histone result like this one is only barely detected by IIF on HEp-2 cells, the antibody screening method that we use in our laboratory. But when dealing with two different techniques, it can be explained by the greater resolution of the first, using purified protein, with respect to the antigenic mixture of the screening methods.

The drug metamizole is not frequently involved in the development of this disease,⁴ but this should be taken into consideration in patients that develop “lupus like” signs and symptoms.

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