

asociada a la EII puede relacionarse con la aparición de pancreatitis³. También se ha descrito una estenosis inflamatoria de la ampolla de Vater o una ampolla incompetente con reflujo de enzimas activadas hacia el interior del conducto pancreático principal⁶. Otros mecanismos menos frecuentes son la afectación primaria del páncreas con la infiltración granulomatosa directa y la presencia de un trayecto fistuloso hacia el interior del páncreas con inflamación secundaria. Otro grupo etiológico que cabe considerar son los factores autoinmunes, dado que se han detectado autoanticuerpos antipáncreas en pacientes con EC con una prevalencia del 33-39%, si bien más en relación con cierto grado de insuficiencia pancreática que con lesiones histológicas de PA^{4,7}. También se ha postulado que la mayor agregabilidad plaquetaria en la EII daría lugar a la formación de tromboembolismos que provocarían inflamación⁸. Por último, una pequeña proporción de casos (aproximadamente un 1%) corresponde a una forma de pancreatitis idiopática, que podría englobarse dentro de las manifestaciones extraintestinales de la enfermedad⁹. Como conclusión, la PA es una complicación poco frecuente de la EII que suele aparecer durante la evolución natural de la enfermedad. Excepcionalmente, es una presentación inicial de la EII, y puede incluso preceder al diagnóstico de ésta. Por este motivo, se debe tener en cuenta en el diagnóstico diferencial de la pancreatitis una EII subyacente, lo que permitirá una evolución clínica más favorable de ambas entidades.

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ACUTE HEPATITIS ASSOCIATED TO LEFLUNOMIDE IN A PATIENT WITH RHEUMATOID ARTHRITIS

Sr. Director: Rheumatoid arthritis (RA) is a chronic disease which affects predominantly women. Patients with RA often require immunosuppressive treatment. Disease-modifying anti-rheumatic drugs (DMARDs) are the cornerstone of the long term immunosuppressive treatment. The most used DMARD is methotrexate although leflunomide is now more commonly prescribed by rheumatologists and internists. Leflunomide is already approved to reduce signs and symptoms and retard structural damage in acti-

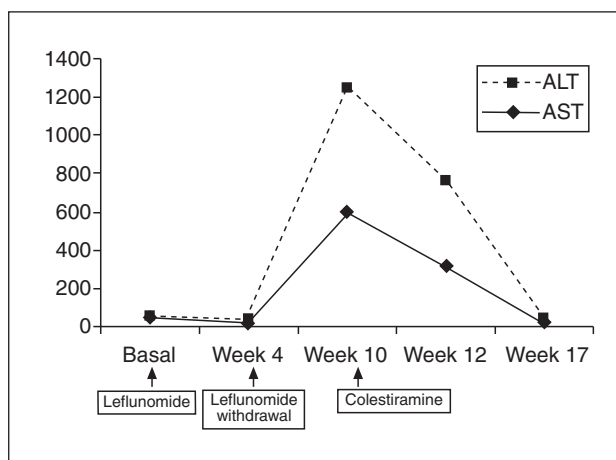


Fig. 1. Laboratory result according to the use of leflunomide and colestiramine.

ve RA in adults. Leflunomide is a relatively newer pyrimidine synthesis inhibitor. Leflunomide is an isoxazole immunomodulatory agent which inhibits dihydroorotate dehydrogenase (an enzyme involved in de novo pyrimidine synthesis) and has antiproliferative activity. Methotrexate and leflunomide must be evaluated bimonthly mainly for liver toxicity.

We present the case of a 48 year-old woman with RA involving hands, elbows, knees and feet. She was seropositive for rheumatoid factor and anticyclic citrullinated peptide antibodies. Erythrocyte sedimentation rate was 30 mm/hr. Basal aspartate aminotransferase (GOT/AST) and alanine aminotransferase (GPT/ALT) levels were 38 U/l and 18 U/l, respectively. No history of blood transfusion, surgery, diabetes or hypertension was referred. After the diagnosis of RA she received immunosuppressive treatment with leflunomide 20 mg/day, hydroxychloroquine 200 mg/day and etoricoxib 90 mg/day. One month later her general state was good with diminution of the articular symptoms and morning stiffness. Five weeks after the start of the treatment with leflunomide she referred fever, anorexia, chills and jaundice. At that moment she stopped all drugs for RA. Laboratory results of GOT/AST and GPT/ALT increased significantly to 597 U/l and 644 U/l, respectively. Abdominal ultrasound revealed hepatomegaly. Blood tests for A or B hepatitis were negative. Colestiramine was started in a dose of 8 grams every 8 hours for 10 days and the liver function tests slowly returned to normal values. One month later all her laboratory results were normal (fig. 1) and she was asymptomatic concerning hepatitis with mild rheumatoid arthritis activity treated with hydroxychloroquine and etoricoxib without any adverse reactions. Although it is well known the potential of leflunomide for liver toxicity, including jaundice, cholestasis and acute hepatic necrosis that may be fatal; reports of acute hepatitis are very rare. In the majority of the patients liver enzyme elevations occurred within the first 6 months of therapy and resolved during continued follow-up. However once liver inflammation due to leflunomide is suspected it is very important to start the treatment with colestiramine and maintain a close monitoring of enzyme levels and the patient's clinical status.

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