CASE REPORT

Abnormal liver function tests in inflammatory arthritis: think beyond the DMARDs

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Abstract

Abnormal liver function tests are often seen in patients with inflammatory arthritis. These are commonly associated with disease-modifying anti-rheumatic drugs, however, clinicians must hold a high index of suspicion for less common causes. This article details two of such cases where hereditary haemochromatosis and acute hepatitis E infection were actually responsible for deranged serum liver enzymes. Correct identification of these conditions leads to disease specific management and improved patient outcomes.

INTRODUCTION

Liver function test abnormalities are not uncommon in patients with inflammatory arthritis and are commonly due to disease-modifying anti-rheumatic drugs (DMARDs). Up to 22% of patients taking methotrexate will have deranged LFTs at some point, with a further increased association if there is a history of underlying liver disease or daily alcohol use [1]. Most of these results are transient and are not associated with significant underlying liver injury/fibrosis.

Here we report two cases of abnormal liver function tests in patients with inflammatory arthritis.

CASE REPORT

Case 1

A 68-year-old woman was re-referred to the rheumatology clinic with worsening joint pain and morning stiffness in both hands. She was first diagnosed with seronegative rheumatoid arthritis at 32 years of age. She had previously taken penicillamine and then sulfasalazine which were stopped due to primary inefficacy. Subsequently her disease went into remission and she had been off all DMARDs for 7 years.

Her past medical history included hypertension and a gastric ulcer for which she was taking losartan and ranitidine. She was taking paracetamol and codeine as required. She had never smoked and drank 35 units of alcohol per week.

On examination she had a bronzed appearance but no stigmata of chronic liver disease. She had active synovitis at the left wrist and second MCP joint. The plan was to commence methotrexate but she was found to have a raised ALT of 156 IU/L with otherwise normal liver function tests and clotting. Her liver function tests had been normal 2 years previously.

She underwent a full liver screen and was found to have a serum ferritin of >2000 μg/L and transferrin saturation of 92%. An abdominal ultrasound was normal. Given her increased alcohol intake a fibroscan was performed which showed a score of 4.6 kPa correlating to no significant liver fibrosis. Haemochromatosis
genotyping revealed she was YYHY genotype with C282Y mutations in a homozygous state consistent with hereditary haemochromatosis and she was entered into a venesection programme.

Haemochromatosis can result in a small joint polyarthritis and so her diagnosis of RA was revisited. However, on repeat testing she was strongly positive for both rheumatoid factor (>130 U) and anti-CCP (221 U) and previous x-rays of her feet showed typical marginal erosions consistent with RA. Haemochromatosis would be unlikely to result in significant iron overload causing joint symptoms in a premenopausal woman aged 32 due to regular menses.

 Genetic liver disorders such as haemochromatosis can mimic RA. Iron overload occurs due to mutations in the haemochromatosis HFE gene leading to haemosiderin deposition throughout the body, including the joints and the liver [2]. The arthropathy associated with this condition is classically non-inflammatory and centred around the second and third MCP joints, proximal interphalangeal joints (PIP) and wrists [3]. The key features differentiating haemochromatosis arthropathy from RA are summarized in Table 1.

### Table 1: Features of haemochromatosis arthropathy compared to rheumatoid arthritis [2]

| Feature                      | Haemochromatosis | Rheumatoid arthritis |
|------------------------------|------------------|----------------------|
| Age at onset                 | < 50 years       | >45 years            |
| Chondrocalcinosis            | Common (30–60% cases) | Rare                 |
| MCP joint involvement        | Very common (typically second and third MCP) | Very common |
| Signs of synovitis           | Uncommon         | Very common          |
| Radiographs                  | Degenerative changes second to fifth MCP joints | Marginal erosions |

MCP = metacarpophalangeal.
Adapted from Rheumatology Network [3].

In patients with compromised immune systems, such as patients on chemotherapy or transplant maintenance medication, chronic HEV infection, where HEV RNA persists for >3 months, is well documented [4]. Although frequently self-limiting these infections can rarely lead to liver cirrhosis [6].

Patients with inflammatory arthritis receive similar immunosuppression from DMARD therapy and therefore are at increased risk of chronic HEV infection [7]. Similar to healthy individuals HEV infected RA patients are frequently asymptomatic however common complaints include jaundice, right upper quadrant abdominal pain and fever [8].

A retrospective study, although low powered, showed good rates of clearance of HEV in these patients within three months. This was achieved either spontaneously or through DMARD withdrawal/dose reduction. The antiviral agent, ribavirin, is indicated when LFTs remained persistently raised [8].

Follow up virology testing, monitoring viral load and HEV IgM levels (positive in this patient), is important in these patients to confirm HEV clearance especially when LFTs remain abnormal [9].

HEV serology should be performed in patients on with DMARDs who develop abnormal liver function tests.

**DISCUSSION**

Derangements of liver function tests are frequently seen in patients with inflammatory arthritis and are commonly caused by DMARDs. These two case reports illustrate the importance of considering alternative diagnoses for persistently elevated liver enzymes in this patient group.

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**CONFLICT OF INTEREST STATEMENT**

No conflict of interest.

**FUNDING**

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**ETHICAL APPROVAL**

No ethical approval required for this case report.

**CONSENT**

Written consent has been provided by the patients from both case reports 1 and 2. Please find attached the consent forms as part of the article submission.

**GUARANTOR**

Alexander Fahmy is the nominated guarantor of this case report submission.

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