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## Carta al Director

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# Multiple liver abscesses in Crohn's disease in infliximab therapy, successfully treated with antibiotic therapy

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Sir,

The tumour necrosis factor alpha inhibitor antibody (anti-TNF) has proven to be effective in induction and maintenance of remission in Crohn's disease (CD). Infliximab is the option more commonly used [1]. Its use can be associated with immunosuppression and predispose to the patients for severe infections [2, 3]. Liver abscess is an uncommon disease in the global paediatric population, but also in CD patients. The reported incidence of this disease in patients with CD is 114-297 per 100,000, a rate that is about 10-15 times higher than that found in the general population [4]. Liver abscesses are seen often in patients with major debilitating diseases, immunosuppression and abnormalities in the biliary tract and can lead to fatal complications [2, 5, 6]. It is also still considered a rare complication of infliximab therapy [2, 5, 7, 8].

We present the case of a 14-year-old boy diagnosed of CD 21 months ago. He was initially treated with enteral nutrition and azatioprin. This drug was withdrawn after an episode of acute pancreatitis. Therefore, methotrexate and infliximab (5 mg/kg/8 weeks) were established for 5 months. He was attended in the emergency room because of fever and vomits for the last 24 hours, without any other symptom and was admitted to the ward. At admission, the vital signs were: temperature 40ºC, heart rate 100 beats/min, respiratory rate 20 breaths/min and blood pressure 110/50 mmHg. The physical examination showed no abnormalities. Laboratory results were: white blood cell count 6,210/mL (5,520 neutrophils, 370 lymphocytes), with liver function test, bilirubin and amylase within the normal ranges; erythrocyte sedimentation rate 29 mm/h, C-reactive protein 95.3 mg/L and procalcitonin 50.7 ng/mL (table 1). Chest x-ray was normal and abdominal ultrasound scan showed a terminal ileitis, without pathologic findings in the supramesocolic organs. Four blood cultures were taken, immunosuppression therapy was withdrawn, an exclusive enteral feeding with a polymeric formula and empirical antibiotic therapy with cefotaxime 2 g/ 8 h were established. After 48 hours he continued with spiking fever and developed right upper quadrant tenderness with enlarged liver. Liver function test had slightly worsened with ASAT 93 U/L, ALAT 88 U/L and bilirubin 2.01 mg/dL. C-reactive protein and procalcitonin were, respectively, 185.1 mg/L and 20.7 ng/mL. White cell count was 4,550/mL (3,820 neutrophils). Right upper quadrant ultrasonography scan revealed a thickened gallbladder wall, with a layered appearance, and a small amount of fluid on the base with an echoic content without shadow. He was diagnosed of acute acalculous cholecystitis, and antibiotic was changed to piperacillin-tazobactam 4 g/ 8 h. The hepatomegaly and the right

**Table 1** **Laboratory data at admission.**

| Parameter | Value | Normal range value |
|---|---|---|
| Leucocyte count/µL | 6,210 | 4,000-11,000 |
| Neutrophil count/µL | 5,520 | 1,700-7,500 |
| Lymphocyte count/µL | 370 | 1,000-3,500 |
| Bilirubin, total (mg/dL) | 0.93 | 0.2-1.2 |
| Aspartate aminotransferase (IU/L) | 39 | 4-50 |
| Alanine aminotransferase (IU/L) | 31 | 5-40 |
| Amylase (IU/L) | 47 | 25-125 |
| Prothrombin time (s) | 13.8 | 10.7-15.5 |
| Procalcitonin (ng/mL) | 50.07 | > 2[a] |
| C-reactive protein (mg/L) | 95.3 | 0-5 |
| Erythrocyte sedimentation rate (mm/h) | 29 | 0-20 |

[a]Severe infection, sepsis, shock

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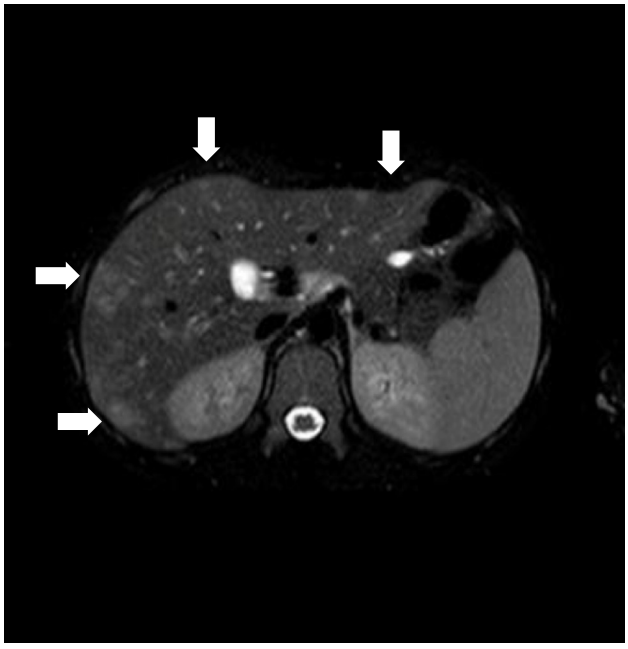

**Figure 1** | **MRI of liver microabscesses (arrows).**

upper tenderness disappeared and there was a progressive normalization of laboratory data, including inflammatory reactants and liver function tests. Blood cultures were negative.

Cholangio-MRI phase T1, enhanced with gadolinium, performed after 14 days, revealed a normal gallbladder and biliary tree, with multiple focal liver lesions within both lobes, predominantly in the peripheral areas, some of them with a hypointense center and enhanced surface in arterial phase, consistent with liver microabscesses (figure 1). Ultrasound guided needle percutaneous aspiration was performed in one of the subcapsular lesions in segment VII. Gram stain showed numerous white blood cells without any microorganism. Cultures for aerobic, anaerobic, fungi and *Mycobacterium* and universal bacterial and *Mycobacterium tuberculosis* PCR were negative. Immunoglobulins, neutrophils oxidative metabolism and lymphocyte population in peripheral blood were normal. The blood biomarkers improved. When he was 23 days in antibiotics, CRP was 7.3 mg/L, procalcitonin, below 0.05 ng/mL and the white blood cell count 2,900/μL (1400 neutrophils). He remained on piperacillin-tazobactam for 28 days and, afterwards, therapy was switched to oral amoxicillin-clavulanate and ciprofloxacin for another 28 days. Two weeks after the antibiotic therapy was completed, he remained asymptomatic, with normal laboratory data, disappearance of the microabscesses and there were neither clinical nor biological activity changes in CD (phoecal calprotectin 17-136 μg/g). His habitual enteral feeding and immunosuppressive therapy with methotrexate and infliximab were restarted. After 72 months of the diagnosis of the liver abscesses, he remained asymptomatic.

It's well known that a liver abscess can be an extraintestinal manifestation in patients with inflammatory bowel disease, but they are usually considered to be mainly of infectious origin. In our patient we think that the etiology was bacterial, because of the severe elevation of biomarkers, mainly procalcitonin, and the good response to antibiotic therapy. Unfortunately, cultures were negative. The sensibility of blood cultures is low usually and the cultures of the hepatic aspiration were taken after several days of antibiotic therapy.

Liver abscesses should be suspected and actively searched in febrile patients with CD, especially if they are in treatment with anti-TNF agents. An early diagnosis and antibiotic therapy can further improve the outcome without need of performing invasive techniques. Withdrawal of the immunosupresive therapy carries a high risk of activate CD. Enteral feeding, whose effectiveness is demonstrated in the initial treatment of this disease, may be a therapeutic option in these patients.

## FUNDING

None to declare.

## CONFLICTS OF INTEREST

The authors declares that they have no conflicts of interest.

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