A challenging case of fever of unknown origin (FUO)

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Introduction

FUO is challenging for patients as well as for physicians and may be caused by over 200 malignant/neoplastic, infectious, rheumatic/inflammatory and miscellaneous disorders (Cunha et al. Fever of unknown origin: a clinical approach. Am J Med. 2015). The diagnosis often requires numerous noninvasive and invasive procedures that sometimes even fail to explain the fever.

Clinical case

Our patient is a 24-year-old Caucasian female who presented the first time to the emergency department with fever (38,5°C) and stomach ache. Anamnesis and physical examination showed no particular findings except occasional smoke and treatment with contraceptive vaginal ring. Haematological parameters showed thrombocytosis (728000/mmc), microcytic anemia (Hb 10,2 g/dl,MCV 78,4 fL) and high values of C-reactive protein CRP (90 mg/L). Ultrasonography of the abdomen revealed a 4 cm hepatic angioma. She was diagnosed a gastropathy and treated with PPI with only slight improvement of symptoms.

Then she was studied deeper because of elevated inflammation markers (CRP 90-130 mg/L, fibrinogen 1082 mg/dl, ESR 77 mmh, persistent thrombocytosis and low-grade fewer combined with fatigue and stomach ache. Further blood tests were carried out; in particular we report ferritin 75 ng/ml, iron 27 µg/dl, transferrin 2,6 g/l, sat.transferrin 7%, low level of vitamin B12 (72 pmol/L),polyclonal hypergammaglobulinemia (total proteins 9,4 g/dl, gammaglobulin 25,9%).Renal function,liver function, thyroid function, folic acid, albumin, beta 2 microglobulin, LDH, urinary kappa/lamda ratio, calcitonin, cromogranin, procalcitonin, tumor markers, PT, aPTT, antitrombin, RAST for food allergies were normal. The patients were underwent to bone marrow biopsy that was normal. Search for Jak-2 mutation was negative.

Multiple blood and urine cultures and serology for multiple microbial agents (CMV, antistreptolysin titer, Syphilis, Typhus O and H, Paratyphus A and B, Brucella, Borrelia, HCV, HIV) were negative. Serology for Parvovirus B19, Toxoplasma and EBV were suggestive of previous infection. PCR test for Leishmania, T.Whippeli and Rickettsia were negative. Multiple coproparassitological examination, pharyngeal and nasal swab, Quantiferon and Mantoux test were negative.

Instrumental examinations were performed; echocardiography, PET/CT, panoramic radiograph, brain MRI, transvaginal sonography and gynecological examination were normal. Esophagogastroduodenoscopy was macroscopically normal but the histological examination (> 30 intraepithelial lymphocyte T on 100 cells at the duodenale level) was suggestive of mild celiac disease. Thus, this diagnosis was unlikely because serologic tests (antigliadin and anti endomysium antibody) were negative and haplotypes DQ2 and DQ8 weren't present. Colonoscopy were normal and histological examination by biopsies in more points showed no pathological findings.

CT for neck, chest and abdomen showed and confirmed the presence of a hig flow hepatic angioma at the right lobe. Then the patient was underwent to abdomen MRI that showed a expansive lesion (40 mm) with semeiological characteristics, although not univocal, that orientated towards the hypothesis of adenoma

The clinical case was discussed with the surgeons and it was decided to subject the patient to resection of the lesion. The patient were underwent to surgery and the histological examination showed a morphological picture compatible with the diagnosis of hepatocellular adenoma inflammatory variant.

One month after surgery the patient is well, the fever has disappeared, the hemoglobin values have improved (11.9 g / dl) and the value of the platelets has dropped (433.000 / µl).

Conclusions

Hepatic adenomas are uncommon benign epithelial liver tumors that develop in an otherwise normal-appearing liver. They are seen predominantly in young women (20 to 44 years old), are frequently located in the right hepatic lobe, and are typically solitary (70 to 80 percent), although multiple adenomas have been described in patients with prolonged contraceptive use, glycogen storage diseases, and hepatic adenomatosis. Adenomas range in size from 1 to 30 cm. Symptoms such as abdominal pain are more likely with larger lesions (Grazioli et al. Hepatic adenomas: imaging and pathologic findings. Radiographics. 2001;21(4):877.) In the literature there is a case of FUO resolved after removal of a liver lesion identified as adenoma by MRI and proved to be an inflammatory myofibroblastic tumor on histological examination. (Kruth et al. (A rare case of fever of unknown origin: inflammatory myofibroblastic tumor of the liver. Case report and review of the literature. Acta Gastroenterol Belg. 2012 Dec;75(4):448-53). Our patient has probably developed a hepatic adenoma during contraceptive therapy and this lesion was responsible for the onset of FUO.

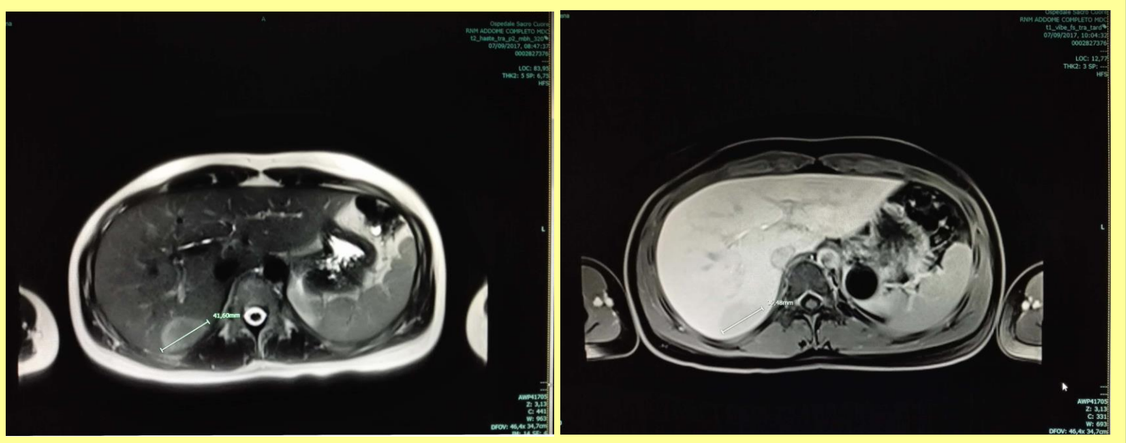

Figure 1: liver slightly increased in size, at net margins. In the posterior segments of the right lobe, in segment VII in the sub-Glisson's capsule region, it is expansive lesion with finely irregular margins and major axis of 40 mm with hyperintense signal in T2, with restriction notes of diffusion coefficient , and with isointense signal in T1-dependent pre-contrast enhanced images. During the dynamic study (not shown), it is hypervascularized in the arterial phase, then tends to the intensity of the surrounding parenchyma in the subsequent phases of the dynamic study. In the biliary excretion phase (not shown) the lesion is hypointense.