

### Acute hepatitis E virus infection and association with a subacute thyroiditis

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Dear Editor:

We read with interest the review of Mar Riveiro Barciela, *et al.*<sup>1</sup> which shows that in developed countries a minority of acute hepatitis cases are attributed to Hepatitis E virus (HEV) infection and they are mainly undiagnosed. This review describes that infection by HEV has been related to extra hepatic manifestations, including neurological, renal, muscular and hematological disorders. These manifestations include inflammatory polyradiculopathy, Guillain-Barré syndrome, bilateral brachial neuritis, encephalitis, proximal ataxia, myopathy, membranoproliferative glomerulonephritis and relapses of IgA nephropathy. As in hepatitis A, HEV infection has been related to the haematological disorders such as severe thrombocytopenia and pure red cell aplasia.<sup>1</sup> However, this concise review does not describe extra hepatic endocrine manifestations. Secondary thyroiditis to viral infections is well-known but the association with viral hepatitis has only been reported in cases of infectious mononucleosis<sup>2</sup> and hepatitis A.<sup>3</sup> The association of acute hepatitis E, hepatitis B and thyrotoxicosis has been recently published<sup>4</sup> as well as another case about autoimmune thyroiditis and HEV,<sup>5</sup> but no cases of subacute thyroiditis have been reported. As it is known, both the T3 and T4 regulate the cells metabolism including the hepatocytes ones and then, in turn, the liver function. The liver is involved in the metabolism of thyroid hormones by regulating their systemic effects. This dual relationship explains why

thyroid dysfunction can disrupt liver function and the liver disease can have an effect on thyroid metabolism.<sup>6,7</sup> We report the first case of association between acute hepatitis E and subacute thyroiditis. The patient is a 45-year-old male. He developed asthenia, myalgia, arthralgia, weight loss of 3 kilos, temperature of 37.7 °C and anterior neck pain a month before. He had hypertension, body mass index 25 kg/cm<sup>2</sup>, and alcohol intake 20 g/week. The physical exam showed: pulse regular at 88 beats per minute, anicteric hot skin, no features of chronic liver disease and thyroid nodule on palpation of apex of right lobe of 1 cm. His laboratory results showed: alanine aminotransferase (ALT) 805 UI/L (normal range 0-40) and aspartate aminotransferase (AST) 416 IU/L (normal range 0-40), alkaline phosphatase 1198 U/L (normal range 60-260), INR 1, thyroid-stimulating hormone (TSH) < 0.005 µIU/mL (normal range 0.6-3.7), T3 2.45 ng/mL (normal range 0.8-2), T4 14.88 µg/mL (normal range 5-14), T4L 2 ng/dL (normal range 0.8-2) and antibody thyroperoxidase 29 UI/mL (reference value < 35). Abdominal ultrasonography showed mild hepatomegaly and the thyroid ultrasonography showed a heterogeneous structure gland, right lobe nodule of 9 mm with peripheral vascularization.<sup>131</sup> I uptake was 1% at 24 h and the scintigraphy showed a hyperenhancement of nodule in the right lobe. All biochemical tests were negative for acute hepatitis: IgM anti-HAV, HBsAg, IgM anti-HBc, Anti-HCV, Anti-HIV, Epstein-Barr IgM antiVCA, IgM Cytomegalovirus, smooth-muscle antibodies (SMA), antinuclear antibodies (ANA), antibodies to liver-kidney microsomes (LKM), soluble liver antigen (SLA) and anti-liver cytosol antibody Type 1 (LC1). Anti-HEV antibodies were positive by a commercial assay detecting IgM + IgG antibodies (DiaPro Diagnostic Bioprobes, Milan, Italy). A fragment of 148 bases from the Open Reading Frame (ORF) 2 and a fragment of 295 bases from ORF 1 of the HEV RNA were sequenced. They both belonged

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to subgenotype 3a. Both of them showed a homology of 92 to 94% with human and swine 3a variants from Japan. The homology with other human HEV 3a variants characterized in Argentina varied between 72 and 85%.<sup>8</sup> The patient had spontaneous improvement with a gradual decrease in the symptoms. Eight weeks later the patient showed ALT 27 IU/L and AST 26 IU/L, with an increase in TSH 2.93  $\mu$ IU/mL, T4 5.53  $\mu$ g/dL and disappearance of the thyroid nodule. After 6 months, the patient had a normal thyroid function. The diagnosis of a new case of autochthonous HEV shows the circulation of this virus as an agent of liver disease in Argentina and contributes to the knowledge of the epidemiology of this virus in the region. The patient is a healthcare worker and has not travelled abroad. This is the first case of subacute thyroiditis linked to HEV. Suspicion and early diagnosis of this entity with its affection of the thyroid allowed a better management of the disease.

We believe our findings could be of interest to the readers because they bring new and strong evidence that the extrahepatic manifestations are real.

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