

Unusual association of diseases/symptoms

Acute hepatitis E virus infection and autoimmune thyroiditis: yet another trigger?

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A middle aged woman, previously healthy with the exception of mild seasonal asthma was presented with signs of acute hepatitis. The further investigation showed acute hepatitis E virus infection associated with autoimmune thyroiditis. Treatment was started with propranolol and carbimazol whereupon hepatitis and hyperthyroidism resolved. The authors think that the observed association of acute hepatitis E virus infection and autoimmune thyroiditis suggests a role of hepatitis E virus as putative trigger of autoimmune thyroiditis. The alternative possibility of thyroid dysfunction due to pre-existing autoantibodies cannot be completely excluded but seems to be unlikely given the very mild course of seasonal asthma in this patient.

BACKGROUND

Autoimmune thyroiditis has been associated with various viral infections^{1–2} as well as with liver diseases – notably autoimmune hepatitis, viral hepatitis and interferon therapy of chronic hepatitis C.^{3–6} To the best of our knowledge, an association of acute hepatitis E virus infection and autoimmune thyroiditis has not been reported.

CASE PRESENTATION

A middle aged previously healthy woman presented with low-grade fever, fatigue, reduced appetite, myalgia, pruritus and dark urine. The medical history was unremarkable with the exception of mild seasonal allergic asthma controlled by intermittent inhalation of steroids. There was no history of recent travel nor did she take any other medications; she had been vaccinated against hepatitis A virus 2 years before presentation. On physical examination, her blood pressure was 110/70 mm Hg with a heart rate of 112/min; she showed mild jaundice with tenderness in the right upper quadrant of the abdomen upon palpation.

INVESTIGATIONS

The laboratory investigation showed highly elevated aspartate and alanine aminotransferases, marked elevation of alkaline phosphatase and γ glutamyl transpeptidase with slight hyperbilirubinaemia as well as frank hyperthyroidism (table 1). Further testing revealed positive antihepatitis E virus IgM and IgG antibodies as well as autoantibodies for thyroid peroxidase (360.90 U/ml; reference <60) and thyroglobuline (370.70 U/ml; reference <60). The titre for antinuclear antibodies was moderately increased (1:320/ reference range <1:80). Testing for hepatitis B and hepatitis C virus, viruses of the herpes group (cytomegalovirus and Epstein–Barr virus) and immunoglobuline levels (IgA, IgG, IgM), smooth muscle and liver kidney microsomal antibodies and thyroid stimulating hormone receptor antibodies were all negative or unremarkable. An ECG on admission

showed sinus tachycardia. Abdominal ultrasound showed a slight enlargement of the liver with slightly hypoechoic parenchyma, several enlarged (2 cm) lymph nodes in the liver hilum, gallbladder stones without signs of biliary obstruction. Ultrasound of the thyroid showed normal volume of the thyroid with patchy hypoechoic parenchymal structure consistent with acute thyroiditis.

DIFFERENTIAL DIAGNOSIS

Regarding acute hepatitis: viral hepatitis as well as autoimmune hepatitis but also – rarely – Wilson's disease or disturbances in liver perfusion (eg, Budd–Chiari Syndrome) should be considered in the differential diagnosis of acute hepatocellular damage.

Regarding hyperthyroidism: focal autonomia as well as less common types of thyroiditis should be investigated. In addition, transient hyperthyroidism due to antithyroid antibodies occasionally associated with asthma bronchiale should be considered.

TREATMENT

The patient was started on propranolol 2×40 mg and carbimazol 1×20 mg. Liver function test was monitored and returned to normal values within 3 weeks. Thyroid hormone levels also decreased under treatment.

Table 1 Laboratory results (value/reference range)

ASAT	656 U/l	(10–35)
ALAT	1395 U/l	(10–35)
GGT	270 U/l	(<39)
Alkaline phosphatase	397 U/l	(35–104)
Bilirubin	2.44 mg/dl	(<1.2 mg/dl)
TSH	0.005 μ U/ml	(0.270–4.200)
Free T4	5.200 ng/dl	(0.900–1.700)
Free T3	1.660 ng/dl	(0.182–0.462)

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; GGT, γ -glutamyltransferase; TSH, thyroid stimulating hormone.

OUTCOME AND FOLLOW-UP

The patient's symptoms subsided within 2 weeks. Since hyperthyroidism did not subside within a year the patient was treated with radioiodine and after a follow-up of now over 2 years is without complaints on substitution with 125 µg of levothyroxine.

DISCUSSION

We report here a patient with acute hepatitis E virus infection who also suffered from autoimmune thyroiditis. To our knowledge this is the first case report on an association of acute hepatitis E virus infection and hyperthyroidism.

The association of liver disease with autoimmune thyroiditis is not a rare event. It has been reported for autoimmune liver disease as well as for hepatitis B and C virus infection, in particular under treatment with interferon α .³⁻⁶ In fact, components of several viruses have been found in the thyroid gland of patients with autoimmune thyroiditis and activation of auto-reactive T cells as well as collateral damage of other antiviral responses might be involved in the pathogenesis of autoimmune thyroiditis.⁷ On the other hand, a variety of auto-antibodies including antinuclear antibodies – as were present in our patient – have been described for autoimmune thyroiditis⁸⁻⁹ but also in patients with asthma bronchiale.¹⁰

In our patient autoimmune thyroiditis has most likely been triggered by acute hepatitis E virus infection. Although we have no autoantibody screen from the time before the episode of acute hepatitis we do not feel that thyroiditis resulted from pre-existing antithyroid antibodies since the patient suffered from mild seasonal asthma which was clinically inapparent at the onset of hepatitis/thyroiditis and did not exacerbate under β blocker therapy. Rather, the observation of acute hepatitis E virus infection associated with autoimmune hepatitis suggests the possibility that this virus – as well as other viruses – might be a trigger for autoimmune thyroiditis.

Learning points

- ▶ Autoimmune thyroiditis associated with liver disease is not a rare event in case of chronic viral hepatitis and/or interferon therapy and autoimmune hepatitis.
- ▶ In addition, it should also be considered in patients with acute hepatitis E virus infection with signs of hyperthyroidism.

Competing interests None.

Patient consent Not obtained.

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