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Review

Hepatitis E and neuralgic amyotrophy: Five cases and review of literature

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ABSTRACT

Hepatitis E virus infection – mainly genotype 3 – is increasingly common in industrialized countries. Infection is usually asymptomatic, but cases of central or peripheral neurological symptoms with hepatitis E have been described. The most frequent is Guillain-Barre but somes cases of neuralgic amyotrophy have been described. In our center, since 2010, we have identified five cases of neuralgic amyotrophy associated with acute hepatitis E in immunocompetent patients. For all these patients, neuralgic amyotrophy was diagnosed with electromyogram and positive IgM for hepatitis E, and detectable HEV RNA in 4 of the cases. Including our patients, we count 26 cases in literature. The mean age of the patients was 44 years old, with a large predominance of males (88%). The disorder is bilateral and asymmetric in 69% of cases. Peripheral nerves other than the brachial plexus were affected in 6 patients (23%). In industrialized countries, any neuralgic amyotrophy, particularly if there is bilateral, asymmetric associated with involvement of nerves outside the brachial plexus, should lead physicians to consider a diagnosis of acute hepatitis E.

Contents

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1. Introduction

Hepatitis E virus (HEV) is endemic in non-industrialized countries, where it is responsible for 50% of acute hepatitis infections. It has a seroprevalence of between 25 and 40% in these countries, particularly in Asia [1]. Four genotypes of HEV have been identified. Genotypes 1 and 2 only infect humans, whereas genotypes 3 and 4 have also been detected in animals. Genotypes 1, 2 and 4 are present in developing countries.

Native cases of hepatitis E are becoming more frequent in industrialized countries. The population affected tends to be older (mean age 55 years) than that in countries where the virus is strongly endemic, and the majority of clinical cases are men (60–75%) [1,2]. In this context, genotype 3 is the most frequently encountered [1,2].

The most likely source of this infection is from pigs due to the consumption of inadequately cooked pork meat [3–5]. In 2009, HEV's seroprevalence in French pig farms was estimated at 65% [6].

Blood-borne transmission has also been described [7–9]. In southern England, between 2012 and 2013, 0.04% of blood donations had been tested positive for HEV RNA, with a rate of transmission of 42% after transfusion of contaminated batches [7]. In France, since 2006, 15 cases of post-transfusion hepatitis E were detected [8]. The seroprevalence in French blood donors is 52% in Toulouse, region of southwest France [2].

In most cases, HEV infection is asymptomatic; symptomatic presentations are more frequent in patients who regularly consume alcohol [1,2]. An increasing number of incidences of central or peripheral neurological symptoms associated with genotype 3 hepatitis E have been described, especially Guillain-Barré syndrome [10–16]. A recent study [10] found anti-HEV IgM in 5% of patients with Guillain-Barré syndrome, compared to 0.5% in the control group. In Kamar et al. [11], 5.5% of the 126 acute or chronic hepatitis E cases were complicated by central or peripheral neurological disorders. Similarly, Woolson [12] described 7.5% of neurological complications in 106 acute hepatitis E cases diagnosed in South-West England.

Neuralgic amyotrophy is a multiple mononeuropathy predominantly affecting the nerve roots and the brachial plexus causing amyotrophy [17]. Neuralgic amyotrophy is characterised by an acute and severe neuropathic pain followed by multifocal paresis [17]. The physiopathology of this disease is currently unknown.

In our center there were 24 cases of neuralgic amyotrophy between 2009 and 2014. In this article, we report five cases of neuralgic amyotrophy associated with acute HEV infection since 2010 and we present the results of a literature review.

2. Methods

We describe five cases of neuralgic amyotrophy associated with hepatitis E diagnosed at Grenoble university hospital (France). A literature review was performed to identify other published cases. We searched PubMed using the following combinations of keywords: hepatitis E and neuralgic amyotrophy; hepatitis E and Parsonage Turner; hepatitis E and brachial neuritis; and radiculoneuropathy and hepatitis E.

The serologic test for HEV is Assure HEV IgM rapid test. The HEV RNA is evaluated by kit hepatitis E: KHHEV for clinical samples, this is a qualitative test.

3. Results

3.1. Case 1

A 54 years old man—with a history of high blood pressure, developed sudden cervicodynia irradiating down to the upper limbs in 2010. Upon taking his familial history, it was noted that his son had been diagnosed with Parsonage Turner syndrome, and that this disease was suspected in his daughter. Clinical examination revealed paresis of the deltoid and biceps muscles, as well as loss of reflexes in the upper limbs. Biochemical assessment indicated cytolysis with elevated ALT (1036 UI/L; normal level: <78 UI/L) and AST (259 UI/L; normal level <37 UI/L), as well as cholestasis (GGT:344 UI/L, AP:180 UI/L) with no evidence of inflammation. The only infection detected was HEV, with an IgM-positive serological test and a positive RT-PCR from a blood sample. The genotype was identified as type 3f. Analysis of the cerebrospinal fluid (CSF) was normal. A cervical magnetic resonance imaging (MRI) did not show any medullar compression.

An electromyogram (EMG) indicated involvement of the root of C6 on the right-hand-side. Idiopathic or hereditary neuralgic amyotrophy associated with hepatitis E was diagnosed. The patient was treated with analgesics, physiotherapy and corticosteroid therapy at decreasing doses for three months.

Two months later, the patient developed dyspnoea associated with orthopnoea. Clinical examination revealed amyotrophy of the muscles in the scapular region and level 4/5 motor deficiency in the upper limbs. Thoracic X-ray indicated a raising of the left hemidiaphragm. Respiratory functional exploration (RFE) indicated a pure restrictive syndrome resulting from paresis of the diaphragm. A second EMG identified sensory anomalies of the musculocutaneous nerve with denervation and neurogenic traces in several muscles in the regions associated with the right and left C5 and C6 nerves, thus confirming bilateral neuralgic amyotrophy. No mutation of the SEPT9 gene was identified, a diagnosis of idiopathic or hereditary neuralgic amyotrophy associated with acute hepatitis E was retained.

Progression at 10 months was marked by recovery of muscle strength but persistence of orthopnoea and a painful limitation of mobility of the right shoulder.

3.2. Case 2

A Caucasian 54 years old man, chronic alcoholic with an alcohol intake of 10 g per day, consulted in July 2013 for intense subacute pain in the upper left limb associated with paresis. The clinical picture was rapidly completed by the appearance of neuropathic pain in the scapular muscles, and then in the lower limbs. Neurological examination indicated hypoesthesia of the root nerve connected to the lower right limb and the regions connected to the root of C6. No motor effects were noted and all deep tendon reflexes were maintained.

Biochemical assessment revealed hepatic cytolysis with elevated ALT (812 UI/L) and AST (332 UI/L), without cholestasis (GGT:66 UI/L, AP:89 UI/L, total bilirubin:8 μmol/L) with no evidence of inflammation.

Lumbar puncture revealed albuminocytological dissociation with high protein levels (0.99 g/L) and few white elements (<5/mm^3). The electrophoretic profile for CSF proteins was normal. A serological testing for HEV was IgM-positive. This was confirmed by RT-PCR for HEV in stool samples, but not in the blood nor CSF. The genotype was identified as type 3f.

The biochemical profile had normalised by the tenth day. The neuropathic pain gradually improved, but the right scapular muscles remained tender and amyotrophy of this region appeared after three weeks. At six weeks, shoulder MRI identified a strong T2 signal indicating intramuscular oedema in the serratus. EMG revealed moderate neurogenic signals in the biceps and along the right supinator and, more punctually, of the extensor digitorum communis, compatible with involvement of the right C6 root. We therefore concluded on a diagnosis of neuralgic amyotrophy associated with acute hepatitis E.