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Dual infection with hepatitis A and E virus presenting with aseptic meningitis: A case report

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ABSTRACT

We report the case of a young male who presented with features of aseptic meningitis and elevated serum liver enzymes, but no symptoms or signs suggestive of an acute hepatitis. Subsequently, he was diagnosed with dual infection with hepatitis A and E viruses, and recovered completely with symptomatic therapy. Isolated aseptic meningitis, unaccompanied by hepatitic features is an unusual presentation of a hepatotrophic viral infection, and is yet to be reported with hepatitis A and E virus co-infection.

1. Introduction

Dual infection with hepatitis A and E virus is a potentially under-reported condition, especially from the developing world in the absence of adequate laboratory facilities. A Cuban study by Lay *et al*[1], demonstrated such co-infection in up to 12.8% of epidemic and sporadic cases of acute viral hepatitis. Such a figure is not unsurprising, considering the similar epidemiological profile of these viruses, both sharing an enteric route of transmission. Unfortunately, data on whether and how such cases of dual infection differ from mono-infection with hepatitis A and E in terms of clinical presentation and natural history are lacking.

2. Case report

A 33-year-old Asian Indian male with no premorbid illnesses presented with high-grade fever since the past 15 days, associated with chills and rigors. He also complained of severe holocranial headache, recurrent vomiting and mild photophobia since the past five days. He denied any history of substance abuse.

General physical examination revealed conjunctival suffusion, and a fever of 102 °F. Neurological evaluation showed grade 1 nystagmus to the left and minimal ataxia in the left upper limb. Although nuchal rigidity was present, Kernig's and Brudzinski's sign could not be elicited. Examination of other systems was normal.

Preliminary blood investigations showed hepatitis (serum AST 142 U/L, serum ALT 400 U/L, serum ALP 403 U/L) and elevated total leucocyte count (13 100/mm^3). Cranial MRI imaging was performed as the patient had focal neurological deficits and was a normal study. A lumbar puncture was done; cerebrospinal fluid (CSF) analysis revealed lymphocytic pleiocytosis (80 cells/mm^3, 90% lymphocytes), and elevated protein (86 mg/dL). CSF glucose was normal (69 mg/dL). Gram staining showed occasional pus cells but no organisms; culture remained sterile. Fluorescein stain was negative for acid fast bacilli, and polymerase chain reaction (PCR) was negative for tuberculosis.

Pending results of serological tests to determine the cause of fever, the patient was empirically initiated on parenteral ceftriaxone (2 g IV q12H), considering a possibility of early pyogenic meningitis. Subsequently, the patient tested positive for both hepatitis A and hepatitis E virus infection by ELISA method. Simultaneously, evaluation for malaria, leptospirosis and enteric fever was negative. Blood cultures drawn at admission, as well as in the course of hospital stay

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were persistently sterile.

In the absence of an alternative etiology, the CSF picture of aseptic meningitis was attributed to dual infection with hepatitis A and E viruses. Antibiotic therapy was therefore discontinued. The patient was kept under observation, and reported steady subjective improvement. Serial monitoring of liver function tests and leucocyte counts showed complete recovery.

3. Discussion

Hepatitis A infection has been linked in sporadic reports with a range of neurological manifestations including meningoencephalitis, acute disseminated encephalomyelitis (ADEM)[2,3], Guillaine-Barre syndrome[4], acute myelitis [5,6] and peripheral neuropathy[7]. In children, hepatitis A infection has been reported in association with pseudotumour cerebri[8] and abducens and palatal palsy[9].

Davoudi *et al*[10] suggested that the close relationship of hepatitis A virus with other enteroviruses known to cause meningitis in humans might explain this phenomenon. Furthermore, the frequently anicteric nature of hepatitis A infection and the low index of suspicion might hinder the identification of such cases, lowering the apparent incidence of such disease.

Hepatitis E infection has also been reported in association with a variety of neurological presentations such as meningoencephalitis[11] and polyradiculoneuropathy[12,13]. Other associations include pseudotumour cerebri[14] and acute transverse myelitis[15].

Pathogenetic mechanisms that have been postulated include immune-medicated damage to axolemmal and Schwann cell antigens, direct neuronal injury by viral invasion of the central nervous system, and the presence of neurotropic HEV quasispecies[16].

Kamar *et al* [16], described a case of central and peripheral nervous system involvement in a patient with chronic hepatitis E infection on immunosuppressant therapy. A multi-center study by Kamar *et al*[17], found evidence of neurologic disease in upto 5.5% of patients with acute or chronic hepatitis E infection. Of the 126 patients involved in this study, 55 were drawn from an organ-transplant unit. Evidence such as this suggests that chronic hepatitis E infection on a background of immunosuppression is a risk factor for neurologic involvement.

Interestingly, our patient was immunocompetent, and both hepatitis A and E viral infections were demonstrated by IgM ELISA techniques, making chronic infection unlikely. One possibility we did consider was whether acute synergistic co-infection with two viruses might have resulted in overt neurologic disease. However, if such synergism could indeed occur, it would be much more likely to affect the liver first, producing a more severe and virulent form of hepatitis than that observed in our patient.

To conclude, our case represents a unique manifestation of dual infection with hepatitis A and E viruses, in an immunocompetent individual. Further studies are required in patients with hepatitis A and E co-infection to determine whether this presentation was an isolated event or not.

Conflict of interest statement

We declare that we have no conflict of interest.

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