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Guillain-Barre Syndrome Associated With Acute Hepatitis A Infection

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Abstract

Guillain-Barre syndrome is an acute polyradiculoneuropathy, often triggered by a preceding bacterial or viral infection. Campylobacter jejuni, mycoplasma pneumoniae, cytomegalovirus and Epstein–Barr virus are the common triggering agents. Infectious agents induced molecular mimicry is supposed to be involved in the pathogenesis of GBS. Rarely, it has been observed in association with hepatotropic viruses (Hepatitis A, B, C and E). However, the nature of the shared epitopes has not been characterized in hepatotropic viruses. We report a case of Guillain-Barre syndrome following acute hepatitis A in a young Indian female.

Keywords

Guillain-Barre Syndrome, Hepatitis A

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1. Introduction

Guillain-Barre syndrome is an acute polyradiculoneuropathy, characterized by rapidly evolving ascending motor weakness, hyporeflexia or areflexia and mild sensory loss. GBS is currently the most common cause of acute flaccid paralysis in the world and constitute one of the serious emergencies in the neurology.[1] GBS is considered a post-infectious, immune-mediated disease. Molecular mimicry and a cross-reactive immune response play a crucial part in its pathogenesis. In two-third of cases, symptoms of a preceding upper respiratory tract infection or gastrointestinal infection are reported, one to three weeks prior to the onset of GBS. Campylobacter jejuni infection is associated with the axonal GBS and Miller Fisher syndrome, whereas cytomegalovirus and Epstein–Barr virus are associated with the demyelinating GBS.[2] Hepatotropic viruses like hepatitis A, B, C and E are increasingly recognized to be triggering microbes. [3]

2. Case Report

A 25 years old female software engineer had high grade fever, vomiting and jaundice. She consulted local physician. She was evaluated at local hospital and diagnosed to have acute hepatitis with serum bilirubin of 5.4mg/dl, aspartate transaminase of 1070IU/L, alanine transaminase of 1206IU/L. There were no features of hepatic decompensation. She was given symptomatic treatment. After one week, she developed neurological symptoms, beginning with paraesthesia in both hands and soles and pain in the back and shoulder. She developed rapidly progressive ascending weakness in all four limbs on next day. She also developed difficulty in speaking and breathing. There was no history of bowel or bladder involvement. These symptoms led the patient to be hospitalized in the neurology department of our institution.

On presentation, she had jaundice and hepatomegaly without any features of hepatic encephalopathy. She was conscious, alert and following verbal commands. She was hemodynamically stable but tachypnoeic. She had bifacial

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lower motor neuron weakness with mild bulbar weakness. Her motor examination revealed generalized hypotonia, areflexic quadriparesis with proximal more than distal weakness [Upper limb power- medical research council (MRC) grade 2, lower limb power- MRC grade 1] and neck muscle weakness. Sensory examination was unremarkable. Diagnosis of Guillain-Barre syndrome was considered in view of rapidly progressive ascending flaccid quadriparesis with areflexia along with bifacial weakness and bulbar involvement.

Blood investigations revealed total bilirubin of 6.06 mg/dl (direct- 3.93, indirect 2.13), aspartate transaminase of 172 IU/L, alanine transaminase of 286 IU/L, gamma glutamyl transferase of 254. Renal functions, coagulation parameters and serum ammonia were unremarkable. Hepatitis B surface antigen, antibodies to hepatitis C, IgM anti-HEV and HIV were absent. IgM Hepatitis A Virus Antibody was positive. Her vasculitis markers and autoimmune hepatitis markers were negative. Ultrasonography of abdomen revealed mild hepatomegaly. Her motor nerve conduction study revealed inelicitable CMAP from right peroneal nerve and significantly reduced CMAP from left peroneal, bilateral median, ulnar and tibial nerves with decreased conduction velocities in right ulnar, right tibial, left peroneal nerves and prolongation of distal latencies in all tested nerves. There was no conduction block. The F response was delayed and impersistent in bilateral median and right ulnar nerves and inelicitable from rest of nerves. H-reflex was absent bilaterally. Sensory nerve action potentials were absent in median, ulnar and sural nerves. These findings were suggestive of proximal and distal symmetrical large fibre sensorimotor predominant polyradiculoneuropathy involving both lower limbs and upper limbs, consistent with acute motor and sensory axonal neuropathy (AMSAN) variant of GBS. GM1 antiganglioside antibody was negative.

A diagnosis of Guillain-Barre syndrome associated with acute hepatitis A was made. Intravenous immunoglobulins were given at a dose of 0.4 g/kg per day for five days. This treatment significantly improved the patient's neurological condition. Her facial weakness had almost completely resolved. Her limb power also improved and she was able to walk with support at the end of 3 weeks. Liver enzymes and bilirubin completely normalized by 3 weeks.

3. Discussion

Guillain-Barre syndrome is considered to be an autoimmune disease triggered by a preceding bacterial or viral infection. The most commonly identified triggering agents are campylobacter jejuni, cytomegalovirus, and mycoplasma pneumonia. Epstein-Barr virus, HIV, shigella, clostridium and haemophilus influenza.[4] The most frequent antecedent infection is campylobacter jejuni infection, which is associated with 30% of cases of the Guillain–Barre syndrome and 20% of cases of the Miller Fisher syndrome.[2] Rarely, it has been associated with acute hepatitis B, acute hepatitis C, hepatitis D, hepatitis E and Hepatitis A.[5] Although GBS is presumed to be autoimmune disease, the molecular pathogenesis of GBS is uncertain. The classic pathological findings in acute inflammatory demyelinating polyneuropathy are inflammatory infiltrates and areas of segmental demyelination, often associated with signs of secondary axonal degeneration. It can be detected in the spinal roots, as well as in the large and small motor and sensory nerves.[6] Ganglioside antibodies may perturb nerve conduction and, in a complement-dependant fashion, disrupt the molecular topography of nodal and paranodal proteins and induce motor axonal degeneration. It is postulated that infected cells can produce ganglioside-like epitopes that trigger the immune response.[7] The proposed pathology is molecular mimicry between virus and peripheral nerve. Hepatitis A infection induces an immune response because of the sharing of cross-reactive epitopes. It will cross-reacts with peripheral nerve components.[8]

Hepatitis A virus-associated GBS appeared to run a course similar to typical GBS. The outcome of GBS did not correlate with the severity of acute hepatitis.[9] GBS with Hepatitis A is reported with younger age of onset and male preponderance. Prognosis of Hepatitis A virus associated GBS was favourable, both in our patient as well as in earlier case reports.[10] Unlike campylobacter jejuni, hepatitis A virus associated GBS could be a marker of a favourable prognosis. We expect increasing numbers of patients with Hepatitis A associated GBS to be reported. It will help in better characterization of this rare association in future.

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