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GUILLAIN-BARRE SYNDROME ASSOCIATED WITH HEPATITIS B VACCINE AND A REVIEW OF THE LITERATURE

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ABSTRACT:
We present a new case of Guillain-Barre syndrome following hepatitis B vaccine and review other cases in the literature. A 14-year-old male patient developed flaccid paralysis after immunization with recombinant hepatitis B vaccine 14 days before. Cerebrospinal fluid analysis revealed acellular fluid with a high protein level. The nerve conduction study was compatible with motor polyneuropathy. Other potential causes of Guillain-Barre syndrome were ruled out. Mechanisms of this very rare complication are proposed along with a literature review.
Key words: Guillain-Barre syndrome, hepatitis B vaccine, review.

HEPATİT B ASISINA BAĞLI GUİLLAİN BARRE SENDROMU OLGUSU VE LİTERATÜRÜN GÖZDEN GEÇİRİLMESİ
ÖZ:
Hepatit B asısına bağlı yeni bir Guillain Barre olgusu sunarak literatürü gözden geçirdik. 14 yasında erkek hasta 14 gün önce yapılan Hepatit B asısını takiben flask paralizi gelisti. Beyin omurilik sıvısı incelemesinde hücre yoktu ve proteini yüksekti. Sinir ileti çalısması demyelinizan polinöropati ile uyumlu idi. Guillain Barre nin diğer muhtemel sebepleri gösterilemedi. Bu nadir komplikasyonun mekanizmaları literatür gözden geçirilerek tartısılmıstır.
Anahtar Kelimeler: Guillain Barre Sendromu, Hepatit B Asısı, Gözden Geçirme.

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INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute postinfectious polyneuropathy that causes symmetric and ascending motor paralysis with the loss of deep tendon reflexes. The syndrome mainly affects motor nerves but sometimes sensory nerves. The initial symptoms include varying degrees of weakness or tingling sensations in the legs. In many cases, the weakness and abnormal sensations spread to the arms and upper body. These symptoms can increase in intensity until the muscles cannot be used at all and the patient is almost totally paralyzed. In more than half of the patients, the paralysis seems to happen after a viral or bacterial infection, like a sore throat or diarrhea.[1] Besides infections, the syndrome has been reported following various vaccines.[2,3]

We present a unique case of GBS associated with hepatitis B vaccine and look over other reported cases of hepatitis B vaccine induced GBS in the literature.

CASE REPORT

A 14-year-old male patient was referred to our hospital due to rapid progression of muscle weakness and inability to walk for 3 days. He did not have a history of upper respiratory tract infection, gastroenteritis, or fever. He had been vaccinated with the first dose of hepatitis B vaccine (Gen Hevac B) 2 weeks before his complaints began.

His physical examination revealed stable vital functions with a respiratory rate of 24/min and heart rate of 93/min. On admission, muscle weakness was present in the distal parts of all four limbs and he could not walk. He had flaccid paralysis (muscle power 2/5) with areflexia. The sensorial examination was normal. The cranial nerves were intact. There was no bowel or bladder involvement. He did not have respiratory insufficiency.

Investigations revealed normal haematological and biochemical data. The urine examination was also normal. Acute phase reactants (erthyrocyte sedimentation rate, CRP) were within normal ranges. A lumbar puncture on the same day revealed 2 cells/mm^3 and protein of 100 mg/dL. Cytomegalovirus (CMV), herpes simplex virus (HSV), and Epstein Barr virus (EBV) antibodies were negative. Serologic testing for Campylobacter jejuni was negative. Antibodies against gangliosides were negative. On the same day the nerve conduction study was suggestive of motor neuropathy involving both perineal and tibial nerves (AMAN type). He was followed in the intensive care unit. Intravenous immunoglobulin (IVIG) (400 mg/kg/day) was administered for 5 consecutive days. He showed clinical improvement and remained static for another 7 days. He responded well to IVIG treatment and supportive

care. Limb power improved gradually and clinical condition showed complete recovery 5 weeks after the initial presentation of his neuropathy.

DISCUSSION

In the present case, the clinical examination revealed GBS. The nerve conduction study and cerebrospinal fluid analysis supported the diagnosis. The pathogenesis of GBS is not clear. Recently described autoantibodies support a close association of GBS and autoimmunity.[4,5] This autoimmune process leads to demyelination or axonal degeneration.

Up to 70% of cases of GBS follow a preceding respiratory or gastrointestinal infection and vaccinations. Associations with various infectious agents have been described including Campylobacter, Mycoplasma, CMV, and EBV.[6] The most common preceding infection is Campylobacter jejuni enteritis and is associated with antiganglioside antibodies against components of the peripheral nerve.[7] In the present case, serum was negative for campylobacter, EBV, CMV and Mycoplasma antibody with the enzyme-linked immunosorbent assay (ELISA). Antiganglioside antibodies were negative.

An increased risk of GBS may also be related to vaccination, but with the presently used vaccines this increase remains below one case of GBS per one million doses. GBS has been reported following influenza, tetanus toxoid, BCG, rabies, small pox, mumps, rubella, oral polio virus vaccine, either plasma derived or recombinant hepatitis B vaccine, and diphtheria vaccine.[8]

Our patient had a history of hepatitis B vaccination 10 days before the symptoms started. Although the pathogenesis of hepatitis B vaccine associated GBS has not been completely elucidated, three mechanisms have been proposed. Molecular mimicry between viral antigens and neural host tissues could be postulated as the first hypothetical mechanism underlying the triggering of the autoimmune diseases like GBS. The DNA sequence of HBV was found to be homologous to myelin basic protein.[9] Coincidental infections like EBV, CMV, and human T lymphotrophic virus (HTLV-3) might be another possible underlying mechanism of GBS in vaccinated patients. Alternatively, in the course of hepatitis B infection, immune complexes that consist of HBsAg, anti-HBsAg, and complement are formed. Deposition of such immune complexes participates in the pathogenesis of arthritis, glomerulonephritis, uveitis, and GBS following hepatitis B virus infection (10). Administration of HBV vaccine may lead to the simultaneous presence of a large amount of antigen and small amounts of antibodies in the serum (similar to that seen in the prodromal phase of hepatitis B), and may, in turn, induce the formation of soluble antigen–antibody complexes, thus initiating clinical disease. The immune complexes may transfer via the blood–nerve barrier and may be deposited in the neuronium and destroy nerve fibers. Administration of IVIG or plasmapheresis may abate these immune complexes. Our patient received IVIG (400 mg/kg) for 5 consecutive days. Five weeks later, he showed an apparent improvement.

Our search of the literature revealed only a handful of hepatitis B vaccine associated GBS cases thus far reported. In 1988, Shaw et al. documented neurological adverse events in the first 3 years of commercial use of the plasma derived hepatitis B vaccine.[11] They reported nine patients with neurological adverse events following vaccination. Nine subjects presented with symptoms 7 weeks after vaccination. One had an atypical presentation. Shaw et al. concluded that there was a slightly higher association in the vaccinated group. McMahon performed a similar study in Alaska in 1992. They reported 2 patients developing GBS after vaccination. They claimed that adverse events are due to the preservative material, thiomersol. In addition to these, 10 case reports of GBS following hepatitis B vaccination have been reported.[12-20]

To the best of our knowledge, this is the second case of GBS associated with hepatitis B vaccination reported from Turkey. As hepatitis B vaccination is recommended in routine immunization programs in this country, physicians should be aware of the serious potential neurological side effects like GBS.

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