



OLGU SUNUMU/CASE REPORT

A recurrence of Guillain-Barré syndrome or a case of acute-onset chronic inflammatory demyelinating polyneuropathy in the course of chronic hepatitis B?

Kronik hepatit B seyrinde Guillain-Barré sendromu rekürrensi mi, akut başlayan kronik inflamatuvar demyelinizan polinöropati olgusu mu?

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Abstract

Chronic inflammatory demyelinating polyneuropathy is a demyelinating polyneuropathy characterized by distal/proximal weakness, which shows gradual progression over a period of 8 weeks or longer. Guillain-Barre Syndrome is a condition characterized by acute monophasic paralysis typically following an infectious assault, and it usually peaks in severity over 3-4 weeks at most. Although rare, there are acute-onset chronic inflammatory demyelinating polyneuropathy cases that show progression over a period shorter than 4 weeks, as is the case in Guillain-Barre Syndrome. This report discusses a case of chronic inflammatory demyelinating polyneuropathy in a HBsAg-positive patient, which started as Guillain-Barre Syndrome but showed 3 recurrences within 6 months, each with rapidly progressing quadriplegia, respiratory arrest, and elevated liver enzymes and HBV DNA.

Key words: Hepatitis b;polyneuropathy;antiviral therapy

Öz

Kronik inflamatuvar demyelinizan polinöropati, 8 hafta ya da daha uzun süre içerisinde kademeli olarak ilerleyen, distal/proksimal kuvvetsizlik ile karakterize demyelinizan bir polinöropati tablosudur. Guillain-Barre Sendromu ise sıklıkla enfeksiyon tablosu sonrası izlenen akut monofazik, en geç 3-4 haftada en üst düzey bulgulara ulaşan paralizisi durumudur. Nadir de olsa Guillain-Barre Sendromu gibi 4 haftadan kısa süre içerisinde progresyon gösteren akut başlangıçlı kronik inflamatuvar demyelinizan polinöropati vakaları da mevcuttur. Burada HBsAg pozitif hastada, Guillain-Barre Sendromu gibi başlayan ancak 6 ay içerisinde 3 kez rekürrens gözlenen ve her rekürrens sırasında hızla ilerleyen quadripleji, solunum arresti gelişen ve karaciğer enzimlerinde ve HBV DNA' da yükseklik saptanan kronik inflamatuvar demyelinizan polinöropati olgusu sunulmuştur.

Anahtar kelimeler: Hepatit B, polinöropati, antiviral tedavi

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a progressive neuropathy characterized by distal/proximal weakness, which shows gradual progression over a period of 8 weeks or longer, or have a course characterized by relapses. Guillain-Barre Syndrome (GBS), on the other hand, is a condition that has a monophasic course, with most of its symptoms and signs reaching a

maximum within a period of 4 weeks^{1,2}. These two distinct neuropathies that have many signs and symptoms in common during the acute phase are immune-mediated conditions³. It has been reported that 16% of patients with CIDP develop a rapid, progressive weakness within the first 8 weeks following the onset of the disease. Such cases are considered as the acute-onset CIDP (A-CIDP)^{3,4}.

On the other hand, 8-16% of patients with GBS are characterized by one or more worsening of

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symptoms shortly after the stabilization or improvement achieved by intravenous immunoglobulin (IVIG) or plasma exchange (PE), which are called Treatment-Related Fluctuations (TRF)^{2,3}. It may prove difficult in clinical practice to differentiate the secondary deterioration in the first week or month due to GBS-TRF and a secondary episode related to A-CIDP. An additional condition confused with these two conditions is the GBS recurrence.⁵ Differentiating these three variants are important, since the treatment strategies and prognoses of these three conditions are different from one another. An additional point we would like to emphasize in our case is the hepatitis B infection detected during the course of the acute clinical picture. Polyneuropathy can be rarely encountered during the course of acute and chronic hepatitis B infection. This report discusses a case of CIDP in a HBsAg-positive patient, which started as GBS but showed 3 recurrences within 6 months, each with rapidly progressing quadriplegia, respiratory arrest, and elevated liver enzymes and HBV DNA.

CASE

A previously healthy, 46-year-old man presented to the neurology outpatient clinic with numbness in hands and feet and weakness in arms and legs for 5 days, and hoarseness and difficulty swallowing for one day. On physical examination he had proximal 2/5, distal 3/5 symmetrical paresis at upper extremities and proximal 4/5, distal -5/5 symmetrical paresis at lower extremities as well as reduced deep tendon reflexes (DTR) and superficial reflexes. He was admitted to hospital with the initial diagnosis of acute polyneuropathy. As EMG examination suggested a mixed-type, demyelinating, moderate-to-severe polyneuropathy primarily involving motor neurons, GBS was primarily diagnosed and a lumbar puncture was performed. CSF analysis showed albuminocytological dissociation (CSF protein: 70 mg/dL, cell count 1/mm³). He later developed peripheral facial paralysis, worsened difficulty swallowing, and mild dyspnea on second day after admission, and was put on plasmapheresis (PE). Hepatitis markers were ordered due to elevated liver enzymes (AST: 91 U/L, ALT: 224 U/L). Serological tests for Hepatitis A, C, D, E were all normal. However, he had HBsAg positivity while HBeAg and AntiHBcIgM were both negative. Therefore, acute hepatitis was ruled out.

He had AntiHBc IgG positivity and a HBV DNA amount of 832.000 u/mL. Anti-nuclear antibody (ANA), smooth muscle antibody (ASMA), kidney liver microsomal antibody (LKM), anti-mitochondrial antibody, ANCA, and anti GM1 and GQ1 antibodies were negative. Brucella, gruber Widal, Rubella IG M were all negative.

He developed respiratory arrest on the second day of plasmapheresis, and he was intubated and transferred to the intensive care unit. He developed anisocoria, IR weakness on the right side and IR loss on the left side, tachycardia, excessive sweating, left peripheral paralysis, and quadriplegia. He began improving after the 7th session, and he was extubated at the 10th session. He continued to improve step-by-step after every session, and his liver enzymes also returned to normal after PE. A liver biopsy was then carried out, which revealed fibrosis grade I, histological activity 6; the patient was put on lamivudin 100 mg/day. The patient was discharged at 1st month while he had absent lower and upper extremity neural action potentials on EMG; he was also quadriparetic and diplegic, and he could walk with assistance at that time. His liver enzymes were normal at the time of discharge (AST: 21U/L, ALT: 23U/L). He returned 2 weeks after discharge with numbness in hands and progressive muscle weakness. His liver enzymes were once again found to be elevated (AST: 138U/L, ALT: 198U/L).

Despite plasmapheresis, he experienced rapid progression, respiratory difficulty, and need for intubation; he was therefore admitted to the intensive care unit where he developed quadriplegia. That recurrence also improved gradually after PE, and he was discharged while he can walk with slight assistance 1 month later. His liver enzymes were normal at the time of discharge (AST: 21U/L, ALT: 23U/L).

Six weeks later, he was readmitted to the intensive care unit with similar symptoms followed by respiratory arrest. He developed rapid progression under intravenous immunoglobulin (IVIG) and plasmapheresis was begun on the 3rd day. One week later, prednisolone was commenced due to inadequate response. His ALT was 70U/L and AST was 128U/L. It was found out that the patient had discontinued his lamivudin therapy for 3 weeks. HBV DNA was 654.000U/mL. Lamivudin was reinstated. Three months after the onset of the last attack he was discharged on oral

methylprednisolone 60 mg/day, antiviral treatment, and IVIG 30 gr/day twice a week for 6 months. At the time of discharge he was able to walk with the assistance of two persons and he had partially persistent difficulty swallowing. At 24th month of the onset of his disease, the patient is on antiviral

therapy and cyclosporine, and he is quadriparetic and diplegic, although he is able to walk without assistance and can meet his own daily needs. His liver enzymes are normal and HBV DNA is currently negative. Liver enzyme and HBV DNA values are summarized in Table.

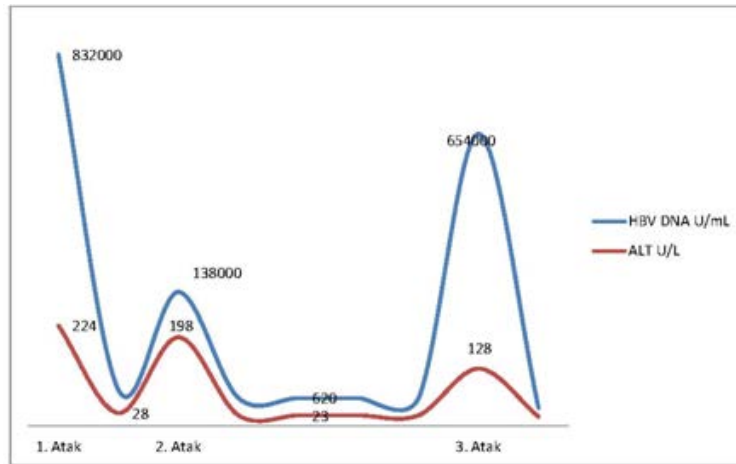


Table. Liver enzyme and HBV DNA values

DISCUSSION

The reported case was diagnosed with GBS since the disease onset was similar to that of GBS and it fulfilled the National Institute of Neurological Disorders and Stroke (NINDS) criteria ⁶. However CIDP was primarily considered owing to course of the disease, 3 recurrences, and low responses to plasmapheresis and immunoglobulin treatments. Ruts et al. reported that 5% of the cases diagnosed with GBS were later diagnosed with A-CIDP, with 10% showing TRF at least once. They also recommended considering A-CIDP as the main diagnosis when there are 3 or more exacerbations since the onset of the disease or exacerbation occurs in 9 weeks after onset ³. Although prospective studies have reported a phrenic nerve involvement rate of 80-90% in patients with CIDP, respiratory involvement and need for mechanical ventilation are quite rare (%1.7-9) ⁷. Furthermore, autonomic dysfunction, bulbar involvement, and facial weakness are common in GBS whereas they are less frequent in patients with A-CIDP ^{4,8}. Bulbar and autonomic involvement, diplegia, and need for

mechanical ventilation observed in our case are considerably rare in A-CIDP cases.

GBS and A-CIDP differ from each other by not only the duration of progression and prognosis, but also by treatment responses. In cases with CIDP there is frequent a need of steroid or immunosuppressant therapy in addition to IVIG or PE ⁸. The main issue in our patient was, as in other similar patients, to differentiate GBS and A-CIDP from each other in the second relapse early during the disease course ⁹. Our patient had a course characterized by unexpected and severe findings unusual for CIDP, and he needed mechanical ventilation. Unfortunately, there exist no criteria to make the distinction during the 2nd attack. GIB-TRF was considered as a possibility in the 2nd attack, and no steroid or immunosuppressant treatment was begun. Here the main concern is the possibility of using medications with severe side effects unnecessarily in GBS, and the risk of serious attacks and severe sequelae of CIDP relapses resulting from a delay in the diagnosis. There is a need for studies facilitating the distinction of these two conditions.

An additional point we would like to emphasize in our case is the hepatitis B infection detected during the course of the acute clinical picture. Polyneuropathy can be rarely encountered during the course of acute and chronic hepatitis B infection. This complication is thought to result from an immune complex containing HBV surface antigen in endoneural capillaries and endoneurium that induces a cytotoxic T cell response^{10,11,12}. In addition, immune response directed at HBV as a result of the similarity of HBV DNA and myelin basic protein may lead to antibody-mediated injury in myelin sheath¹³. Tsukada demonstrated HBV containing immunocomplexes in vasa nervorum in a patient with CIDP considered to be related to chronic HBV infection¹⁴. Furthermore, another study of the authors reported a correlation between remission and exacerbation periods of the neurological symptoms and liver dysfunction¹⁵. There are published cases of inflammatory neuropathy after hepatitis B vaccine or during the course of acute hepatitis B^{11,13,16}. CIDP cases developing during the course of chronic hepatitis B have been rarely reported¹⁷. Further studies on the relationship between hepatitis B and neuropathy should be conducted. The antiviral treatment did not reach adequate duration in the first two attacks of our patient; the patient discontinued the treatment in the third attack. Elevated liver enzymes and HBV DNA in each attack may suggest hepatitis B infection stimulating CIDP. The absence of any polyneuropathy recurrence at 18th month with normal liver enzymes and negative HBV DNA under antiviral treatment may support our theory.

In conclusion, taking complaints such as weakness or numbness serious during the course of acute or chronic hepatitis B is critical for early diagnosis and treatment of neuropathy. It is also vital to prevent hepatitis B exacerbation by using antiviral treatment in CIDP cases in which immunosuppressant therapy is a possibility.

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