

# Guillain - Barre' Syndrome Following Recombinant Hepatitis B Vaccine and Literature Review

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## Abstract

A 17 year-old woman developed progressive quadripareisis with bilateral facial diplegia after immunization with recombinant hepatitis B vaccine 3 days prior. Cerebrospinal fluid analysis revealed acellular fluid with high protein level. The electrodiagnosis was compatible with demyelinating polyneuropathy. Other potential causes of Guillain-Barre' syndrome (GBS) were ruled out. Her motor power gradually improved and returned to normal later. The temporal relationship between GBS and vaccination was suggestive of a vaccine-induced cause. Mechanisms of this very rare complication are proposed with a literature review.

**Key word :** Guillain-Barre' Syndrome, Recombinant Hepatitis B Vaccine

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Numerous cases of vaccine - induced Guillain - Barre' syndrome (GBS) have been reported. Most common are those from influenza vaccine<sup>(1)</sup>. Other sporadic reports include rabies, Bacille Calmette, mumps, rubella, measles, poliovirus, *Hemophilus influenzae* B and hepatitis B vaccines<sup>(1,2)</sup>. Most reports of hepatitis B vaccine associated GBS are plasma-derived vaccine manufactured from human plasma<sup>(2)</sup>. We herein report a case of Guillain - Barre' syndrome after administration of a recombinant hepatitis B vaccine.

## CASE REPORT

A 17-year-old woman was admitted to Songklanagarind Hospital because of progressive weakness for one week. Ten days before admission, she received the first dose of a recombinant hepatitis B vaccine (H-B-vax II; Merck Sharp & Dohme). Three days later, she developed headache, fatigue and weakness. She had no antecedent viral illness and was not taking any medication. Systemic examination was normal. Neurological examination revealed quadripareisis with more predomi-

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nant proximal muscle weakness (MRC grade III/V) than distal muscle weakness (MRC grade IV/V). Bilateral facial diplegia was also observed. The sensation was normal. All deep tendon reflexes were absent.

The laboratory findings revealed a normal complete blood count and urinalysis. The virologic studies included hepatitis B surface antigen and anti hepatitis B surface antibody. They were negative. Serum for anti-HIV antibody, anti CMV (cytomegalovirus) Ig M antibody, and anti VCA (viral capsid antigen) Ig M antibody were also negative. The cerebrospinal fluid had normal pressure and was acellular, with normal sugar level and protein of 208 mg/dl. CSF culture for aerobe was negative. The motor nerve conduction studies demonstrated prolonged distal latency, normal velocity, amplitude and F-wave latency. Sensory nerve conduction studies were also normal. Physical rehabilitation and symptomatic treatment were started. Her muscle strength gradually improved and returned to normal in 2 months.

## DISCUSSION

Various adverse effects from human plasma-derived hepatitis B vaccine are well known<sup>(3)</sup>. These include local and systemic effects such as fever, headache, fatigue, nausea and dizziness<sup>(3)</sup>. GBS, optic neuritis, transverse myelitis, Bell's palsy, convulsion, lumbar radiculopathy and brachial plexus neuropathy have also been reported<sup>(2)</sup>. Among these neurological complications, GBS was found to be significantly associated with the vaccine<sup>(2)</sup>. Since 1986, recombinant DNA hepatitis B vaccine has become commercially available<sup>(4)</sup>. The mild adverse reactions of recombinant hepatitis B vaccine are reported to be similar to plasma-derived hepatitis B vaccine<sup>(4)</sup>. Neurological complications of recombinant Hepatitis B vaccine are very rare<sup>(5-8)</sup>. Only five cases associated with it have been noted<sup>(5-8)</sup>. These include central

nervous system demyelination (2),(5) cerebellar ataxia (1),(6) myelitis (1)<sup>(7)</sup> and GBS (1)<sup>(8)</sup>. The clinical features develop 2-6 weeks after vaccinations of varying doses<sup>(5-8)</sup>. The neurological deficit is usually moderately severe<sup>(5-8)</sup>. The prognosis is good<sup>(5-8)</sup>. The patients usually strikingly improve, but with neurologic sequelae in some cases<sup>(5-8)</sup>.

Our patient developed quadriplegia 3 days after the first dose of the vaccination. She had no antecedent viral illness and was not taking any medication. Her clinical course and laboratory findings were consistent with GBS. Other potential causes were ruled out. The time interval relationship between GBS and recombinant hepatitis B vaccine suggested a causal link between them. Although the incubation period of our case is shorter than previous reports, it is similar to that of some GBS resulting from human-derived hepatitis B vaccine<sup>(2)</sup>.

The pathogenesis of recombinant hepatitis B vaccine - induced GBS is unclear. It may be an immunologic mechanism activated by hepatitis B surface antigen protein in the vaccine which diffused from systemic circulation into neural tissue as occurs in GBS after acute hepatitis B virus infection<sup>(9)</sup>. Hepatitis B surface antigen-antibody complexes were found in the CSF of a GBS -patient after acute hepatitis B virus infection<sup>(9)</sup>. Other probable mechanisms of GBS after recombinant hepatitis B vaccination due to thimerosal,<sup>(10)</sup> a mercurial compound used as a preservative, or to aluminum hydroxide used as an absorbant<sup>(10)</sup>. Both compounds are also used in human plasma-derived vaccine<sup>(3)</sup>. Although we could not definitely prove a causal link between GBS and the vaccination, GBS occurring after the first dose suggested that further doses be withheld.

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## กลุ่มอาการกีฬง แบบ ภัยหลังฉีดวัคซีนตับอักเสบ บี ชนิดรีคอมบิแนนท์และทบทวนรายงานในอดีต

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ผู้ป่วยหญิงอายุ 17 ปี มีอาการอ่อนแรงแขนขาทั้งสองข้างร่วมกับอัมพาตของใบหน้าทั้งสองด้านภัยหลังได้รับวัคซีนป้องกันไวรัสตับอักเสบ บี ชนิดรีคอมบิแนนท์ 3 วันก่อน การตรวจน้ำไข้ลับหลังไม่พบเชลล์ แต่มีปริเด็นสูง การตรวจทางไฟฟ้าของเส้นประสาทเข้าได้กับโรคเส้นประสาทส่วนปลายที่มีการเสื่อมของปลอกในอิลิน และไม่พบสาเหตุอื่นของกีฬงแบบ ภัย การอ่อนแรงของผู้ป่วยดีขึ้นและหายเป็นปกติในเวลาต่อมา ความล้มพั้นธ์ตามระยะเวลาระหว่างกีฬงแบบ ภัยและวัคซีน เชื่อได้ว่าวัคซีนเป็นสาเหตุของกลุ่มอาการกีฬง แบบ ภัย ซึ่งพบได้น้อยมาก กลไกของการเกิดโรคได้ถูกสมมติฐานขึ้นร่วมกับการทบทวนรายงานในอดีต

**คำสำคัญ :** กลุ่มอาการกีฬง แบบ ภัย, วัคซีนตับอักเสบ บี ชนิดรีคอมบิแนนท์

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