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Case Report

Rare Twist: Post-rabies Vaccine Guillain-Barré Syndrome Unveiled

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Abstract

Guillain-Barre syndrome is an autoimmune neurological disorder characterized by rapid worsening weakness, often starting in the legs and spreading upward. Guillain-Barre syndrome is usually preceded by respiratory or gastrointestinal infections. Two-thirds of cases of Guillain-Barre syndrome are diagnosed following infection; however, vaccination has also been linked to Guillain-Barre syndrome pathogenesis. The most commonly known etiology of Guillain-Barre syndrome is an infectious disease notably caused by Campylobacter Jejuni. A very small fraction of people can develop Guillain-Barre syndrome due to vaccines such as meningococcal, poliovirus, influenza, and rabies. Vaccine-associated Guillain-Barre syndrome is defined as those with the onset of Guillain-Barre syndrome symptoms within six weeks after receiving the vaccine. Among the vaccines associated with Guillain-Barré Syndrome, one is for rabies. Given the invariably fatal nature of rabies, post-exposure prophylaxis should be administered in accordance with World Health Organization guidelines. There are two types of vaccines globally available to protect against rabies in humans; which are Nerve Tissue Vaccine 2 (NTV) and Cell Culture Vaccine (CCV). Even though, the World Health Organization has strongly recommended discontinuing the Nerve Tissue Vaccine and replace with the modern cell culture-derived vaccine, a few low-income countries including Ethiopia are still using the vaccine as post-exposure prophylaxis following rabies exposure, because of the affordability and accessibility problems related to modern cell culture vaccines. The vaccine has been predominantly used in Ethiopia since 1944. We are reporting a 22-year-old Ethiopian woman who presented with a progressive weakness for six days. The weakness initially started from the lower limb. It progressed caudally after she had received 12 doses of the Nerve Tissue anti-rabies vaccine, which was administered following a dog bite to her right lower extremity.

Keywords

Guillain-Barre Syndrome, Rabies, Nerve Tissue Vaccine, Post-vaccine GBS

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1. Introduction

Guillain-Barre syndrome (GBS) is a neurological disorder characterized by rapid worsening weakness, often starting in the legs and spreading upward. It's an autoimmune condition characterized by acute onset of peripheral and cranial nerve dysfunction. The pathophysiology of GBS is not thoroughly understood. Evidence suggests a key role of molecular mimicry. Viral respiratory or gastrointestinal infection, immunization, or surgery often precedes neurologic symptoms by 5 days to 4 weeks [1]. The most common preceding infectious diseases are Campylobacter Jejuni, Cytomegalovirus, and Epstein-Barr virus. A small proportion of individuals may experience GBS due to vaccinations, such as meningococcal disease, poliovirus, influenza, and rabies [2].

Rabies, caused by rabies virus (RABV) genotype 1, is one of the most common fatal infections worldwide. It is mainly associated with dog bites in Europe, Asia, and Africa and with bats in the Americas [3]. The clinical stages of rabies are incubation, prodrome, acute neurological signs, coma, and death [4]. Initially, a patient might present with weakness at the bitten extremities, then can progress into either furious or paralytic rabies [5]. Cardinal features of furious rabies are fluctuating consciousness, hydrophobia, inspiratory spasms, and autonomic dysfunction. Conversely, lower motor neuron ascending weakness with only motor disturbance is the initial manifestation of paralytic rabies [5]. Rabies is estimated to cause 59,000 human deaths annually in over 150 countries, with 95% of cases occurring in Africa and Asia [6]. Due to its fatal nature, WHO recommends administering a post-exposure prophylaxis vaccine.

Even though WHO recommends using cell culture vaccine (CCV) for post-exposure prophylaxis against rabies, Ethiopia uses nerve tissue vaccine (NTV) due to affordability and accessibility issues [7].

2. Case Presentation

An Ethiopian female in her 20s presented to the Emergency Department (ED) with progressive weakness over six days. It initially manifested in her lower extremities, starting from her right leg and progressing to her left leg within two days. By the third day, the weakness progressed to involve her upper extremities. This occurred after receiving 12 doses of anti-rabies vaccine following a dog bite to her right lower extremity 17 days prior. Symptoms began on the 11th day of her vaccination regimen.

She had no history of behavioral changes, headache, respiratory complaints, diarrhea, fever, difficulty in swallowing, altered bowel movements, loss of consciousness, trauma, or chronic illnesses. No prior comorbidities or illness.

Upon physical examination, the patient was alert, oriented, and had stable vital signs: BP 110/70 mmHg, pulse rate 88 bpm, RR 20/min, temperature 36.5 ℃, SpO_2 98% on room air. Single breath count was 26. A healed bite area with a 1×2cm scar was observed on the right lower extremity. Neurologically, the patient was alert with a Glasgow Coma Scale of 15/15. Muscle tone was hypotonic, power 0/5 in both lower extremities and 4/5 in upper extremities. Deep tendon reflex was 0 in biceps and triceps bilaterally, +1 in brachioradialis, knees, and ankles bilaterally. Sensation was intact with no atrophy or fasciculations.

Her blood work showed a white blood cell count of 6.5 x 103/μL, a hemoglobin level of 13.8 g/dL, a hematocrit of 40%, and a platelet count of 247 x 103/μL. The renal function test, liver function test, and electrolyte panel were all within the normal range.

In the cerebrospinal fluid analysis, the WBC count was 0.023 x 109/L and the red blood cell count was 0.002 x 1012/L. The monocyte percentage was 73.9% and the polymorphonuclear neutrophil percentage was 26.1%. The glucose level was 50 mg/dL and the total protein level was 4 g/dL.

3. Outcome and Follow-up

The patient was investigated in the emergency room but was discharged against medical advice due to financial constraints.

4. Discussion

GBS is the most common cause of acute, flaccid, neuromuscular paralysis in the United States [8]. Guillain-Barr é syndrome (GBS) and its variants are considered post-infectious, immune-mediated neuropathies. One of the suggested mechanisms is molecular mimicry, where an immune response triggered by prior infection cross-reacts with peripheral nerve components, damaging their myelin sheath [2].

A systematic review from 1985 to 2020 found the incidence rate of GBS ranged from 0.30 to 6.08 per 100,000 population. Males are affected at a slightly higher rate than females [9]. The mean age of diagnosis was 49.8 years (range 16-86) [10]. Although rare, GBS significantly impacts healthcare systems. The estimated cost per patient can reach $318,966 [8]. In addition to that, mortality rates were 2.8% at 6 months and 3.9% at 12 months, with most deaths occurring in among the elderly or severely affected patients during recovery [11].

Clinically, patients present with proximal and distal flaccid weakness, areflexia or hyporeflexia, and sensory symptoms. Facial diplegia and dysphagia may occur due to facial and vagus nerve involvement. The major cause of morbidity and mortality is dysautonomia [8].

GBS is largely a clinical diagnosis, but ancillary tests assist in atypical cases [12]. CSF typically shows albuminocytologic dissociation- normal WBC count with elevated protein [8]. Additionally, Electromyography and nerve conduction studies can help differentiate GBS from its mimics [8].

The finding in our patient was progressive bilateral weak-

ness of the lower extremities which later involved the upper extremities after receiving Nerve Tissue anti-rabies vaccine. On her physical exam, muscle tone was hypotonic and deep tendon reflexes were absent. On the Lab investigations, CSF analysis revealed classic albuminocytologic dissociation with a protein level of 4 g/dL.

There are two current standard treatments: intravenous immunoglobulin (IVIG) and plasma exchange [8]. IVIG likely acts via immune modulation, though its exact mechanism is unclear. The dose is 2 g/kg divided over 5 days [13]. Plasma exchange removes pathogenic antibodies, humoral mediators, and complement proteins. A 2016 meta-analysis found no superiority between IVIG and plasmapheresis in GBS management [13].

In terms of rabies prevention, the nerve tissue vaccine is considered a first-generation rabies vaccine, still in use after Louis Pasteur first administered it in 1885. It is derived from animal brain or spinal tissues and thus has been linked to adverse reactions, including serious neurologic complications such as encephalitis [14]. The rate of neurological complications for nerve tissue vaccines varies in different sources, ranging from 0.14 per 1,000 to 7 per 1,000 cases per treatment [15]. Whereas for cell culture vaccines, less than 10 cases of GBS-like polyradiculopathy have been reported so far, and with the high prevalence of GBS (1.2-3 per 100,000 population), a positive correlation has been difficult to establish [16].

The higher prevalence of acute neurological and non-neurological complications associated with NTVs has led the World Health Organization to strongly recommend its discontinuation in favor of the cell culture vaccine since 1984 [17]. However, it remains in use primarily in LMICs due to its affordability and accessibility compared to the cell culture vaccine [18, 19]. With the persistence of this vaccine access inequity, our case further underscores the need for higher vigilance post-rabies vaccine administration, particularly for nerve tissue-derived ones.

5. Conclusion

Our findings emphasize the importance of monitoring and understanding the potential side effects of vaccines, particularly in the context of rare complications like GBS. It is also crucial to reduce the gap in the availability of Rabies Nerve Tissue Vaccine in low-income countries to reduce vaccine-related Side effects.

Abbreviations

NTV	Nerve Tissue Vaccine
CCV	Cell Culture Vaccine
GBS	Guillain-Barré Syndrome
RABV	Rabies Virus
WHO	World Health Organization
BP	Blood Pressure
RR	Respiratory Rate
bpm	Beats per Minute
SpO_2	Peripheral Capillary Oxygen Saturation
CSF	Cerebrospinal Fluid
IVIG	Intravenous Immunoglobulin
WBC	White Blood Cells
LMICs	Low-middle Income Countries

Author Contributions

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Data Availability Statement

The data used to prepare this case report is available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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