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Treatment-related fluctuation of Guillain-Barré syndrome associated with positive autoantibodies: a pediatric case report

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ABSTRACT

Guillain–Barre syndrome (GBS) is an acute inflammatory polyneuropathy usually considered as a post-infectious autoimmune disease. It is generally monophasic, but treatment related fluctuation (TRF) and recurrences could occur. The main challenge is to differentiate TRF from acute onset chronic idiopathic demyelinating polyneuropathy (A- CIDP). These entities have different outcomes and prognosis, thus the importance of a thorough workup. Genetic and/or immunological host factors may play an important role. In this report, we describe a case of TRF_GBS associated with positive anti-GAD (Glutamate decarboxylase) and anti-VGKC (canals potassium voltages depended) autoantibodies in an 11-year-old boy. With a focus on management and differential work up. Through this case report, we aim to raise awareness among healthcare providers about this rare but potentially severe entity.

Keywords: *TRF – Guillain Barré – anti GAD – Anti VGKC.*

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1. INTRODUCTION

Background:
Guillain-Barre syndrome (GBS) is a potentially life threatening acute immune-mediated polyneuropathy, that typically follows a monophasic pattern [1]. However, in some cases, is shows a different outcome with either r**eoccurrence (**2–5% of pediatric cases)[1] or the development of treatment related fluctuation (TRF) [2]. TRFs are observed in 6–10% and often raise diagnostic challenges in distinguishing GBS from acute-onset chronic inflammatory polyneuropathy (A-CIDP) [3]. In this report, w**e describe a case of TRF-GBS, in an 11-year-old Tunisian boy associated with positive** anti-GAD (Glutamate decarboxylase) and anti-VGKC (canals potassium voltages depended) **autoantibodies. Aiming to** raise awareness among healthcare providers about this rare but potentially severe entity.

Case presentation:
An 11-year-old boy presented with a rapidly progressive symmetrical and ascending muscular pains and weakness in the lower limbs, swallowing disorders, abolition of osteotendinous reflexes, preserved sensitivity, and without sphincter disorders, 07 days after a flu like symptoms.

ENMG was highly suggestive of GBS, with increased protein level in cerebrospinal fluid. The immediate outcome was favorable with complete recovery after a course of intravenous immunoglobulin (IvIg) and motor physiotherapy. Three weeks later, he presented again with reappearance of motor deficit but no sensory deficit. Cerebro-medullary MRI showed

an enhancement of the medullary horn and the horse's tail roots in favor of GBS, hence a second course of IvIg. Further workup showed positive anti-GAD (glutamic acid decarboxylase), anti-VGKC (voltages gated potassium channel) antibodies with negative anti-MOG (myelin oligodendrocyte glycoprotein), anti-acetylcholine receptor, anti-MUSK, anti-ganglioside, anti-neuron, anti-NMDA receptor, and anti- NMO antibodies. After the second course of IvIg he had a partial improvement. He then received a monthly injection of IvIg for 3 consecutive months along with physiotherapy with a total recovery without further relapses for 2 years, and normal ENMG.

2. DISCUSSION:

GBS typically follows a monophasic pattern, however some patients experience TRFs or recurrences, posing diagnostic challenges in differentiating GBS from A-CIDP [3]. TRFs are defined as disease progression occurring within 2 months following an initial treatment-induced clinical improvement or stabilization [1], while relapse is considered with two or more episodes of GBS, with a minimum time between episodes of 2 months (when fully recovered in between) or 4 months (when only partially recovered) [4]. Whereas, chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic acquired immune-mediated neuropathy, typically characterized by clinical worsening over the course of at least 8 weeks. Yet, 16% of patients with CIDP, may present acutely with a nadir in less than 8 weeks simulating GBS, followed by a chronic or relapsing course beyond 8 weeks [3]. The Overlap between these disease courses makes it difficult but crucial, to differentiate them as they implicate different therapeutic strategies and prognosis [2, 3, 5, 6]. In our present case symptoms reappearance occurred 3 weeks after recovery which led us to consider TRF. However, the incomplete response to the second course of IvIg makes A-CIDP also possible but the absence of new flares for 2 years is more in favor of TRF. The distinction between these two entities is delicate, and remains challenging. Clinical elements rely essentially on timing of symptoms occurrence, their nadir and the frequency of relapses [3, 5, 7]. Besides, according to Dionne et al, [7] A-CIDP patients had more sensory signs, and less autonomic nervous system involvement, facial weakness, a preceding infectious illness, or need for mechanical ventilation

However, in a recent literature review, Berin et al, [3] did not find conclusive criteria for differentiation among electrophysiological studies, ultrasonography, and immunological markers.

The particularity of our case is the detection of positive anti-GAD and anti-VGKC antibodies with negative anti-MOG, anti-acetylcholine receptor, anti-MUSK, anti-ganglioside, anti-neuron antibodies, anti-NMDA receptor, and anti- NMO antibodies. In fact, in a national Danish cohort, of 28 patients with anti-VGKC positive testing; 17 showed associated anti LGI1 (Leucine-rich glioma-inactivated 1) antibodies consisting with limbic encephalitis. The remaining LGI1 negative phenotypes were GBS, Creutzfeldt-Jakob disease, neuromyotonia and anti-N-methyl-D-aspartate receptor encephalitis [8]. As for Anti Gad antibodies, they were described in cases of Miller Fisher syndrome [9]. To our knowledge, the association of these two autoantibodies was not described in GBS patients before. Our case may suggest their role in the pathogenesis as well as the recurrence of the disease. Further immunological investigations are needed to better determine their clinical and pathogenic significance in this syndrome.

3. CONCLUSION:

The spectrum of demyelinating neuropathies is large and overlapping. Boundaries between acute and chronic entities are not clear. Immunological workup may help a better pathogenic comprehension and management.

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