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СИНДРОМ ГИЙЕНА-БАРРЕ С ПОЗДНИМ НАЧАЛОМ ПОСЛЕ COVID-19: СВИДЕТЕЛЬСТВО ДЛИТЕЛЬНОЙ ИММУННОЙ ДИСРЕГУЛЯЦИИ У ПАЦИЕНТА С ПРЕДШЕСТВУЮЩИМ АУТОИММУННЫМ ЗАБОЛЕВАНИЕМ

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DELAYED ONSET GUILLAIN-BARRÉ SYNDROME FOLLOWING COVID-19: EVIDENCE OF PROLONGED IMMUNE DYSREGULATION IN A PATIENT WITH PRE-EXISTING AUTOIMMUNITY

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Резюме. В этой статье описывается случай развития синдрома Гийена-Барре (СГБ) примерно через 20 месяцев после тяжелой инфекции SARS-CoV-2 у 68-летней женщины с уже существующим панникулитом Вебера-Кристиана, получавшей хроническую терапию кортикостероидами, что представляет собой клиническую картину, не описанную ранее, но подчеркивает тройной иммунный каскад.

Ключевые слова: синдром Гийена–Барре, COVID-19, аутоиммунное заболевание, болезнь Вебера–Крисчена, кортикостероиды.

Resume. This article reports a case of Guillain-Barré syndrome (GBS) developing approximately 20 months after severe SARS-CoV-2 infection in a 68-year-old female with pre-existing Weber-Christian panniculitis on chronic corticosteroid therapy representing a clinical constellation not described previously while highlighting a triple immune cascade.

Keywords: Guillain-Barré syndrome, COVID-19, autoimmune disease, Weber-Christian panniculitis, corticosteroids.

Relevance. Weber-Christian panniculitis affects fewer than 1 in a million people. Guillain-Barré syndrome affects roughly 1 in 100,000. The odds of one patient carrying both - separated by a two-year delay triggered by covid 19 should have been essentially zero. Patients with pre-existing autoimmune diseases have a significantly increased risk of developing new-onset autoimmune conditions following COVID-19 infection [3], with reported incidence rates of approximately 3.8% (38.10 per 1,000 individuals) following COVID-19 infection.

Aim: to elucidate the pathophysiological mechanisms underlying the delayed onset of GBS two years following COVID-19 infection, with particular focus on how pre-existing autoimmunity and prolonged corticosteroid therapy may alter immune signaling. Specifically, this study explores how these factors may predispose to GBS while modulating and delaying its neuroinflammatory clinical presentation.

Objectives:

1. Characterize the triple autoimmune cascade: Weber-Christian panniculitis, then COVID-19, then GBS.
2. Analyze the mechanisms of delayed onset of GBS following COVID-19.

3. Evaluate the role of corticosteroids in altering the neuroinflammatory threshold.

Materials and methods. A retrospective analysis of a single patient case from the 6th Clinical Hospital, Minsk, Belarus was conducted, supplemented by a focused review of current literature from scientific databases.

Results and their discussion. This is a case of a 68-year-old female (DOB: 24.12.1955) with a history spanning three hospitalizations across six years. The patient's clinical course unfolded as a sequential triple autoimmune cascade, each hospitalization setting the stage for the next.

Tbl. 1. Summary of patient's three hospitalizations

	Hospitalization 1 (2018)	**Hospitalization 2 (2022)**	**Hospitalization 3 (2024)**
Department	Rheumatology	Pulmonology / COVID-19 Unit	Gastroenterology → ICU
Presentation	Painful, itchy rashes on extremities; numbness of three fingers (right hand); joint pain; general weakness, fatigue COMORBIDITIES IHD, Arterial hypertension grade 2, CHF NYHA II	Dry cough, high fever, dyspnea, general weakness	Chest pain, constipation – GBS not yet suspected; 8-days in gastroenterology
Diagnosis	Recurrent Weber-Christian Panniculitis + secondary vasculitis (M35.6)	Severe COVID-19; bilateral interstitial polysegmental pneumonia; new-onset atrial fibrillation	AIDP- Guillain-Barré Syndrome; deep tetraparesis
Key findings	ANA positive; ESR elevated;	Ag SARS-CoV-2+; bilateral CT infiltrates; SpO_2↓; leukocytosis; elevated CRP/ESR; steroid-induced hyperglycemia	CSF protein 1.739 g/L (4–11× above normal); 0 cells/μL; pathognomonic albuminocytological dissociation; DVT; probable PE
Treatment	Methylprednisolone pulse 125 mg × 3 days; oral methylprednisolone 4 mg (long-term); hydroxychloroquine	Remdesivir; dexamethasone; fraxiparine; rivaroxaban	IVIg 0.4 mg/kg/day × 5 days; intubation (11 Mar); tracheostomy (14 Mar); anticoagulation; Death: 19.03.2024

GBS was confirmed on ICU transfer (8 March). Neurological findings included deep tetraparesis, areflexia, bulbar involvement (swallowing and speech affected), respiratory muscle weakness, autonomic dysfunction (hemodynamic instability), and arrhythmia. CSF analysis revealed the hallmark finding: protein 1.739 g/L (4–11× above normal, severely elevated) with 0 cells/μL (normal), markedly elevated protein with normal cell count is pathognomonic for GBS. The main diagnosis was confirmed as Acute Inflammatory Demyelinating Polyradiculoneuropathy -AIDP (Guillain-Barré Syndrome).

Tbl. 2. CSF analysis: hallmark albuminocytological dissociation confirming AIDP-GBS

Parameter	Patient's Result	Normal Range	Significance
Protein	1.739 g/L	0.15–0.45 g/L	4–11× above normal - severely elevated
Cell count	0 cells/μL	0–5 cells/μL	Normal
Glucose	Normal	Normal	-
Appearance	Clear / xanthochromic	Clear	Elevated protein effect

Covid-19 as the immunological trigger: Patients with pre-existing autoimmune diseases have a significantly elevated risk of developing new autoimmune conditions after COVID-19 infection, with an incidence rate of 38 per 1,000 person-years, compared to 15 in those without prior autoimmunity.[3]

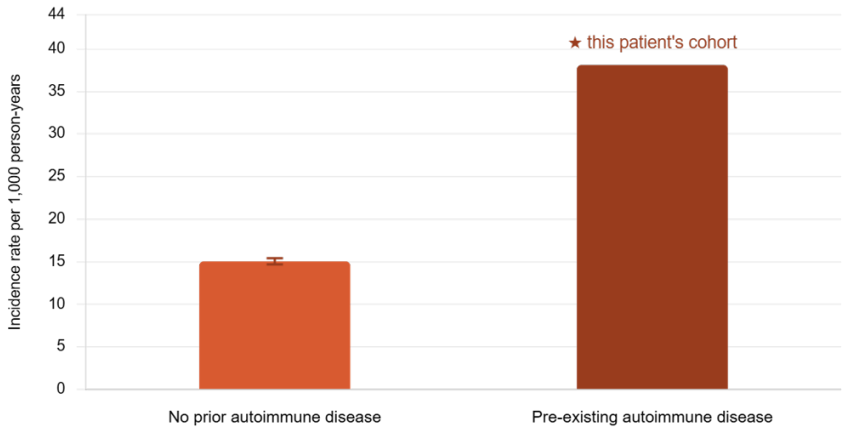

Fig. 1 – Incidence of developing autoimmune conditions after COVID-19

Persistent viral reservoirs may remain detectable for up to two years.[5] COVID-19 may act as an immunological stressor superimposed on an already dysregulated immune system, potentially triggering a prolonged subclinical phase. SARS-COV2 causes an overactivation of the immune system leading to the formation of various autoantibodies.[2]

Role of corticosteroids:The patient had been on long-term methylprednisolone therapy for nearly seven years prior to the diagnosis of GBS which could have led to the suppression of inflammation and attenuation of pain (common side-effects of chronic corticosteroid therapy) thereby obscuring early neuropathic symptoms such as paresthesia and mild weakness. Additionally, steroid-induced myopathy may have contributed to the

misattribution of proximal muscle weakness to medication side effects rather than an evolving neuropathic process. As a result of these processes, an increase in threshold of inflammatory activity required to produce clinically detectable nerve damage may have been observed.[1,4]

All published post-COVID GBS cases report onset within 1 to 6 weeks of acute infection[6], but it took this patient approximately 20 months. We propose that it was not a single cause but a cumulative threshold effect that caused this.

The patient entered COVID-19 with autoantibodies already present from her Weber-Christian Panniculitis, her immune system was already misdirected. Severe COVID-19 then generated additional autoantibodies through molecular mimicry and immune overactivation. Simultaneously, chronic corticosteroid-induced immunosuppression partially restrained the inflammatory cascade slowing it, but not stopping it. Over approximately 20 months, this subclinical autoimmune process gradually accumulated until it crossed the threshold required to produce clinically manifest GBS.

This is not GBS appearing out of nowhere two years later. This is GBS that was building slowly, restrained by steroids, until it became clinically manifest.

Conclusions. Clinicians evaluating post-COVID patients with pre-existing autoimmune disease should maintain heightened GBS vigilance even beyond the classical 6-week window, and especially when autonomic symptoms such as constipation, chest pain and hemodynamic instability predominate over the classic ascending paralysis.

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