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Acute Onset Chronic Inflammatory Demyelinating Polyneuropathy Following COVID-19

COVID-19 Sonrası Akut Başlangıçlı Kronik İnflamatuar Demiyelinizan Polinöropati

Miruna Florentina ATEŞ
0000-0001-5953-4240
Sude KENDİRLİ
0000-0002-6152-6730
Sibel KARŞIDAĞ
0000-0002-2887-9235
Şevki ŞAHİN
0000-0003-2016-9965
Nilgün ÇINAR
0000-0003-3868-3137

Department of Neurology, Maltepe University Faculty of Medicine, İstanbul, Turkey

ABSTRACT

The cases of Guillain Barre Syndrome (GBS) have been reported following the coronavirus disease 2019 (COVID-19). Here, we describe a case that evolved from GBS to chronic inflammatory demyelinating polyneuropathy (CIDP) after COVID-19 in terms of contributing to the literature due to its different aspects. In the cerebrospinal fluid examination of the acute onset mixed type polyneuropathy case, albuminocytological dissociation was not detected. The patient was given a loading dose and monthly maintenance intravenous immunoglobulin (IVIG) for six months. Blood ferritin levels gradually decreased in parallel with clinical improvement. Four months after the IVIG treatment was terminated, the findings recurred and the CIDP was developed and IVIG treatment was continued. Long-term follow-up of post-COVID-19 GBS patients is important in terms of recurrence and chronicity. Ferritin level may be a biochemical marker in the clinical follow-up of these cases.
Keywords: COVID-19; GBS; ferritin; axonal; recurrence; prognosis.

ÖZ

Koronavirüs hastalığı 2019'u (coronavirus disease 2019, COVID-19) takiben Guillain Barre Sendromu (GBS) vakaları bildirilmiştir. Burada farklı yönleri nedeniyle literatüre katkı sağlaması açısından COVID-19 sonrası GBS'den kronik inflamatuar demiyelinizan polinöropatiye (chronic inflammatory demyelinating polyneuropathy, CIDP) evrilen bir olguyu tanımladık. Akut başlayan mikst tipte polinöropati olgusunun beyin omurilik sıvısı incelemesinde albüminositolojik dissosiasyon saptanmadı. Hastaya yükleme dozu ve altı ay boyunca aylık idame intravenöz immünglobulin (IVIG) verildi. Kan ferritin düzeyleri klinik iyileşme ile paralel tedricen azaldı. IVIG tedavisi sonlandırıldıktan 4 ay sonra bulgular tekrarladı, CIDP gelişti ve IVIG tedavisine devam edildi. COVID-19 sonrası GBS hastalarının uzun süreli takibi nüks ve kroniklik açısından önemlidir. Bu olguların klinik takibinde ferritin düzeyi biyokimyasal bir belirteç olabilir.
Anahtar kelimeler: COVID-19; GBS; ferritin; aksonal; nüks; prognoz.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) primarily involves the respiratory system but also causes central and peripheral nervous system findings. Acute polyradiculopathy is among the rare neurological complications of COVID-19 infection (1). Guillain Barre syndrome (GBS) develops following many viral diseases such as *campylobacter jejuni*, Epstein-Barr virus, influenza or cytomegalovirus (2). It has been reported recently that COVID-19 can cause GBS, recurrent GBS, and the worsening of chronic inflammatory demyelinating polyradiculopathy (CIDP) (3). It has been reported GBS associated with COVID-19 did not show classical and electrophysiological features and it had a lot of variations (4).

Corresponding Author
Sorumlu Yazar
Miruna Florentina ATEŞ
miruna.ates@gmail.com

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Here, we present a case of acute motor-sensory axonal neuropathy (AMSAN) as a variant of GBS after COVID-19 and relapsed ten months later.

CASE REPORT

A 39-year-old female, hospitalized with dry cough, dyspnea, and fever. A positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was found in the RT-PCR assay at the nasopharyngeal swab and ground-glass opacities in the lung at computed tomography (CT) scan were seen. One week after her discharge, she was admitted to the neurology outpatient clinic with difficulty in walking and generalized pain. Neurological examination revealed for 3/5 weakness in the distal of the upper and lower extremities. Cranial nerve, cerebellar system, and sensory examination was normal. Deep tendon reflexes could not be detected in the lower extremities; the Babinski reflex was negative.

Nerve conduction studies showed prolonged distal motor latencies (DML), small compound muscle action potentials (CMAPs) and decreased nerve conduction velocities (NCVs) in the tibial and median motor nerves bilaterally. Sensory nerve conduction studies showed prolonged sensory latencies, small sensory nerve action potentials (SNAPs) and decreased NCVs in the sural nerves bilaterally. The latencies of the tibial F-waves were prolonged bilaterally. Abnormal spontaneous potentials were recorded in the lower extremity muscles in needle electromyography (EMG). These EMG findings were found compatible with the AMSAN variant of GBS.

A mild elevated white blood cells count (70 /mm^3), normal protein level (10 mg/dl), and normal sugar level (65 mg/dl) was detected in the cerebrospinal fluid (CSF) analysis. PCRs for Herpes simplex virus 1-2, SARS-CoV-2, serologic antibody tests for Epstein-Barr virus, cytomegalovirus, and *Borrelia burgdorferi* were found negative in CSF. The patient's had normal IgG index (0.1) without oligoclonal bands of the CSF. Anti-ganglio side antibody, including anti-GM1, GM2, GM3, GD1a, GD1b, Gt1b, and GQ1b was negative.

Intravenous immunoglobulin (IVIG) treatment was given 0.4 gr/kg/day for 5 days as starting dose. Since the neurological findings showed partial improvement, maintenance IVIG (1 gr/kg monthly) was continued. Treatment was terminated because nerve conduction studies returned to normal in the repeated EMG at 6 months. Modified Erasmus GBS Outcome score (mEGOS) reduced from 6 to 3, gradually. Ferritin levels were also gradually got normal limits in the six months (monthly ferritin values: 1259, 946, 488, 282, 271, and 170 ng/ml, respectively, normal range: 10-204 ng/mL). However, difficulty in walking and sensory complaints in the hands developed again after 10 months. Repeated EMG showed slowing in tibial motor NCVs, small CMAPs in median and tibial motor nerves. Decreased NCVs in sural sensory nerves was detected. The IVIG treatment was restarted as 1gr/kg monthly.

DISCUSSION

SARS-CoV-2, like other viruses, can trigger GBS in the post-infectious period. The first COVID-19 related GBS case has been reported by Zhao et al. (5) in 2020. Acute polyneuropathies have been reported with severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV), which have been previously caused epidemics (6).

A large Italian study reported an incidence of GBS as 0.42% after COVID-19 (7).

GBS symptoms typically start several days to a few weeks after acute viral illnesses. In recent studies, the mean time interval from COVID-19 to GBS symptoms was reported 11±6 days (4). GBS cases related to COVID-19 have a wide spectrum. The most common electrophysiological pattern is acute inflammatory demyelinating polyneuropathy (AIDP), less frequently acute motor axonal neuropathy (AMAN), and AMSAN (4). It has been reported abnormalities in the central nervous system together with GBS symptoms. Albuminocytological dissociation is reported in the CSF in 75% of the cases. The absence of typical areflexia in some cases has been reported as an interesting finding. It was reported that 73-75% of the patients showed varying degrees of improvement in 5 days to 8 weeks. CSF protein elevation is known as an important biomarker determining the severity and extent of the disease (8). In our patient, the CSF protein level was low, and the clinical course showed a slow recovery. We detected serum ferritin level as an important biomarker.

mEGOS has been shown to be a significant predictive parameter in GBS patients. The Brighton criteria are helpful to confirm the diagnosis of GBS variants, evaluating different features (10). The patient's clinical presentation, CSF findings, nerve conduction studies evaluate and score between 1 and 4 (level 1: the highest certainty). Srivastava et al. (11) determined 66% of the COVID-19-related GBS patients as level 1, 24% as level 2, 6% as level 3, and 3% as level 4 according to the Brighton criteria. Our patient shows level 3 diagnostic acuity according to the Brighton criteria.

The mortality rate was reported as 5.8% in GBS cases after COVID-19. Partial and complete recovery was reported in 72% of patients (3).

Ferritin is one of the acute phase reactants as such C-reactive protein, haptoglobin, fibrinogen and it has a critical role in inflammation (12). Lino et al. (13) observed a strong relationship between serum ferritin level at the first days of hospital admission and mortality in COVID-19 patients. Some research focused that ferritin levels in the first seven days were the sign of early hyper inflammation secondary to cytokine storm (14). A meta-analysis showed that ferritin is a marker of progression to critical illness (15). So far, it has been emphasized that hyperferritinemia syndrome in the early days may help identify high-risk patients. In our case, hyperferritinemia persisted although other acute phase reactants returned to normal in the first month. It may be important in following the course of the disease in GBS cases after COVID-19.

Recurrent GBS (rGBS) is defined as 2 or more episodes of GBS that recur with ≥4 months intervals in incompletely healed cases and ≥2 months intervals in patients who fully recover. rGBS develops in 2-5% of patients with previous GBS (16,17). McDonnel et al. (18) reported a case of rGBS triggered by COVID-19, who had two GBS attacks before. GBS treatment-related fluctuation is defined as at least one grade worsening in disability scores within 2 months after discontinuation of immunotherapy (17). CIDP is characterized by a slow

progressive relapsing course that gradually worsens over 8 weeks (19). Suri et al. (20) defined acute onset CIDP as worsening of GBS symptoms after 8 weeks from onset or worsening attacks of the neurological findings at least 3 times. It is difficult to distinguish rGBS, treatment-related fluctuations, from CIDP. There may be spectrum-like transitions between rGBS and CIDP. Partial worsening of neurological findings developed after 4 months from the cessation of immune therapy in our patient. This is differing from treatment-associated fluctuation.
Although relapses reported in 2-5% of GBS patients (21), repeated clinical relapses may suggest a more chronic disease process or the diagnosis is an acute CIDP initially in this patient.

CONCLUSION

Post-COVID-19 GBS may occur in different patterns and it may progress to CIDP. GBS cases should be followed up in terms of recurrence and chronicity. Ferritin level may be a biochemical marker in the clinical follow-up of these cases.

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