Case report

Atypical miller-fisher syndrome after COVID-19 and sleeve gastrectomy: Contribution of neurochemical markers to early diagnosis

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began in late 2019. More recently, there have been sporadic reports of development of Miller-Fisher Syndrome, a rare variant of Guillain-Barré Syndrome in COVID-19 patients.

Case report: We report here the case of a young French woman presenting with ophthal-moplegia, cerebellar ataxia, and universal areflexia following a bariatric surgery (sleeve gastrectomy). A concomitant COVID-19 diagnosis was retained based on microbiological testing. The patient was successfully treated after high-dose intravenous thiamine, but areflexia persisted. Underlying COVID-19 related Miller-Fisher Syndrome was established on physical examination and confirmed by pathologic neurophysiological findings and elevated level of phosphorylated neurofilament heavy chain protein in cerebrospinal fluid analysis.

Conclusions: Guillain-Barré Syndrome and its variants after SARS-CoV-2 infection are extremely rare. The measurement of phosphorylated neurofilament heavy chain protein should be considered as an easy tool to detect an early affection of the peripheral nervous system.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a multi-symptomatic disease with potentially lethal direct and indirect complications, which can particularly cause neurologic damage [1]. Guillain-Barré Syndrome (GBS) and Miller-Fisher Syndrome (MFS), classified as rare variant of GBS, are emerging as known consequences of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2,3].

MFS is an autoimmune disease of the peripheral nervous system characterized symptomatically by ophthal-moplegia, ataxia, and areflexia and biochemically by elevated cerebrospinal fluid (CSF) protein concentration and the presence of autoantibody against ganglioside GQ1b [4]. The annual incidence is around one patient per one million population [5]. Furthermore, a variety of recent factors associated with surgical complications, mortality rates and consequences have been reported in COVID-19 surgical patients [6,7]. We described herein a rare clinical presentation of MFS overlap with Wernicke Encephalopathy (WE) in a French young adult patient with SARS-CoV-2 infection and emphasized the contribution of neurophysiological studies and neurochemical markers such as neurofilament heavy chain protein (pNFH) in CSF to early diagnosis, in this context.

2. Case report

On March 01, 2021, a 25-year-old woman with a severe obesity (BMI=36.8 kg/m²) and no other significant medical past history underwent laparoscopic sleeve gastrec-
tomy (SG). After surgery, an enteral feeding (first liquid then semi-liquid food) was introduced with no intestinal intolerance or disorders.

On April 20, 2021, the patient sought care after two weeks of gastro-intestinal (GI) symptoms such as nausea and vomiting, general weakness (weight loss about 14 kg), polypnea (24 breaths/minute) and tachycardia (120 to 150 beats/minute). Abdomino-pelvic computed tomography was normal. On April 23, she developed severe gait disorder with repeated falls, double vision, myalgia of the lower limbs and painful sensation of electric discharges. So, the patient was hospitalized in our department of neurology. Neurologic examination revealed multi directional bilateral nystagmus, bilateral abducens nerve palsy, cerebellar gait ataxia and universal areflexia.

At admission, concomitant COVID-19 was diagnosed from results of real-time reverse transcription PCR (RNA nucleocapsid gene (N) of SARS-CoV-2 was detected with a cycle threshold (Ct) value of 44) and SARS-CoV-2 serology (positive for IgG 58 U/mL). The patient was isolated and neither antimicrobial drugs nor steroids were begun.

Brain magnetic resonance imaging (MRI) (with diffusion weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) sequences) was normal. Lumbar puncture showed clear CSF with normal blood cell count (1/mm³), normal protein concentration (0.3 g/L), moderately elevated Lactate level of 3.3 mmol/L and one monoclonal band. Phosphorylated neurofilament heavy chain protein (pNfH) was moderately elevated in the CSF, at 784 pg/mL (normal levels below 560 pg/mL). On neurophysiological examination, we found early signs of acute inflammatory demyelinating polyneuropathy (demyelination of the nerve roots): extended F-waves were found of right fibular nerve. F-waves were not detected on bilateral median nerve, right ulnar nerve, right tibial nerve, left fibular nerve. A-waves were found on right fibular nerve, right tibial nerve, left median nerve. The diagnosis of MFS was established based on physical examination and electromyography (EMG) findings. There was no evidence of other predisposing infectious or autoimmune factors in CSF analysis and MRI.

Further investigations such as serum anti-ganglioside antibodies including GQ1b and campylobacter serology were negative.

The vitamin B1 (thiamine) test showed a low blood level at 61 mmol/L (normal range: 83–245 mmol/L). The patient received high-dose intravenous (IV) thiamine (300 mg daily for 10 days). Symptoms subsided (abducens nerve palsy and nystagmus disappeared, pulse frequency was normalized and cerebellar ataxia improved considerably after 48 hours). However, universal areflexia persisted. No other specific treatment has been associated. After the good clinical outcome, we decided against IV immunoglobulins.

3. Discussion

Wernicke Encephalopathy (WE) in non-alcoholic patients has been reported after bariatric surgery [8], even as a very early complication after surgery [9], such as our patient.

Despite absence of cognitive impairment, the diagnosis of WE was initially suspected in regard to clinical presentation with bilateral abducens nerve palsy, nystagmus (ocular signs) and cerebellar ataxia [10] and confirmed with low vitamin B1 blood level with favorable outcome after the correction of thiamin deficiency.

Nevertheless, universal areflexia and early EMG findings of acute Guillain-Barré type demyelinating polyneuropathy in very early state cannot be explained by WE diagnosis. We want to focus on the initial clinical history of this patient, which has associated general, GI, and respiratory symptoms and concluded to mild symptomatic form of COVID-19. This was approved in regard to RT-PCR SARS-CoV-2 and serology results with a first negative RT-PCR at surgery moment (On March 01, 2021).

The latency period between COVID-19 clinical features and neurologic symptoms (about 2 weeks after onset of first clinical symptoms) suggests a neurologic complication following COVID-19, which led us to retain early manifestations signs of MFS after SARS-CoV-2 infection.

Currently, the neuro-invasive mechanism of SARS-CoV-2 has been demonstrated and it’s known that multiple neurological complications including GBS [2] and MFS [3] have been associated with COVID-19. Obviously in addition to previous publications [11,12] the immune-mediated mechanism is different compared to traditional MFS cases with positive anti GQ1b antibodies [12,13]. Senel et al. [11]. suggested that measurement of neurochemical markers such as pNfH in the CSF might be considered an easy tool to detect early affection of the peripheral and central nervous system following SARS-CoV-2 infection, such as our patient. Moreover, the period from COVID-19 to the appearance of neurological symptoms was similar to that of almost cases reported in medical literature [2,3].

In effect, ataxia and opthalmoplegia can be explained by underlying WE related to thiamin deficiency after bariatric surgery. However, we could also conclude that ataxia and opthalmoplegia, but not nystagmus, were also caused by post-COVID 19 MFS; there are a few concerns that limit the robustness of our conclusions: (1) The cardinal features for a clinical diagnosis of MFS [14] is significantly confounded by this patient’s thiamine deficiency. The high response to thiamine for suspected cardinal findings of opthalmoplegia and ataxia lead one initially to doubt on the additional specific diagnosis of MFS. Further investigations with features of proximal nerve root involvement due to multiple absent F waves (and prolonged F waves) and collateral sprouting resulting in A
waves, and along with areflexia as described in GBS and MFS as a GBS variant sustains diagnosis of MFS. (2) The role of pNFH in CSF has mainly been described to show moderate association with worse long-term outcomes in GBS [15]. The case report uses it to aid in the diagnosis [11], however we know, MFS is predominately a clinical diagnosis, and would avoid highlighting a diagnostic role of this investigation as it is mainly been described as potentially prognostically useful.

4. Conclusion

In this case, we want to highlight a scarce presentation of MFS after infection with COVID-19 in a context of WE after bariatric surgery, for which carrying out the diagnosis has proven difficult. Neurochemical markers should be considered to detect early MFS, GBS and its variants following SARS-CoV-2 infection.

Availability of data and material

Not applicable

Code availability

Not applicable

Authors’ contributors

BH and SZ drafted the manuscript. HZ, NB and TK revised the final manuscript. We especially thank Dr Isabelle QUADRIO (Hospices Civils de Lyon, France) for her help.

Declaration of competing interests

All authors declare no competing interests.

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Ethics approval

Not applicable.

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