Postcovid Guillain-Barré syndrome with severe course – case series two patients including clinical evaluation of smell and examination of olfactory event-related potentials (OERPs)

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Introduction. We report a case series two patients of Guillain-Barré syndrome (GBS) associated with previous COVID-19 that both patients survived. GBS is an immune-mediated disease that affects peripheral nerves and can cause life-threatening complications.
Case Reports. In both cases (53-year-old female and 59-year-old male) with severe GBS with complications, the smell of sense was investigated subjectively using Sniffin' sticks identification tests and objectively using objective olfactometry by the evaluation of olfactory event-related potentials (OERPs). Both patients had good results of the subjective Sniffin' sticks identification test without patholgical findings. Results of objective examination of OERPs: the P2-N1 wave complex was equipotent. No olfactory disturbance could be detected in either case, OERPs were plentiful in both cases.
Conclusion. The presentation of a case series two patients of post-covid GBS are an example of one of the many complications of COVID-19 that can cause prolonged recovery. Despite the severe course of GBS and the long recovery time, both patients returned to normal life. An expanded prospective study is planned for the future to investigate post-covid olfactory impairment. The prevalence of GBS associated with COVID-19 is still unknown but it is evident that both mild and severe forms of GBS have been described in patients.

Key words: Guillain-Barré syndrome, COVID-19 infection, Sniffin stick tests, olfactory event-related potentials, objective olfactometry

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INTRODUCTION

An increasing number of neurological complications are being recognized in association with COVID-19 infection, including patients with severe Guillain-Barré syndrome (GBS) and its variants. It presents with several subtypes ranging from acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN) and acute inflammatory demyelinating polyradiculoneuropathy (AIDP). Guillain-Barré syndrome commonly occurs after viral infections, including COVID-19. Life threatening complications occur with GBS. Neurologic symptoms are present in about 57% (ref.[1]) of patients with COVID-19 and include hyposmia, parosmia, dysgeusia, myalgias and headache, which appear at an early stage of the disease[1-4].

Viral diseases cause prolonged olfactory loss, most likely due to a protective response of neurons to prevent the spread of the virus intracranially. Loss of olfaction is the most commonly reported symptom in patients with COVID-19. The spontaneous recovery rate is high. Persistent olfactory disorders are estimated at 30% (ref.[5-8]) of patients one year after COVID-19 (ref.[5-8]). No treatment is, to date, significantly effective on persistent post-viral olfactory disorders with the exception of olfactory training[6,8].

There are subjective and objective methods of examining the sense of smell. Frequently used subjective tests include the Sniffin' sticks identification test[6,8-10].

The Sniffin' sticks test kit contains 16 odourant-impregnated pen-like odour dispensing devices which should be identified by the patient[8].

Objective methods are mainly represented by objective olfactometry. It is based on the principle of presenting the odourant by an olfactometer into the patient's nasal cavity and detecting the odourantevoked electric activity of neurons in the olfactory pathway.

Vanillin or 2-Phenylethanol (Rose odour), which selectively stimulates the olfactory nerve and CO2 for the trigeminal nerve are used as odourants. The objective olfactometer measures olfactory event-related potentials (OERPs). OERPs consisting of a negative component, N1, followed by two positive components, P2 and P3 (ref.[8,9,11-14]).

Observation

We report two case reports of AIDP associated with previous COVID-19 infection. We performed an olfactory examination using Sniffin' sticks identification (Burghart) tests and objective olfactometry, which is a electrophysiological technique and measures OERPs. We used the objective olfactometer OL 24 (Burghart) – see Fig. 1 (Objective olfactometer OL 024 Burghart – measurement of olfactory event-related potentials (OERPs), from corresponding author's archive).

The patients presented in this manuscript signed an informed consent for the olfactory examination.

The study was approved by the local ethics committee: number 108/1–4/2021.

CASE REPORT 1

A 53-year-old female, unvaccinated for COVID-19, experienced a mild course of COVID-19 from November 19, 2021, without loss of smell or taste. COVID-19 was confirmed by PCR test. With a latency of 14 days, the first neurological symptoms appeared: weakness of the lower limbs, inability to walk, paresthesia of the upper limbs. She was admitted acutely to the neurology department because of suspected ascending AIDP, clinically progressive symmetric flaccid quadriparesis and quadruparesis, without borderline sensory deficits. Computed tomography (CT) scans of the lungs showed signs of COVID-19 pneumonia. The Electromyography (EMG) findings showed signs of severe motor conduction disorder of the mixed type. An examination of the cerebrospinal fluid revealed proteinocytological dissociation. The clinical picture and results of paraclinical examinations support the diagnosis of the ascending form of AIDP. The patient underwent one cycle of five plasmaphereses.

On hospital day 5, the patient was hyposaturated and had a worsening of right upper paresis. She developed dysarthria, tachycardia and a fever of 38 °C. A laboratory examination showed elevation of inflammatory parameters, which concluded as methicillin-susceptible staph sepsis (MSSA) with catheter phlebitis and respiratory infection responding well to empirically administered antibiotic cefotaxime. The patient showed no signs of respiratory insufficiency and was transferred to the Department of Anesthesiology and Resuscitation to complete treatment with plasmapheresis.

The antibiotic treatment was adjusted to Vancomycin and then to Oxacillin. After completion of plasmapheresis treatment, the patient was transferred back to the neurological intensive care unit (ICU), while spontaneous ventilation was maintained.

The upper limb mobility, muscle strength and fine motor skills improved, poor paraparesis and lower limb dysesthesia persisted. She was then transferred to a rehabilitation centre. The patient was discharged from the hospital with normal topical neurologic findings and continued in an outpatient physical therapy program. Total length of hospitalization was 53 days.

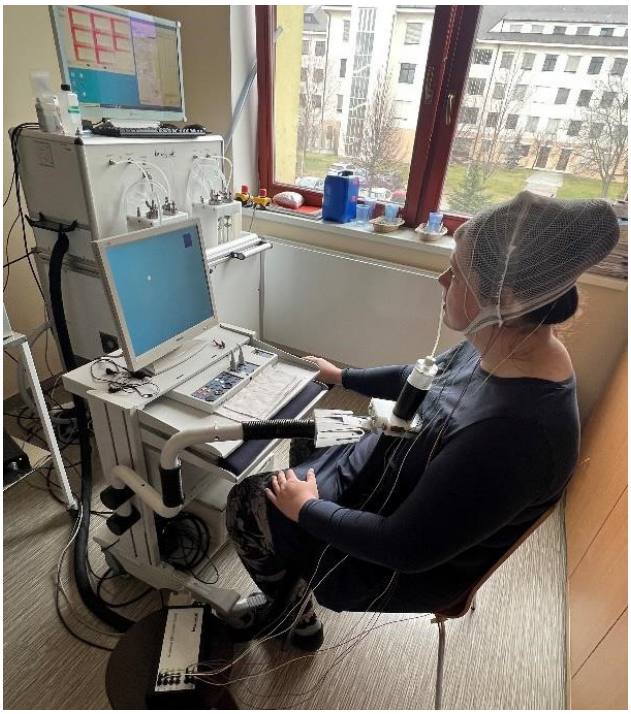

Fig. 1. Objective olfactometer OL 024 Burghart – measurement of olfactory event-related potentials (OERPs) (from corresponding author's archive).

The otorhinolaryngological examination was performed in November 2022 and included an assessement of the olfactory function. Results of the Sniffin' sticks identification test: the patient had 13 correct and 3 incorrect answers and did not report any subjective loss or impairment of smell. Objective examination of OERPs: the results with the rose odourant showed that the P2-N1 wave complex was equipotent. Rose odourant stimulus ended at time 750 ms. The N1 wave had a value of -4 uV and a latency of 983 ms, while the P2 wave showed a value of 5 uV and a latency of 1107 ms.

In conclusion, the objective olfactometry revealed normal OERPs.

(See Fig. 2 – normal olfactory event-related potentials, Female, 53-year-old, from corresponding author's archive.)

CASE REPORT 2

A 59-year-old male patient not vaccinated against COVID-19 tested positive for COVID-19 on a PCR test on February,15, 2021. The disease was of mild course initially; he did not complain about any loss of smell or taste. With a latency of 21 days, the first neurological symptoms appeared – a rapidly progressive proximally spreading quadruparesis of the limbs followed by flaccid quadriparesis and inability to walk. The patient was afebrile. He was admitted to the neurology department for suspected AIDP. A lumbar puncture was performed and the assessment of the cerebrospinal fluid revealed lympho-

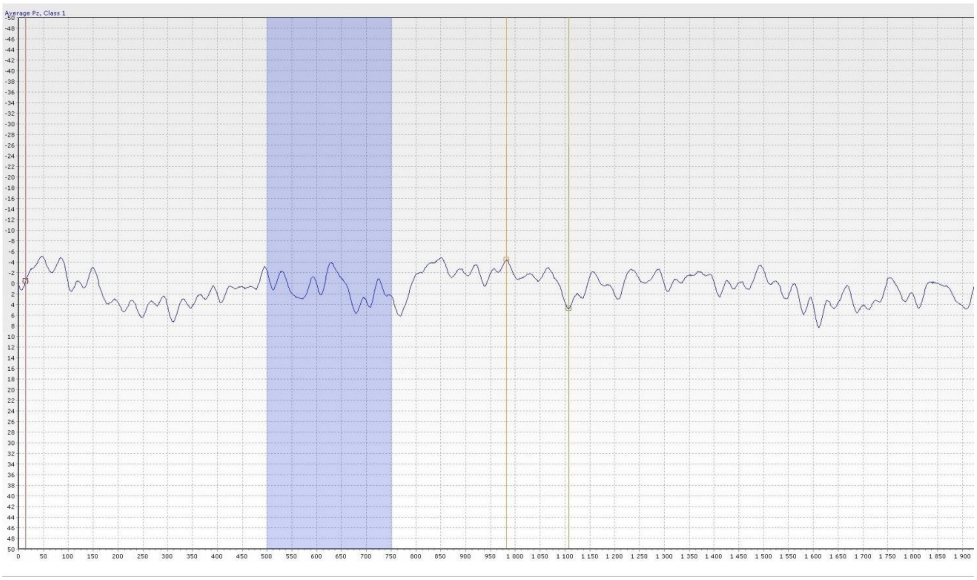

Fig. 2. Normal olfactory event-related potentials (OERPs), Postcovid Guillain-Barré syndrome, Female, 53-year-old (from corresponding author's archive).

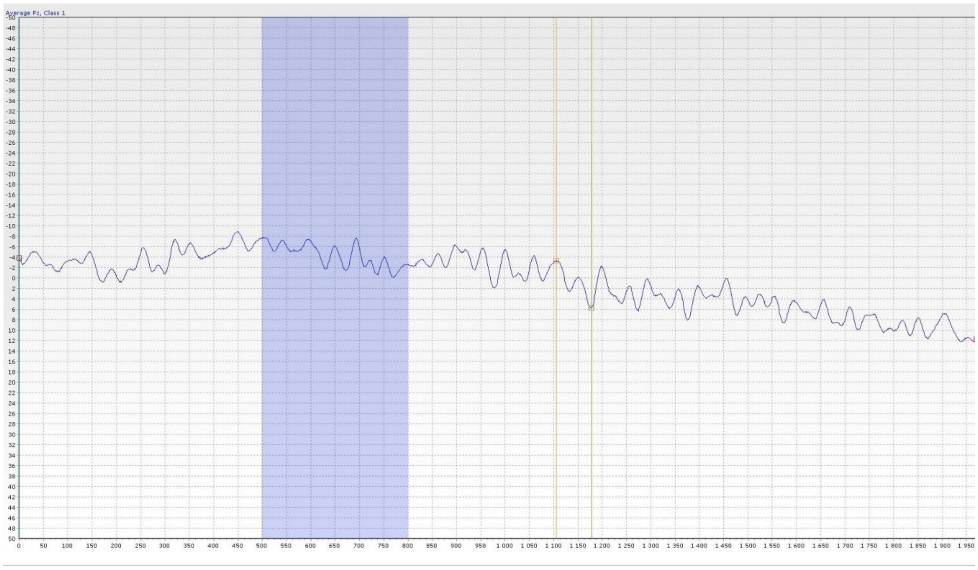

Fig. 3. Normal olfactory event-related potentials OERPs, Postcovid Guillain-Barré syndrome, Male, 59-year-old (from corresponding author's archive).

cyte dissociation. An EMG examination supported the diagnosis of acquired demyelinating polyneuropathy of the GBS type, it showed multiple prolongations of distal motor latency on lower and upper limbs, multiple prolongations of motor conduction velocities on lower limb nerves. Subsequently, the patient had rapid decline of his ability and five-day immunotherapy with Immunoglobulinum humanum normale (IVIG Privigen) was indicated. Due to the progression of bulbar syndrome, dysphagia and worsening of ventilatory parameters with signs of respiratory failure, the patient was transferred to ICU on day 4 of hospitalization. He was intubated and had to be ventilated artificially. On day 9, a percutaneous dilatation tracheostomy was performed. Neurologically, the patient was fully conscious but started experiencing panic attacks. Further improvement in bulbar and quadrature symptomatology was observed. Because of a respiratory and urinary infection, empiric antibiotic therapy was ongoing during hospitalization. The patient was successfully weaned from artificial pulmonary ventilation. On day 41 of hospitalization, decannulation of the patient's tracheostomy tube was achieved and a follow-up EMG revealed that the inflammatory polyneuropathy with impaired motor and sensory conduction in the lower extremities persisted. The patient was transferred to the spinal unit for intensive rehabilitation on day 56 of hospitalization. He was discharged to home care with mild flaccid quadriparesis with dominant L5 bilaterally disability. Total length of hospitalization was 150 days.

A follow-up neurological examination was performed one year after AIDP, with only residual foot hypesthesia bilaterally found; otherwise the topical neurological findings were normal.

In March 2022, he underwent an otorhinolaryngogic examination included an assessement of the olfactory function. Results of the Sniffin' sticks identification test: the patient had 12 correct and 4 incorrect answers and did not experience any loss or impairment of the sense of smell subjectively. Objective examination of OERPs: Rose odourant stimulus ended at time 800 ms. The results with the rose odourant showed that the P2-N1 wave complex was equipotent, with a N1 wave latency of 1105 ms and

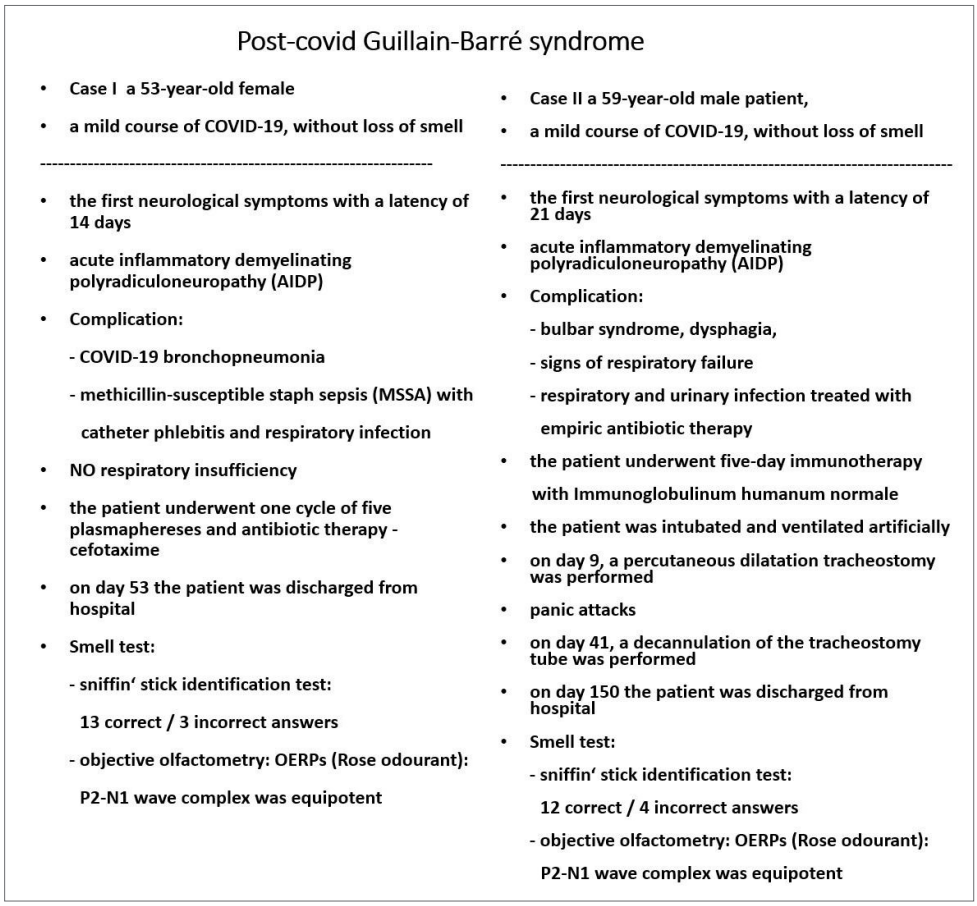

Fig. 4. Case series overview – Postcovid Guillain-Barré syndrome.

a value of -3 uV, and a P2 wave latency of 1178 ms and value of 6 uV.

(See Fig. 3 – normal olfactory event-related potentials, Male, 59-year-old, from corresponding author's archive).

For an overview of the case series see Fig. 4.

DISCUSSION

Both of our patients had a mild course of COVID-19. The average latency between the onset of COVID-19 symptoms and the first neurological manifestations has been described in the literature as 12 days (range: 0–28 days) (ref.[1]). In our two case reports the latency was 14 and 21 days.

Zuberbuhler et al. reported that COVID-19 symptoms preceded GBS in 46 patients, including fever (56%), hyposmia (27%) and diarrhea (25%), as well as dyspnea (13%), headache (10%) (ref.[1,14]).

It has been reported that short-term neurological outcome was favourable in 65% (ref.[1,2,5]), patients with good neurological recovery, 29% (ref.[1,2,5]) had respiratory failure, 23% (ref.[1,2,5]) required mechanical ventilation, 2% (ref.[1,2,5]) required noninvasive ventilation, and 4% (ref.[1,2,5]) died within hours of admission. Respiratory failure in these patients is likely to the combined effect of muscle weakness from GBS and pulmonary infection due to COVID-19 (ref.[1,2,5,15]).

In comparison, one of our cases presented without respiratory failure, whereas the other case had bulbar syndrome with respiratory failure and required intubation, artificial pulmonary ventilation and subsequently tracheostomy. Both patients survived. They were discharged from the hospital to home care on days 53 and 150 respectively.

Unfortunately, the underlying pathophysiological mechanism mediating COVID-19 nerve damage is still unclear. Hyposmia and dysgeusia affect up to 50–85% (ref.[1,5,14,15]), of patients with COVID-19 (ref.[1,5,14,15]). Moreover, in reports of post-viral smell alteration, studies have found that as many as 56% (ref.[8,11]) of patients experience parosmia and phantosmia[8,11].

The Sniffin'sticks identification test is suitable for the routine clinical assessment of olfactory performance[16]. OERPs – this is an objective method to observe changes in olfactory function. The presence of OERP is a robust indicator of a healthy olfactory function; conversely, the absence of OERP suggests an olfactory loss[8,11,13]. However, although the course of GBS was severe, we recorded normal OERPs curves in both our cases. N1, P2 components had normal latencies and amplitudes.

CONCLUSIONS

The two presented case reports suggest a possible association between ongoing COVID-19 infection and GBS. Despite the severe course of the disease, being life-threatening, both of our patients returned to normal life without impaired sense of smell, which was verified by

olfactory tests. An expanded prospective study is planned for the future to investigate post-covid olfactory impairment. The prevalence of GBS associated with COVID-19 is still unknown but it is evident that both mild and severe forms of GBS have been described in patients.

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Informed consent statement: The patients presented in this manuscript signed an informed consent for the olfactory examination.

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