

# Kranialni polinevritis, povezan z okužbo s SARS-CoV-2: prikaz primera

## Polyneuritis cranialis related to SARS-CoV-2 infection: a case report

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### Izvleček

**Namen:** Kranialni polinevritis je manj znana oblika iz skupine Guillain-Barréjevega sindroma in je zelo redko opisovan pri otrocih. V prispevku želimo opisati primer mladostnika, ki je zbolel po okužbi s SARS-CoV-2.

**Poročilo o primeru:** 15-letni fant je bil obravnavan zaradi hkratne paralize več možganskih živcev. Diagnozo smo potrdili z dokazom protiteles GQ1b in nevrofizioloških preiskav. Bolnika smo zdravili s plazmaferezo in intravenskimi imunoglobulini, njegovo klinično stanje pa se je izboljševalo zelo počasi in postopoma.

**Zaključek:** Kranialni polinevritis je redko in hudo nevrološko obolenje, ki ga lahko sproži tudi covid-19.

### Abstract

**Purpose:** Polyneuritis cranialis (PNC) is a less known regional variant of Guillain-Barré syndrome and has rarely been described in children. Here, we report a case of an adolescent, who became perilously ill following severe acute respiratory syndrome-coronavirus 2 infection.

**Case report:** A 15-year-old boy presented with acute multiple cranial nerve palsies. The presence of GQ1b antibodies and nerve conduction studies confirmed the diagnosis of PNC. The patient was treated with plasmapheresis and intravenous immunoglobulins, but clinical improvement was gradual and very slow.

**Conclusion:** PNC is a rare and severe neurologic condition that can be triggered by coronavirus infection.

## INTRODUCTION

Polyneuritis cranialis (PNC) represents a variant of Miller-Fisher syndrome (MFS), which is a form of Guillain-Barré syndrome (GBS), an acute immune-mediated peripheral neuropathy. The descriptive term “oculopharyngeal variant of GBS” has been proposed and partly adopted as an alternative name for PNC, an acute immune-mediated peripheral neuropathy (1,2). There is a significant overlap of MFS variants within the spectrum of GBS and significant differences among clinical descriptions of PNC reported by patients. Although the number and severity of involved cranial nerves can considerably vary, cranial nerves I and II are typically spared. Increased titers of anti-ganglioside GQ1b antibodies (Abs) are found in more than 90% of MFS cases and often present in those with the PNC variant (2).

## CASE PRESENTATION

A 15-year-old boy with no previous history of neurologic or other chronic disease presented with a short episode of fatigue and signs of mild respiratory infection. Two weeks later, his voice deepened and became hoarse. Over the next 3 days, the patient reported episodes of diplopia and dysphagia, which in deteriorated over a period of 2 days to complete piecemeal deglutition accompanied by progressive dysarthria and, ultimately, aphonia.

On admission, he was afebrile, alert, and orientated, but could only communicate through gesticulations and written messages, and exhibited slight asymmetrical facial diplegia, which was complete on the left and very obvious on the right. The patient was also unable to move the right corner of his mouth, but could partially lower his right upper eyelid, or protrude his tongue, while lateral tongue movements were markedly reduced. No gag reflex could be elicited and sialorrhea was observed. The strength of the trapezius muscle was normal, while that of the sternocleidomastoid muscle was reduced. Bilateral inability to turn the eye outwards resulted in convergent strabismus and disturbing diplopia. Function of cranial nerves 2–5 and 8 was normal. The patient also exhibited signs of anosmia, dysgeusia, and ataxia. Finger-to-nose and heel-to-shin testing showed no limb ataxia or dysmetria. The tendon reflexes were clearly present in the lower limbs, but absent in the

upper limbs. Accordingly, muscular strength was normal in the legs, but diminished in the arms and hands, especially on the left. Peristalsis was diminished. Other neurologic indices were normal.

All conventional blood chemistry parameters were normal. Testing of nasopharyngeal swabs for SARS-CoV-2 was negative by polymerase chain reaction analysis, but positive for Abs against SARS-CoV-2. Magnetic resonance imaging (MRI) of the brain revealed no abnormalities. Initial analysis of the cerebrospinal fluid (CSF) was normal (protein, 300 mg/L; 1 cell; immunoglobulin G index, 0.5; negative for oligoclonal bands). Malignancies, tuberculosis, sarcoidosis, borreliosis, and granulomatosis with polyangiitis were excluded, as were botulism and myasthenia gravis. Contrast-enhanced MRI of the brain showed no abnormalities.

Due to signs of dysphagia, parenteral nutrition was started. Exclusion of other possible causes of multiple cranial neuropathies strengthened our suspicion of PNC. We confirmed the presence of immunoglobulin G Abs against GQ1b ganglioside yet later, but we initiated the polyvalent intravenous immunoglobulins (IVIG) administration on hospitalization day 3. Testing for other ganglioside Ab types was negative.

The patient's condition deteriorated on hospitalization day 4 due to the development of fever, dyspnea, and hypoxemia. Serum levels of C-reactive protein increased from normal to 237 mg/L. A second lumbar puncture showed slight pleocytosis (protein, 380 mg/L, 11 cells). An X-ray revealed extensive aspiration pneumonia in the right lung. Hence, the patient was sedated and intubated for mechanical ventilation. In addition, five courses of membrane plasmapheresis every 2 days were started. On day 4 of antibiotic treatment, the patient was afebrile again and all markers of inflammation had gradually normalized. Extubation was attempted, but unsuccessful despite sufficient respiratory muscle strength. Maintaining an open airway could not be sustained due to hypotonia of the oropharyngeal muscles and the inability to swallow saliva. After a few hours, the patient was sedated and re-intubated. Artificial ventilation was continued for 2 weeks. Termination of artificial ventilation by classical surgical tracheostomy improved airway aspiration.

For the first 3 weeks, only parenteral nutrition was possible. Peristalsis was weak and had to be stimulated by laxatives and metoclopramide. Neostigmine was not administered to avoid enhanced salivation. Later, the patient was fed

through a nasogastric tube. Apart from the days requiring deep sedation, his consciousness remained intact and he was able to communicate through writing. The patient consented to tracheostomy, but not gastrostomy for removal of the nasogastric tube. His motor function declined due to muscular wasting.

The patient was transferred to a tertiary rehabilitation center 6 weeks after appearance of the initial symptoms, where feeding with a nasogastric tube and tracheostomy were continued. Because the clinical symptoms improved very slowly, he was referred to our tertiary Pediatric Neurology Department at 8.5 weeks after admission for further evaluation. Follow-up contrast-enhanced MRI of the brain and cervical spinal cord was normal and testing for neurodegenerative diseases was negative. Nerve conduction studies (NCSs) and electromyography (EMG) were conducted at 9 weeks after admission. NCSs of the upper and lower limbs were normal, except for prolonged F response latencies, low F response persistence, and signs of chronodispersion in several nerves of the upper and lower limbs. NCSs of the facial nerves showed very low amplitude compound muscle action potential responses in all branches and markedly prolonged distal latency of one of the six tested facial nerve branches, changes consistent with predominant axonal damage and possible demyelination. Needle EMG changes were consistent with a subacute neuropathic process.

Two additional courses of IVIG at 4-week intervals were administered at the rehabilitation center and symptoms steadily, but slowly, improved. The patient's ability to taste and smell returned at about 8 weeks after the initial symptoms. IVIG was discontinued after the four courses (12 weeks after admission), as the clinical manifestations continued to improve. The patient's ability to swallow was sufficient at 13 weeks to start partial peroral feeding with dense liquids. The tracheal cannula was removed shortly afterward. After decannulation, the patient's voice was very weak and his speech dysarthric, but gradually improved to near normal. While the tracheostomy wound healed, he used special maneuvers to communicate. Discrete facial asymmetry and slight facial muscle weakness, more pronounced on the left side, were still obvious at 18 weeks, but disappeared at 23 weeks. Muscular strength was eventually restored, allowing the patient to walk without problems, while functioning of his arms and hands had returned to normal. The nasogastric tube was removed

once normal eating was possible and diplopia had subsided at 23 weeks.



**Figure 1:** The patient at 6 weeks after admission. Note convergent strabismus, facial diplegia, and inability to swallow. A cuffed tracheostomy tube was used to prevent further problems with aspiration.

## DISCUSSION

Our patient exhibited rapid progression of slightly asymmetrical cranial nerve palsies after an upper respiratory tract infection. Despite early and aggressive treatment, there was no immediate improvement. Most patients with PNC recover and are discharged from the hospital in about 11 weeks (2). A fast and full recovery was reported in a case of a 10-year-old boy with PNC after just two courses of IVIG (3). Because PNC was not the only differential diagnosis in this case, diagnosis was extended to other possible causes. Multiple cranial neuropathies can occur with several infectious, inflammatory, or neoplastic lesions of the skull base or brainstem (4). Systemic diseases, including diabetes mellitus, have also been linked to PNC. However, laboratory tests and neuroimaging excluded these causes in this patient. Myasthenia gravis, which was ruled-out, can

also initially present with involvement of multiple cranial nerves. Albuminocytological dissociation is common with GBS, but only 67% of reported PNC cases (2). Analysis of the first lumbar puncture of this patient was completely normal, while the second showed slight pleocytosis, although no elevated protein levels in the CSF, which is less common but does not exclude a diagnosis of PNC (4). An antecedent respiratory infection is common with PNC, as demonstrated with our patient, who exhibited a complete loss of smell, which was attributed as a consequence of SARS-CoV-2 infection, rather than a sign of the involvement of the first cranial nerve in PNC. Involvement of the upper limbs might represent an overlap to the pharyngeal-cervical-brachial form of GBS, which often involves the presence of anti-GT1a Abs. However, this patient was negative for anti-GT1a Abs. Limb weakness is uncommon in patients with oculopharyngeal involvement and is more suggestive of MFS. Our patient, however, showed no signs of ataxia and deep tendon reflexes were preserved in the lower limbs. Although the nasopharyngeal swabs were negative, the lack of relevant medical history, presence of anti-GT1a Abs, and loss of taste and smell supported the presumption that SARS-CoV-2 triggered PNC in this patient. Several cases of MFS have been reported as an adverse effect of

vaccines against COVID-19 (5). However, our patient was not vaccinated. Common neurologic complications among adults hospitalized for COVID-19 include myalgia, headache, encephalopathy, dizziness, dysgeusia, and anosmia (6). Stroke, movement disorders, motor and sensory deficits, ataxia, and seizures have been described, but are less common. Neurologic deficits can arise both from the direct effects of the virus as well as systemic responses to infection. Anosmia is considered to be a direct consequence of olfactory bulb injury (7). Among immune-mediated complications, several cases of GBS have been described in patients with COVID-19, but only one case of PNC in an adult (8).

## CONCLUSION

Autoimmune response-related complications of COVID-19 might be the most serious. PNC is a rare neurologic condition that can be triggered by COVID-19 and affects children most gravely. Vaccination of the pediatric population not only helps to prevent spread of the virus, but also prevents serious complications, which are also possible in children.

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