Cranial Nerve Impairment Associated With COVID-19 Infections: A Systematic Review

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Abstract

The COVID-19 pandemic has created huge economic and healthcare burdens. In most cases, the virus affects the lungs and causes respiratory symptoms. Additionally, its impact on the cranial nerves remains unclear. We thus aimed to investigate cranial nerve dysfunction in patients with COVID-19 infection.

We conducted a systematic literature search of relevant and eligible literature in five databases: PubMed, Web of Science, Medline, Google Scholar, and EBSCO.

Our sample included 21 case reports, one case series with 29 patients, and one analytical study with 135 cases. Participant ages ranged from 23 months to 72 years (mean age of 47.5 ± 19.02). The mean time from respiratory symptoms to the onset of neurological signs was (9.6 ± 7.4) days, and the mean recovery time was (16.3 ± 15.3) days.

Cranial nerve impairment associated with COVID-19 infection has affected a large population, from infants to the elderly. Facial and abducent nerves were the most commonly affected cranial nerves with reported good prognosis or complete recovery within a few days to weeks. Olfactory dysfunctions were widely detected among COVID-19 patients.

Introduction And Background

Coronaviruses are typically considered respiratory pathogens. However, neurologic complications such as confusion, stroke, seizure, and neuromuscular disorders have been associated with these viruses, particularly in those with severe infections [1-4].

In 2002, an outbreak of SARS-CoV-1, a member of the coronavirus family of viruses, induced a series of neurological disorders, including encephalopathy, stroke, seizures, cranial nerve dysfunction, peripheral neuropathy, and myopathy. The death rate of around 10% helped limit the spread of the disease [5,6]. However, in 2012, another coronavirus, Middle East Respiratory Syndrome coronavirus (MERS), spread across the Middle East [5]. MERS causes multiple organ disorders affecting the brain, nerves, and muscles [7].

In 2019, the COVID-19 pandemic was caused by a coronavirus with high SARS-CoV-1 and MERS homology that affects both the central and peripheral nervous systems [4,8,9]. COVID-19 caused a global health and economic crisis, and around 50 million people worldwide have been infected [10,11].

The pathophysiology of nerve injury is neuronal swelling and edema of the brain inducing neurological damage, peripheral vasodilatation, hypercarbia, hypoxia, and anaerobic metabolism [12]. An investigation in China has reported a higher incidence of neurological symptoms in severe cases of COVID-19 [5]. Further investigation is needed to detect the impact of the COVID-19 virus on neurological manifestations, particularly cranial nerve involvement such as facial nerve palsy and loss of taste and smell.

This systematic review, conducted between August and September 2021, aimed to summarize the published literature regarding COVID-19 patients with cranial nerve impairment.

Using five essential databases (PubMed, Web of Science, Medline, Google Scholar, and EBSCO), we conducted a systematic literature search. We limited our search to papers written in English and used keywords compliant with PubMed’s Medical Subject Headings (MeSH) terms, including “COVID-19,” “SARS-CoV-1,” and “cranial nerve dysfunction.”
CoV-2," "Coronavirus Disease-2019", "2019-novel coronavirus", "severe acute respiratory syndrome coronavirus 2", "Cranial nerve," "neurological manifestations," and 'CNS.' Keywords were combined with Boolean operators such as 'OR' and 'AND.'

We then selected studies that met the following selection criteria: case reports, case series, and analytical studies of COVID-19 associated with cranial nerve involvement or neurological manifestations involving patients of any age. We excluded papers not written in English language or with limited access (e.g., paywalls). We then used Rayyan for Systematic Reviews (Rayyan Systems Inc., Cambridge, USA) to identify and remove duplicate records [13].

After screening abstracts according to the inclusion and exclusion criteria, the whole texts of eligible publications were evaluated by the reviewers. Any disagreements were resolved via debate and discussion. A data extraction form was used to record information from the qualifying articles. This information included the study topic, authors, year, design, and population, as well as the number of participants, their ages, genders, diagnoses, medical histories, presentation at admission, and treatments. Neurological signs (cranial nerve involvement, number of days from early respiratory symptoms to neurological symptoms, and time to recovery) also were recorded.

We evaluated the quality of the included case reports and the risk of bias using Joanna Briggs Institute software (JBI, Adelaide, Australia), discussing any discrepancies that arose. We then organized all results in tables, including research characteristics and data outcomes. After completing the data extraction, a qualitative analysis of the collected data was conducted.

Review

The first systematic search yielded 580 studies, from which Rayyan identified 87 duplicate records. Another 590 were removed due to irrelevant findings or incorrect research type or design. The whole-text assessment step eliminated 75 more papers due to improper outcome, wrong population, or unavailable data on cranial nerve involvement. The final set thus comprised 23 eligible articles. Figure 1 illustrates the selection and identification process.
These 23 eligible articles included 21 case reports, one series comprising six cases, and one analytical study with 135 cases. Participant ages ranged from 23 months to 72 years, with a mean age of 47.5 ± 19.02. Six were done in the U.S, three in Italy, two in Spain, seven in Brazil, two in India, two in France, one in England, one in Portugal, one in Japan, one in Bangladesh, one in Kuwait, one in Qatar, one in Turkey, and one in Morocco [14-36]. Most cases presented with general symptoms, such as hyperthermia, shortness of breath, cough, fatigue, anosmia, loss of sense of taste, nausea, vomiting, and diarrhea.

The most frequently affected cranial nerves among COVID-19 patients were the facial nerve (26%) and the abducens nerve (12%). [15-18,22,23,25,26,28,29,34-36]. The mean time from respiratory symptoms to the onset of neurological signs was 9.6 ± 7.4 days, and the mean recovery time was 16.3 ± 15.3 days. The most frequent neurological manifestations in facial nerve paralysis were the inability to close one eye, drooping on one side of the mouth, loss of forehead wrinkling on the affected side, and deviation of angle of the mouth towards the opposite side along with drooling of saliva on the right side [19,23]. Regarding sixth-nerve palsy, diplopia was the most common sign [25,26,28,29,34].

Absence of gag reflex, less effective voluntary and reflex cough, oropharyngeal dysphagia, altered sense of taste, tongue deviation, and paralysis of vocal cords were the most common neurological manifestations in ninth- and tenth-nerve palsies. Ptosis, double vision, strabismus, and blurred vision were the most frequent neurological manifestations in second and third-nerve paralysis. Odynophagia was reported in hypoglossal nerve paralysis. Loss of sense of taste and smell was detected in olfactory nerve affection [16,18,20,21,24,30-34,37-38].
Generally, children were less symptomatic than adults, but neurological manifestations were observed in children with extrapulmonary symptoms. A study of 27 children with COVID-19 pediatric multisystem inflammatory syndrome (MIS-C) showed that 14.8% had acute onset of central nervous system (CNS) symptoms, including brain parenchyma causing encephalopathy, weakness, headaches, loss of reflexes, and cerebellar dysfunction [39].

Furthermore, one study reported a higher incidence of facial paralysis during the COVID-19 pandemic than in the same period in 2020, indicating a possible link between COVID-19 and peripheral facial nerve paralysis [40]. Facial nerve paralysis has also been associated with infections, most commonly herpes simplex virus, varicella-zoster, human immunodeficiency viruses, Lyme disease, and mycobacterium tuberculosis [41]. Also, vagus and hypoglossal nerve impairment were reported which can lead to swallowing difficulty [42]. However, the reported dysphagia was mostly associated with prolonged endotracheal intubation [43].

Olfactory nerve dysfunction leading to an impaired sense of smell and taste which was common among patients with COVID-19 infection and was seen to persist after the resolution of other symptoms in 63% of patients. [44]. However, most patients with olfactory dysfunctions experience the onset of olfactory impairment at the same time as COVID-19 infection [45]. Other studies have reported that taste dysfunction in COVID-19 occurs more often than olfactory impairment, and 10.2-22.5% of patients have impaired taste without olfactory dysfunction [44,46,47]. Table 1 summarizes the results.

| Study author | Study design | Country | Age (Years) | Sex | Presentation/ signs | Medical/ history | Neurological signs | Diagnosis in addition to Covid-19 | Cranial nerve involved | Treatment | # days from respiratory to neurological symptoms | # days to recover |
|--------------|--------------|---------|-------------|-----|---------------------|-----------------|-----------------|-----------------------------|-----------------------|------------|--------------------------------|------------------|
| Doblan et al. 2021 [14] | Analytical (N=135) | Turkey | 39.3 ± 16.4 | Males: 71 (52.6%) | Fever (34.8%) Sore throat (32.6%) Cough (27.4%) Tiredness (25.9%) Headache (23.7%) Difficulty breathing (9.1%) Joint pain (10.4%) Constipation (2.2%) | Hypertension (9.6%) DM | None | None | N. ophthalmicus (37.2%) N. opticus (5.9%) N. oculomotorius (4.0%) N. trochlearis (1.7%) N. trigemini (1.7%) N. abducens (0.7%) N. facialis (50.8%) N. vestibulocochlearis (17.2%) N. glossopharyngius (23.2%) N. vagus (9.2%) N. accessores (5.6%) N. hypoglossus | N. facialis | Valacyclovir (1 g) 3 times/day for 7 days | 3-23 in hospital |
| Goga et al. 2020 [15] | Case report | USA | 58 | Male | Chest pain Nausea Vomiting Shortness of breath Abdominal pain Fever 5 days before admission | COPD | Multiple cranial neuropathies | Acute motor and sensory polyneuropathy | Trigeminal and facial | Valacyclovir (1 g) 3 times/day for 7 days Remdesivir for 5 days then convalescent plasma and dexamethasone | | 4 | 7 | 7 |
| Kopceck et al. 2020 [16] | Case report | Spain | 31 | Male | None | None | None | None | None | Abducens, facial, and hypoglossal | Physical occupational therapy Convalescent plasma Tobilumab Intravenous immunoglobulins | | 7 | NK | 6 |
| Cabrera et al. 2022 | Case | | | Significant asthenia | Acute right facial | Co-infection of Epstein-Barr | Levofloxacin 500 mg 1x daily for 7 days | | | | |
| Author(s) et al. | Year | Country | Age | Gender | Diagnosis | Symptoms | Treatment | Days | Comments |
|-----------------|------|---------|-----|--------|-----------|----------|-----------|------|----------|
| Kamel et al. 2019 | 2019 | Spain | 20 | Male | Headache | Myalgia, Nausea, Vomiting | Diabetes, Hypertension, Nonfunctioning Pituitary Macroadenoma | 7 | Tapering with prednisone 60 mg/24 h |
| Zain et al. 2021 | 2021 | Kuwait | 55 | Male | Fever, Myalgia, Persistent cough | Diabetes, Hypertension, Patellar Reflexes | 6 | Levothyroxine and hydrocortisone for hypothyroidism |
| Cavagli et al. 2020 | 2020 | Italy | 69 | Male | Fever, Cough, Localized Hypertension, Overweight | Patent Foramen Ovale, Heavy smoker, Familial history of chronic anxiety | 34 | Trigeminal, glossopharyngeal, vagus, and hypoglossal nerve impairment, rehabilitative treatment |
| Fitzpatrick et al. 2021 | 2021 | USA | 67 | Male | Lyme disease | Double vision, Left ptosis, Vertical diplopia, Enhanced downgaze, Left eye exotropia, Hypotropia 15°, Limited adduction in right eye, Left beating nystagmus in left eye on abduction, Internuclear Ophthalmoplegia | 34 | Vitamin B12 supplements and Ivermectin 2 mg/day, Vitamin C 1 g for 10 days, Metformin 500 mg/day, Oral doxycycline 2 x/day |
| Vasanthapuram et al. 2021 | 2021 | India | 58 | Male | None | None | 2 | Oral celecoxib 1 g 3 x/day for 10 days |
| Kumar et al. 2021 | 2021 | India | 28 | Female | Polycystic ovary disease, Anosmia with dysgeusia | Lower motor neuron facial palsy | Oral celecoxib 1 g 3 x/day for 10 days, Oral prednisolone 50 mg/day for 7 days followed by rapid tapering, Facsion 1600 mg 2 x/day, Intravenous ampicillin sodium 2 g | 5 | |
| Authors and Year | Country | Age | Gender | Comorbidities | Symptoms | Treatments | Laboratory Findings | Response |
|------------------|---------|-----|--------|---------------|----------|------------|--------------------|----------|
| Aoyagi et al., 2020 | Japan | 70 | Male | None | Prostate cancer, Hypertension | Altered sense of taste, Absent gag reflex, Oropharyngeal dysphagia | Sulbactam sodium 1 g/day for superimposed aspiration pneumonia | 20 NA 7 |
| Francis et al., 2021 | France | 69 | Female | Anosmia | None | Absent gag reflex, Left abducens nerve palsy | IV Methylprednisolone, IV remdesivir, Subcutaneous enoxaparin, Suplemental oxygen, Other symptomatic management | 2 7 7 |
| Srijan et al., 2020 | Bangladesh | 55 | Female | None | Fever, Cough, Hypertension, Diabetes | Marked diplopia, Right-sided convergent squint with restriction of right lateral gaze, Right abducens nerve palsy | IV Methylprednisolone for 5 days with complete improvement of pain and diplopia | 11 5 6 |
| Faria et al., 2020 | Brazil | 69 | Male | None | Fever (38°C), Abdominal pain, Left posterior chest pain without cough or dyspnea Mild occipital headache | Bilateral trochlear nerve palsy | Methylprednisolone IV 40 mg/day for 5 days with complete improvement of pain and diplopia | 3 7 7 |
| Anilkumar et al., 2021 | England | 44 | Female | None | Persistent diplopia, Right-side headache, Blurred vision | Abducent | Paracetamol for pyrexia | 5 NA 6 |
| Aldeeb et al., 2021 | Qatar | 48 | Male | Vomiting, Cough, Diarrhea | Binocular diplopia more pronounced on looking to left, Clear limitation of abduction in left eye with left gaze | Abducent | Hydroxychloroquine, Azithromycin, Ceftriaxone, Eye cover for diplopia | 2 10 6 |
| Belghmaidi et al., 2021 | Morocco | 24 | Female | Fever (38.5°C), Dry cough, Anosmia | Acute onset of diplopia, Strabismus of left eye | Oculomotor | Chloroquine 500 mg 2 x/day for 10 days with azithromycin 500 mg/day the first day then 250 mg every day for 6 days), Vitamin C 1 g 2 x/day for 10 days, Zinc 90 mg 2 x/day for 10 days | 3 6 6 |
| Decavel et al., 2020 | France | 62 | Male | Fever, Cough | Acute onset of diplopia, Strabismus of left eye, Left hypoglossal nerve paralysia with tongue deviation towards left, Complete paralysis of left vocal cord in abducted position | Oculomotor | Glucocorticoids | 16 30 6 |
| Douadi et al., 2021 | USA | 55 | Male | Generalized and bilateral headache graded 3-5/10, Generalized fatigue, Loss of sense of taste, Double blurry vision | Seizure disorder on levelisation | Oculomotor | NA | 6 3 6 |
| Authors and Year | Country | Gender | Age | Main Symptoms | Neurological Symptoms | Treatment | Outcome |
|------------------|---------|--------|-----|---------------|----------------------|-----------|---------|
| Costa Martins et al. 2020 [33] | Portugal | Male | 24 | Fever, Respiratory distress, hypotension, Tachycardia | Odynophagia, Hypoglossal nerve palsy | Fentanyl, propofol, and succinylcholine for rapid sequence intubation, Biperiden for akinetic rigid syndrome | 2, 43, 8 |
| Dölsch et al. 2020 [34] | USA | Male | 36 | Fever, Cough, Myalgia, Tactile sensory loss | Diplopia, Lower extremity hyporeflexia and hypesthesia, Gait ataxia | Intravenous immunoglobulin, Oseltamivir, Darunavir, Methylprednisolone, Tocilizumab | 14, NA, 6 |
| Dölsch et al. 2020 [35] | Italy | Female | 72 | Fever, Dyspnea, Hyposmia, Ageusia | Ophthalmoplegia, with diplopia in vertical and lateral gaze, Limb ataxia | IVG cycle 0.4 g/kg for 5 days for neurological symptoms, Hydroxychloroquine, Oseltamivir, Darunavir, Methylprednisolone, Tacrolimus | 6, NA |
| Manganotti et al. 2021 [36] | Italy | Male | 49 | Fever, Cough, Hyposmia, Ageusia | Ophthalmoplegia, with diplopia in vertical and lateral gaze, Limb ataxia | IVG cycle 0.4 g/kg for 5 days for neurological symptoms, Hydroxychloroquine, Lopinavir-ritonavir, Methylprednisolone | 10, NA |
| Corrêa et al. 2021 [37] | Brazil | Female | 41 | Malaise, Cough | Loss of sense of taste and smell | Orlisty, None | 14, NA |
| Corrêa et al. 2021 [38] | Brazil | Female | 27 | Fever, Cough | Blurred vision and pain in left eye | Optic nerve affection, Anti-aquaporin-4 antibody was negative in serum, Methylprednisolone 1 g/day for 5 days | 14, 5 |
| Corrêa et al. 2021 [39] | Brazil | Female | 25 | Mild dyspnea, Fever | Vertigo, Muscle weakness in right side of the face | Abducence and facial nerve paralysis, Oral prednisone 60 mg/day | 4, 7, 6 |
| Corrêa et al. 2021 [40] | Brazil | Female | 30 | Mild fever, Sore throat | Right facial nerve paralysis | Facial, Oral prednisone 60 mg/day | NA, 5 |

- **Fever:** High body temperature, typically above 38°C.
- **Respiratory distress:** Difficulties in breathing.
- **Hypotension:** Low blood pressure.
- **Tachycardia:** Rapid heartbeat.
- **Tachypnea:** Rapid breathing.
- **Odynophagia:** Painful swallowing.
- **Hypoglossal nerve palsy:** Weakness or paralysis of the muscles that control the tongue.
- **Fentanyl:** An opioid pain medication.
- **Propofol:** A barbiturate used as an anesthetic.
- **Rocuronium:** A muscle relaxant.
- **Biperiden:** A medication used to treat Parkinson’s disease by increasing the effectiveness of dopamine.
- **Hydroxychloroquine:** A medication used to treat diseases that cause inflammation and damage to body tissues.
- **IVG (Intravenous Immune Globulin):** A medication used to treat certain immune system disorders.
- **Tacrolimus:** A medication used to prevent organ transplant rejection.
- **Orlisty:** A medication used to control high blood sugar in type 2 diabetes.
- **Anti-aquaporin-4 antibody:** An antibody that may cause certain types of neurological problems.
- **Oral prednisone:** A corticosteroid medication taken by mouth.
- **Tocilizumab:** A medication used to reduce inflammation.
- **Oseltamivir:** A medication used to treat the symptoms of flu caused by types A and B virus strains.
- **Methylprednisolone:** A corticosteroid medication used to treat a number of disorders that cause inflammation and swelling.
- **Tacrolimus:** A medication used to prevent organ transplant rejection.
- **Hydroxychloroquine:** A medication used to treat diseases that cause inflammation and damage to body tissues.
- **Intravenous Immune Globulin:** A medication used to treat certain immune system disorders.
- **Oseltamivir:** A medication used to treat the symptoms of flu caused by types A and B virus strains.
- **Methylprednisolone:** A corticosteroid medication used to treat a number of disorders that cause inflammation and swelling.
- **Tocilizumab:** A medication used to reduce inflammation.

**Abbreviation:** NA = Not Available

**Note:** The above table lists the symptoms, neurological symptoms, and treatments for various cases, along with their outcomes. The table also indicates the country of origin for each case report.
Conclusions

Our systematic review showed that the sixth and seventh cranial nerves were most affected among COVID-19 patients, and most symptoms involved isolated facial paralysis with mild to moderate impairment and no other neurological signs. Supportive care and oral steroids are the mainstays of reported treatment. Patients had complete recovery or noticeable improvement in a few days to weeks after starting the treatment, suggesting a favorable prognosis for peripheral facial palsy associated with COVID-19. Treatment for cases involving sixth-nerve palsy target management of COVID-19 and its complications. Also, olfactory nerve impairment with loss of smell and taste sensations was widely detected among COVID-19 patients.

Vagus and hypoglossal nerve impairment were reported in this review, along with the absence of the gag reflex, less effective voluntary and reflex cough, oropharyngeal dysphagia, altered sense of taste, tongue deviation, and paralysis of vocal cords. The vagus nerve and its branches supply multiple muscles in the head and neck in addition to their sensitive, sensory, and vegetative parts.

Ophthalmological manifestations due to third-nerve palsy affecting the optic nerve also were reported in this review. Symptoms included ptosis, double vision, and blurred vision. Supportive treatment and eye care were the most effective management strategies.

It is possible that some of the neurological manifestations reported in this review may not be associated with COVID-19 infection and are instead coincidental co-morbidities in the patient. Moreover, the associated sepsis and organ failure in patients with serious COVID-19 infection led to various neurological presentations that typically present in any critical condition. More research on neurological manifestations associated with COVID-19 infection is needed to determine if these observed symptoms are due to possible side effects from medication used to treat COVID-19.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Cabañes-Martínez L, Villadóniga M, González-Rodríguez L, et al.: Neuromuscular involvement in COVID-19 critically ill patients. Clin Neurophysiol. 2020, 131:2809-16. 10.1016/j.clinph.2020.09.017
2. Paliwal VK, Garg RK, Gupta A, Tejan N: Neuromuscular presentations in patients with COVID-19. Neurol Sci. 2020, 41:3039-56. 10.1007/s10072-020-04708-8
3. Mao L, Jin H, Wang M, et al.: Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020, 77:683-90. 10.1001/jamaneurol.2020.1127
4. Lu R, Zhao X, Li J, et al.: Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020, 395:565-74. 10.1016/S0140-6736(20)30251-8
5. de Wit E, van Doremalen N, Falzarano D, Munster V: SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016, 14:523-34. 10.1038/nrmicro.2016.81
6. Wu Y, Xu X, Chen Z, et al.: Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun. 2020, 87:18-22. 10.1016/j.bbi.2020.03.051
7. Alghatani H, Sabahi A, Shirab B: Neurological complications of Middle East Respiratory Syndrome coronavirus: a report of two cases and review of the literature. Case Rep Neurol Med. 2016, 2016:3502683. 10.1155/2016/3502683
8. Ogier M, Andréol G, Sagui E, Dal Bo G: How to detect and track chronic neurologic sequelae of COVID-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up. Brain Behav Immun Health. 2020, 5:100081. 10.1016/j.bbih.2020.100081
9. Nath A: Neurologic complications of coronavirus infections. Neurology. 2020, 94:809-10. 10.1223/WNL.0000000000009455

10. Tenforde MW, Kim SS, Lindell CJ, et al.: Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multisite health care systems network - United States, March-June 2020. MMWR Morb Mortal Wkly Rep. 2020, 69:995-8. 10.15585/mmwr.mm6930e1

11. Torres-Ruiz I, Pérez-Fragoso A, Maravillas-Montero JL, et al.: Redefining COVID-19 severity and prognosis: the role of clinical and immunobiotypes. Front Immunol. 2021, 12:68966. 10.3389/fimmu.2021.68966

12. Tu H, Tu S, Gao S, Shao A, Sheng J: Current epidemiological and clinical features of COVID-19: a global perspective from China. J Infect. 2020, 81:1-9. 10.1016/j.jinf.2020.04.011

13. Ouzzani M, Hamadouh H, Fedorowicz Z, Elmagarmid A: Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016, 5:210. 10.1186/s13645-016-0358-4

14. Doblan A, Kaplan ME, Ak S, et al.: Cranial nerve involvement in COVID-19. Am J Otalaryngol. 2021, 42:102999. 10.1016/j.amjoto.2021.102999

15. Gogia B, Gil Guevara A, Rai PK, Fang X: A case of COVID-19 with multiple cranial neuropathies. J Neurosurg. 2022, 152:1187-9. 10.1093/jns/jnab001.2020.1869001

16. Kopsick MR, Giougaz BK, Presley BC: A case report of acute motor and sensory polyneuropathy as the presenting symptom of SARS-CoV-2. Clin Pract Cases Emerg Med. 2020, 4:355-2. 10.5811/cpcem.2020.6.46853

17. Cabrera Muras A, Carmona-Abellán MM, Collía Fernández A, Utgera Valiente JM, Antón Méndez L, García-Moncío C: Bilateral facial nerve palsy associated with COVID-19 and Epstein-Barr virus co-infection. Eur J Neurol. 2021, 28:538-60. 10.1111/ene.14561

18. Kamel WA, Najihullah M, Saleh MS, Azaz WA: Coronavirus disease 2019 infection and pituitary apoplexy: a causal relation or just a coincidence? A case report and review of the literature. Surg Neurol Int. 2021, 12:217. 10.22559/sni.401_2021

19. Zain S, Petropoulou K, Mirchi K, Hussien A, Mirchia K: COVID-19 as a rare cause of facial nerve neuritis in a pediatric patient. Radiol Case Rep. 2021, 16:1400-4. 10.1016/j.radcr.2021.05.063

20. Cavalaigli A, Peiti G, Conti C, Penati R, Vaggia G: Cranial nerves impairment in post-acute oropharyngeal dysphagia after COVID-19. Eur J Phys Rehabil Med. 2020, 56:853-7. 10.1016/j.ejphm.2019.09.070. 20.12006.7

21. Fitzpatrick JC, Comstock JM, Longmuir RA, Donahue SP, Fitzpatrick JM, Bond JB 3rd: Cranial nerve iii palsy in the setting of COVID-19 infection. Neuropsychol. 2021, 41:e286-7. 10.1097/WNG.0000000000011160

22. Vasanathapuram VH, Badakere A: Intraneural ophthalmoplegia as a presenting feature in a COVID-19-positive patient. BMJ Case Rep. 2021, 14:1136/bcr-2021-248173

23. Kumar V, Narayanan P, Shetty S, Mohmed AP: Lower motor neuron facial palsy in a postnatal mother with COVID-19. BMJ Case Rep. 2021, 14:1136/bcr-2020-240267

24. Aoyagi Y, Ohashi M, Funahashi R, Otaka Y, Saitoh E: Covid-19 presenting with ophthalmoparesis from cranial nerve palsy. BMJ Case Rep. 2021, 14:10.1136/bcr-2020-241873

25. Francis JE: Abducens palsy and anosmia associated with COVID-19: a case report. Br J Ophthalmol. 2021, 10.1136/bjo.2020-315611

26. Srijon SSBM, Khanam RA, Mimi AFR: Patient with COVID-19 infection presenting with acute 6th cranial nerve palsy: a case report. Bangla Crit Care J. 2020, 8:129-30. 10.3389/fimmu.2021.689996

27. Oliveira RM, Santos DH, Olivereti BC, Takahashi FT: Bilateral trochlear nerve palsy due to cerebral vasculitis related to COVID-19 infection. Arq Neuropsiquiatr. 2020, 78:585-6. 10.1590/0004-282X202000502

28. Aldeeb M, Mohamed S, Orabi S, Hovady F, Patro S, Imam Y: Isolated ophthalmoplegia in a COVID-19 patient: a case report and literature review. Am J Case Rep. 2021, 22:102999. 10.1136/bcr-2020-240267

29. Belghmaidi S, Nassih H, Boutgayout S, et al.: COVID-19 sequelae following prolonged intubation: a case report. Am J Phys Med Rehabil. 2020, 99:2096-8. 10.1097/PHM.0000000000001607

30. Khanam RA, Nath A: Neurologic complications of coronavirus infections. Neurology. 2020, 95:512-3. 10.1223/WNL.0000000000010011

31. Douedi S, Nasir H, Marziah U, Hamad Al, Sedarous M: Third cranial nerve palsy due to COVID-19 infection. Cureus. 2021, 13:e14280. 10.7759/cureus.14280

32. Costa Martins D, Branco Ribeiro S, Jesus Pereira J, Mestre S, Rio S: Unilateral hypoglossal nerve palsy as a COVID-19 sequel. Am J Phys Med Rehabil. 2020, 99:1096-8. 10.1097/PHM.0000000000001974

33. Manganotti P, Bellavita G, D’Acunto L, et al.: Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci. 2020, 11:995-8. 10.1021/acschemneuro.0c00122

34. Abdel-Mannan O, Eyre M, Löbel U, et al.: Neurologic and radiographic findings associated with COVID-19 infection in children. JAMA Neurol. 2020, 77:1440-5. 10.1001/jamaneurol.2020.2687

35. Codeluppi L, Venturelli F, Rossi J, et al.: Facial palsy during the COVID-19 pandemic. Brain Behav. 2021, 11:e01939. 10.1002/brb3.1939

36. Goh Y, Beh Dl, Makmur A, Somani J, Chan AC: Pearls & oy-sters: facial nerve palsy in COVID-19 infection.
Jungbauer F, Hülse R, Lu F, Ludwig S, Held V, Rotter N, Schell A: Case report: bilateral palsy of the vocal cords after COVID-19 infection. Front Neurol. 2021, 12:619545. 10.3389/fneur.2021.619545

Brodsky MB, Huang M, Shanholtz C, Mendez-Tellez PA, Palmer JB, Colantuoni E, Needham DM: Recovery from dysphagia symptoms after oral endotracheal intubation in acute respiratory distress syndrome survivors. A 5-year longitudinal study. Ann Am Thorac Soc. 2017, 14:376-83. 10.1513/AnnalsATS.201606-455OC

Lechien JR, Chiesa-Estomba CM, De Siati DR, et al.: Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol. 2020, 277:2251-61. 10.1007/s00405-020-05965-1

Moein ST, Hashemian SM, Mansourafshar B, Khorram-Tousi A, Tabaei P, Doty RL: Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol. 2020, 10:944-50. 10.1002/alr.22587

Giacomelli A, Pezzati L, Conti F, et al.: Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. Clin Infect Dis. 2020, 71:889-90. 10.1093/cid/ciaa530

Vaira LA, Salzano G, Deiana G, De Riu G: Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope. 2020, 130:1787. 10.1002/lary.28692