

Cranial neuropathy in COVID-19: a case series and review of literature

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SUMMARY

Neurological presentation of COVID-19 is increasingly being recognised. Cranial neuropathy in COVID-19 is an uncommon and under-diagnosed entity. We report a case series of 4 patients who presented with trigeminal neuropathy (two cases) and

facial nerve palsy (two cases) which recovered with conservative treatment along with the review of the literature.

Keywords: COVID-19, trigeminal neuralgia, Bell's palsy.

INTRODUCTION

COVID-19 has spread as a pandemic geographically and has demonstrated multiple systemic manifestations beyond the respiratory system. Neurological manifestations including headache, stroke, seizures, Guillain-Barré Syndrome and Acute disseminated encephalomyelitis have been documented as clinical presentations of COVID-19 [1, 2]. However, rarely COVID-19 can also affect cranial nerves leading to varied and atypical presentations. These can lead to delayed recognition and appropriate therapy. We report a case series of 4 patients who presented with cranial neuropathies within 2 weeks of COVID-19 infection and showed complete recovery, along with a review of literature for the same.

Case 1: A 44-year-old male presented with a 2 days history of fever, generalized body ache and dry cough. Rapid antigen test (RAT) for COVID-19 was done and it came out to be positive. On ex-

amination, the patient's blood pressure (BP) was 132/80 mm Hg, pulse rate (PR) 110/min, respiratory rate (RR) 18/minute and saturation oxygen (SPO₂) -98% on room air. Patient was managed as a case of mild infection as per Indian national guidelines with antipyretics and nutritional supplements with monitoring of vitals in home isolation. On day 5 of illness, the patient had residual mild cough which resolved by day 8-9. On day 11, he developed a paroxysmal, stabbing type of pain on the right side of face. Pain was aggravated by chewing & laughing. On examination, the patient described pain in the mandibular and maxillary region of the trigeminal nerve (right side). Patient was started on Carbamazepine 200 mg twice a day and was symptomatically better in five days. Patient became asymptomatic after one week and discontinued medications. On a follow up visit on day 17 of illness, there were no symptoms or any neural loss.

Case 2: A 32-year-old male presented with a 3 days history of cough, generalized body ache, diarrhoea and fever. On examination, the patient's BP was 118/70 mm Hg, PR 106/min, RR 17/min and SPO₂-99% on room air. Patient was advised to take a rapid antigen test for COVID-19 which

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came out to be positive. Patient was managed as a case of mild infection as per Indian national guidelines with antipyretics and nutritional supplements with monitoring of vitals in home isolation. Patient became asymptomatic on day 6. On day 9, the patient developed pain on the right side of face which he described as a paroxysmal, lancinating type of pain which got aggravated on chewing & touching. On examination, the patient described pain in the mandibular and partially in maxillary region of trigeminal nerve (right side). Patient was started on carbamazepine 200 mg twice a day, but he complained of increased sleepiness, so dose decreased to 100 mg, which subsequently was increased to 200 mg bd after 3 days. On day 6, the patient was symptomatically better but pain was still present, so dose increased to 200 mg thrice a day. Patient presented after 2 weeks with resolution of symptoms, so dose was reduced to 100 mg twice a day for one week, after which it was stopped.

Case 3: An 18-year-old female presented with a history of facial deviation toward the left side, inability to close right eye for 1 day. Patient also had a history of cough and generalized body ache 1 week back for which she got tested positive for COVID-19 antigen. On examination, the patient's BP was 110/72 mm Hg, PR 88/min, RR16/min and SPO2-99% on room air. On neurological examination, there was lower motor neuron (LMN)

type of right facial palsy and the rest of the examination was normal. Patient was started on steroids (1 mg/kg body weight), eye taping during sleep and methylcellulose eye drops. After 1 week, the patient improved significantly and steroids were tapered over the next 2 weeks. After 2 weeks, there was no residual focal neurological deficit.

Case 4: 20-year-old male presented with fever, cough and body ache for 3 days. On examination, the patient's BP was 128/80 mm Hg, PR 116/min, RR 17/min and SPO2-96% on room air. Patient turned out to be COVID-19 polymerase chain reaction (PCR) positive. Patient was also managed as a case of mild infections. On day 11, the patient developed LMN type of facial palsy on the right side. Patient was started on steroids (1 mg/kg body weight), methylcellulose eye drops and advised eye taping during sleep. After 5 days, the patient improved significantly and at 2 weeks, there was no residual focal neurological deficit.

■ LITERATURE SEARCH AND REVIEW

The search of PubMed for {[COVID-19] OR [SARS CoV2]} and {[Cranial neuropathy] OR [cranial nerve]} revealed 221 results as on 9th September 2021. After excluding review articles or letters or which did not have any patient data, cases which were post-COVID-19 recovered patients with tu-

Table 1 - Summary of published literature of cranial neuropathy during COVID-19.

Article	Patients	Cranial neuropathy	Treatment	Outcome
Finsterer J et al. [3]	Systematic review of 36 articles with 56 patients	Single cranial nerve involved in 36 patients, while in 19 patients, multiple cranial nerves were involved. Bilateral involvement was more in GBS group	Steroids (n=18), intravenous immunoglobulins (IVIG) (n=18), acyclovir/valacyclovir (n=3), and plasma exchange (n=1)	The outcome was classified as "complete recovery" in 21 patients and as "partial recovery" in 30 patients. One patient had a lethal outcome.
<i>Other studies not included in the above systematic review</i>				
Tamaki et al. [4]	Cohort of 348008 COVID-19 patients from 41 centres	284 (0.08%) had Bell's palsy. 131 among these had a past history of Bell's palsy	Retrospective study with no details regarding treatment	Retrospective study with no details regarding outcome
Piazza et al. [5]	Case report of 1 patient	Right sixth cranial nerve palsy, CSF had high protein and MRI had white matter changes	High-dose intravenous methylprednisolone	Rapid resolution of clinical symptoms

<i>Article</i>	<i>Patients</i>	<i>Cranial neuropathy</i>	<i>Treatment</i>	<i>Outcome</i>
Moyano A JR et al. [6]	Case report of a 38-year-old female patient	Vagus nerve neuropathy presenting with dysphagia and hypoesthesia in pharynx	Multidisciplinary rehabilitation program that included speech and deglutition therapy	Complete recovery
Francis et al. [7]	Case report of a 69-year-old female patient	Left abducens nerve palsy	Rehabilitation	Complete spontaneous recovery of the abducens palsy within 6 weeks
Gupta et al. [8]	Thirteen articles (case reports) from 2020 including 20 cases of COVID-19 with Bell's palsy	Bell's palsy as the only major neurological manifestation	Not mentioned	Not mentioned
Theophanous C et al. [9]	Case report of a 6-year-old child	Right sided facial palsy	Intravenous acyclovir 150 mg every 8 hours, scheduled dose of IVIG infusion (for underlying agammaglobulinemia). Lubricating eye drops for corneal protection	The symptoms improved at a follow-up at 3 weeks
Halalau A et al. [10]	Case report of a 42-year-old male patient	Right vestibular neuritis presented with persistent vertigo, persistent leftward nystagmus and a positive Romberg sign with a tendency toward the right	Oral prednisone (50 mg once daily for 5 days) and meclizine (25 mg as-needed up to thrice daily)	Improvement over 2 weeks
Kumar V et al. [11]	Case report of a 28-year-old female patient	Drooling from right sided angle of mouth, deviation of face to right and inability to shut her right eye suggestive of Right sided facial nerve palsy	Oral valacyclovir 1 g thrice daily for 10 days and oral prednisolone 50 mg once daily for 7 days followed by tapered doses	Improvement at 10 days
Wei H et al. [12]	Case report of a 62-year-old male patient	Drooping of left eyelid and diplopia. Left sided oculomotor nerve palsy. Respiratory failure with SpO ₂ 90%	Oxygen therapy, moxifloxacin 400 mg, oseltamivir 75 mg, methylprednisolone 40 mg and ribavirin 0.5 mg once daily, lopinavir 400 mg twice daily, IVIg 0.4 g/kg once daily, paracetamol up to 650 mg thrice daily and ibuprofen 600 mg twice daily for 12 days	Died on 12 th day due to respiratory failure
François J et al. [13]	Case report of a woman in her fifties	Right eye optic neuritis and uveitis with bilateral pneumonia and temporal arteritis	Oral and topical corticosteroids	Regained partial eyesight at 45 days

Notes: GBS, Guillain-Barré syndrome; IVIG, Intravenous immunoglobulin; SpO₂, percent saturation of oxygen in the blood.

berculosis, fungal sinusitis or other conditions leading to cranial nerve involvement, a total of 11 studies were enlisted (one systematic review and 10 other studies) in Table 1 [3-13]. It is evident from the literature that cranial neuropathy can occur across all age groups (6-year-old child to 62-year-old adult), can involve various cranial nerves (2nd, 3rd, 5th, 6th, 7th and even 10th cranial nerve), often requires no drug treatment resolving with only rehabilitation and conservative management, sometimes require steroids and rarely additional drugs like Intravenous immunoglobulin (IVIG). Mortality has been seen in two patients with 7th nerve palsy, which was associated with Guillain-Barré syndrome (GBS) leading to respiratory failure [3, 12]. A large systematic review of 36 articles illustrates that facial nerve involvement is the most common manifestation reported among COVID-19 with cranial neuropathy, particularly more common in patients presenting with GBS [3].

■ DISCUSSION

Our case series comprised of young patients with mild COVID-19 with 5th and 7th cranial neuropathy which had a complete recovery similar to reported literature (Table 1). Partial recovery has occasionally been seen in optic and vestibular neuropathy. The two patients with facial nerve palsy in our series were treated with oral steroids. This is in contrast with the reported literature where most patients recovered spontaneously. However, steroid use has shown a rapid response in certain reported cases and moreover, even in post COVID-19 vaccination facial nerve palsy [14]. Our patients were being monitored with telemedicine and in view of rapid recovery, did not require prolonged course of steroids or gradual tapering of doses. The two patients with trigeminal neuralgia were treated with carbamazepine for 1 week and 3 weeks respectively. The use of carbamazepine may have been similar to placebo, but the second patient did report improvement of pain with the prolonged use. A recent case series reported rapid response with use of carbamazepine in four patients with COVID-19 who had recurrence of their underlying idiopathic trigeminal neuralgia [15]. In view of rapid and complete recovery with steroids, the possible pathophysiology of cranial neuropathy in COVID-19 may be immune-mediated.

However, direct entry of SARS CoV-2 into the trigeminal and facial nerve through ACE2 receptors of neuronal and glial cells is also a possibility [16]. The exact etiopathology can only be unravelled by large-scale studies and appropriate investigations. Unfortunately, all of our patients were in home isolation, and thus they could not undergo any neurological imaging or nerve conduction studies.

Anosmia and ageusia was also initially reported from few areas across the world leading to increased recognition and subsequent addition in the list of symptoms of COVID-19 [17]. Similarly, despite varied neurological manifestations ranging from central to peripheral nervous system in COVID-19, cranial nerve palsies are rare and possibly under recognised. Even as pulmonary specialists treat COVID-19, it is imperative to keep a multi-system approach while treating COVID-19. Unfortunately, non-pulmonary manifestations are not included in classifying such patients into moderate or severe cases in Indian guidelines. Eventually, all these patients with no hypoxia get classified as mild cases and are advised home isolation [18].

■ CONCLUSIONS

Thus, a high index of suspicion, close clinical follow-up and constant vigilance is necessary to timely diagnose these evolving neurological manifestations of COVID-19 as they are treatable and often show complete recovery [19]. Besides, in the peak COVID-19 waves, these symptoms should not be ignored as they may be the initial or the only manifestation of COVID-19.

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Conflicts of interest

None.

Consent

Written informed consent was taken from the patients for sharing their clinical details in the article.

Contributors

PI and NB were involved in conceptualization, literature search. NB, PI, KPI and AN were involved in writing, review and editing. All authors have read and agreed to the final draft submitted.

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