



# COVID-19 Associated Neuropathies in Cameroon: A Case Series

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## Introduction

The novel Coronavirus (SARS-CoV-2) hit the world as from December 2019 with a potentially life-threatening respiratory tract infection [1]. However, the Coronavirus Disease 2019 (COVID-19) has a broad spectrum of clinical manifestations that is still to be fully described. Out of the respiratory tract, the virus seems to have a great neural tropism, given the large number of neurological signs that comprise but are not limited to headache, convulsions, anosmia, ageusia and trigeminal neuralgia. We describe a case of Trigeminal Neuralgia (TN) arising in a COVID-19 patient and persisting after the resolution of all the other symptoms and two cases of chemical senses involvement.

## Case Series

### Case 1

Mister ND is a 50-year-old accountant with a past medical history of left chronic otitis media, high blood pressure under captopril + Hydrochlorothiazide 50 mg + 25 mg combination, right knee joint chronic pain under sporadic NSAID (Diclofenac). He came to us with the complaints of nasal pains irradiating to both ears and alternating sensations of empty nose and nasal foreign body. The pain had started twelve weeks ago, along with a flu-like clinical frame comprising a dry cough, anosmia, ageusia, headache, catarrh, diarrhea and epigastralgia. He was diagnosed positive to COVID-19 after a Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) nasopharyngeal swab test. The patient was then put on the Cameroon national protocol against COVID-19, which at that time was Chloroquine (200 mg PO bid for seven days), Azithromycin (500 mg PO on day 1, 250 mg PO from day 2 to day 5), Vitamin C (1 g PO daily for 10 days) and Zinc sulphate (10 mg PO daily). After 14 days of in-home containment, a control test was done and found positive again to COVID-19. The patient underwent a new Chloroquine + Azithromycin full regimen for 7 and 5 days respectively. On day 25, the 3<sup>rd</sup> test finally came negative and the patient was declared healed. A week after he could resume his outdoor activities. To date, he still complains of subjective hyposmia and hypogeusia. All the other symptoms were relieved except the nasal pains. The latter were very worrisome, keeping him in the anxiety of a COVID-19 recurrence and resulting in insomnia and anxiety. It was an excruciating pain, described as “electric current”, estimated as severe as 8-9 over 10 on visual subjective scale, occurring randomly several times in the day and the night, awakening him. It could last seconds to a maximum of 3 min, with no known triggering or alleviating factor, accompanied with a worsening of the nasal foreign body or emptiness sensation. He had taken acetaminophen, diclofenac, ibuprofen, tramadol and tramadol + codeine in vain. He had undergone 2 more RT-PCR and 1 antigen COVID-19 rapid diagnosis tests which were all negative.

We performed an audiogram which revealed a conductive hearing loss on left ear with average loss 50 dB, consistent with the history of chronic otitis media. Hearing was normal on right side. A nasopharyngeal endoscopy was also performed and was normal. The Eustachian tube openings were not obstructed and there was no mass in the nasal cavities or the rhinopharynx.

The patient was reassured and put on carbamazepine (200 mg 12 hourly) and meclizine (25 mg at once at bedtime for 10 days). As from day 2, the pain subsided progressively. It does recur

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randomly, but is estimated at only 2 over 10 on visual subjective scale. The empty nose or full nose sensation have ceased. To this date, after a 3-month follow up, the patient is doing finer.

### Case 2

A 29 year-old lady came for anosmia evolving for 6 months prior to the consultation. The past medical history revealed that during the first wave of COVID-19, she had a sudden anosmia and ageusia accompanied by light headache, a running nose and little fatigue. After about 5 days, she regained her taste sensation and all the symptoms subsided except the anosmia. Upon questioning, the patient revealed a cacosmia occurring from time to time, about once every other day and lasting for a few seconds. In fact, she would smell an offensive odor, always the same, though there is nothing alike in her immediate vicinity. She couldn't describe what the odor corresponded to, but it was not comfortable. Physical examination was normal including other cranial nerves. We performed a nasal endoscopy that was irrelevant. A serological and a real time PCR COVID-test were done. The first revealed positive IgG antibodies and the latter was negative. We prescribed her a nasal steroid spray (Fluticasone furoate: 1 spray in each nostril twice a day) for a month, Betamethasone and vitamin B per os for 10 days. There was no improvement of the initial complaints of the patient. An olfactory bulb MRI-scan was done with no relevant finding. To date, the patient is left without solution.

### Case 3

A 40-year-old female came to complain for decreased taste sensation since her COVID-19 infection. She was diagnosed positive 13 months ago over a clinical frame of catarrh, headache, muscle and joint pains, anosmia and ageusia. She was staged as mild infection and given Cameroon national protocol treatment (Hydroxychloroquine, Azithromycin, Zinc and Vitamin C). Things improved quickly and almost all the symptoms disappeared within a week. But she was left with a partial recovery of taste. She said her tongue was numb, like anaesthetized and the taste sensation was faint compared to before COVID-19 infection (hypogeusia). She also complained of parosmia and phantosmia. Physical examinations with neurological examination were normal. She was given Methylprednisolone and a B multivitamin preparation per os for 10 days to no avail. To date, her smell and taste sensation have not changed any better.

## Discussion

The COVID-19 clinical picture is still under construction as new features of the disease are still emerging along the course of the pandemics. Neurological manifestations are now an undisputable part of the clinical frame of the infection [2-5]. They include a large number of symptoms that can be classified as Central Nervous System (CNS) and Peripheral Nervous System (PNS). CNS manifestation includes dizziness, headache, impaired consciousness, ataxia, acute cerebrovascular disease and epilepsy while PNS comprise hyposmia, ageusia and neuralgia [2].

Trigeminal neuralgia is usually called tic douloureux and is a well-known neurological condition. Its diagnosis is based on clinical findings that can be classified in three criteria: Restriction of the pain to the territory of one or more branches of the 5<sup>th</sup> cranial nerve, paroxysms of pain that are intense, sudden and very short (from less than a second to a few minutes) and described by patients as an electric sensation or shock and the triggering of pain by innocuous touch of the trigeminal territory [6,7]. The prevalence of TN is higher in women than in men.

The features of TN in the reported case 1 differ slightly from the classical presentation. In fact, there was no known triggering factor to his pain. In addition, the pain was associated with subjective nasal emptiness or fullness. Given the numerous types of stimuli that can trigger the pain, including sensory stimuli, the patient may not be aware or may not link a discreet move (such as pronouncing labial letters, eye movements, and tongue movements) to the pain start despite of a thorough interrogatory. We couldn't examine it directly since no episode occurred during consultation.

TN can be due to vascular compression of the 5<sup>th</sup> nerve (classical) or to another disease (multiple sclerosis, tumors) but the final common pathway is demyelination which causes ectopic generation of electric impulses with high-frequency after discharges [8]. Demyelination has already been associated with COVID-19 as a mechanism of its neurological manifestations, along with infection through the cribriform plate and olfactory bulb and dissemination through trans-synaptic transfer.

The typical pain of TN is usually unilateral. However, in the case 1 reported, it was located in both nasal fossa and radiated to both ears. This is consistent with a concomitant aggression of both nasal cavities by the novel coronavirus, leading to the features.

In a series previously reported, Karadas et al. found 3% of their sample of COVID-19 patients to have TN and many other teams report more cases [1,2,4,7].

Treatment strategies of TN include medical treatment (carbamazepine, oxcarbazepin, baclofen, lamotrigin, gabapentin, etc.), surgical treatment (microvascular decompression, stereotaxic radiosurgery and percutaneous destruction neurosurgical techniques) [6]. Carbamazepine is the baseline gold-standard treatment. It provides significant relief of pain in TN. But attention must be paid to the control of liver function since this drug alters them.

Due to lack of financial support, the patient did not perform a brain imagery to rule out other confounding conditions such as a tumor or multiple sclerosis.

Smell and taste are known as chemical senses [9]. There are numerous reports describing their involvement in COVID-19 patients. There are about 200 virus that can cause respiratory infection leading to a decrease of chemosensation while Post Viral Olfactory Dysfunction (PVOD) is caused mainly by rhinoviruses, influenza and parainfluenza and coronaviruses [9,10]. PVOD has a variable persistence course after the infection has resolved, leading to hyposmia or anosmia. Hyposmia usually occurs during the symptomatic phase of the infection due to congestion and discharge. In fact, mediators like bradykinins increase mucus production and cleaning as well as swelling of nasal blood vessels leading reduction of air flow [11]. Beside this mechanism, a direct lesion of the olfactory sensory epithelium has been described. In fact, biopsies have showed large areas of scarring, decreased number of cilia on the olfactory receptor neuron and replacement of olfactory by respiratory epithelium [9,12]. Spontaneous recovery from PVOD occurs within 3 years after the infection in one third of patients while a significant portion of them will continue to experience parosmia and/or phantosmia [13-15]. Most of the PVOD happen in the 4<sup>th</sup> decade when the regeneration ability of the olfactory sensory neurons is decreased. This lesser the chances of recovery [16].

## Conclusion

TN triggered by COVID-19 is a clinical feature of the pandemic

the world is facing for more than a year now. Chemical senses involvement is now a well-known clinical finding. The delay in recovering of those senses is of great concern for the patients who experience a significant worsening of their quality of life.

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