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CASE REPORT

# COVID-19 patient having anosmia as a sole symptom: A case report

## *Patient COVID-19 ayant l'anosmie comme le seul symptôme: Un rapport de cas*

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## ABSTRACT

Smell loss or also called anosmia is a very common symptom of COVID-19 and occurs in a high prevalence of infected patients in associated with or even in the absence of any other frequent symptoms such as fever or cough. Previous studies also showed that an acute loss of smell or anosmia might be the first symptom, and in some patients the sole symptom, of COVID-19 infection.

The prevalence of anosmia in patients with COVID-19 has been reported from 24% up to 70% of confirmed cases. However, this reported prevalence has been depending on the geographical area and technique used to evaluate smelling ability. Although most studies stated that females were more likely to experience anosmia due to COVID-19 compared to males, the relationship between anosmia and gender in patients with CIVID-19 has not been clarified.

The mechanisms underlying anosmia in COVID-19 have been fully explored during the pandemic. Some initial observations showed that although small percentage of people who do develop blocked nose or runing nose (rhinorrhea) could account for hyposmia or even anosmia, the majority of COVID-19 patients who suffer from anosmia typically do not get nasal congestion (blocked nose) or rhinorrhea. Hence, other potential mechanisms have been clarified recently.

Here, we present a case with COVID-19 infection as a sole symptom of the disease.

**KEYWORDS: SARS-COV2; COVID-19; Anosmia; Symptom.**

## RÉSUMÉ

La perte de l'odorat ou aussi appelée anosmie est un symptôme très courant de COVID-19 et se produit dans une forte prévalence de patients infectés en association ou même en l'absence de tout autre symptôme fréquent tel que la fièvre ou la toux. Des études antérieures ont également montré qu'une perte aiguë de l'odorat ou une anosmie pourrait être le premier symptôme, et chez certains patients le seul symptôme, de l'infection au COVID-19.

La prévalence de l'anosmie chez les patients atteints de COVID-19 a été rapportée de 24% à 70% des cas confirmés. Cependant, cette prévalence rapportée dépend de la zone géographique et de la technique utilisée pour évaluer la capacité olfactive. Bien que la plupart des études aient indiqué que les femmes étaient plus susceptibles de souffrir d'anosmie en raison de COVID-19 que les hommes, la relation entre l'anosmie et le sexe chez les patients atteints de CIVID-19 n'a pas été clarifiée.

Les mécanismes sous-jacents à l'anosmie dans COVID-19 ont été pleinement explorés pendant la pandémie. Certaines observations initiales ont montré que bien qu'un petit pourcentage de personnes qui développent un nez bouché ou un nez qui coule (rhinorrhée) puisse expliquer une hyposmie ou même une anosmie, la majorité des patients COVID-19 qui souffrent d'anosmie n'ont généralement pas de congestion nasale (nez bouché) ou rhinorrhée. Par conséquent, d'autres mécanismes potentiels ont été clarifiés récemment.

Ici, nous présentons un cas d'infection au COVID-19 comme seul symptôme de la maladie.

**MOTS CLÉS: SRAS-COV2 ; COVID-19; Anosmie; Symptôme.**

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## INTRODUCTION

Currently, the world has passed more than 200 million cases globally infected with COVID-19 (SARS-CoV-2 virus) and registered hundreds of more than 4 million of deaths. The main symptoms of COVID-19 have been initially described with fever, sore throat, dry cough, difficulty breathing, tiredness, diarrhea [1]. However, health care workers around the world are now recognizing sudden alterations to smell and taste as a specific symptom of COVID-19 infection [2-4]. Smell loss or also called anosmia is a very common symptom of COVID-19 and occurs in a high prevalence of infected patients in associated with or even in the absence of any other frequent symptoms such as fever or cough [5]. Previous studies also showed that an acute loss of smell or anosmia might be the first symptom, and in some patients the sole symptom, of COVID-19 infection [6].

The prevalence of anosmia in patients with COVID-19 has been reported from 24% up to 70% of confirmed cases [7-9]. However, this reported prevalence has been depending on the geographical area and technique used to evaluate smelling ability. Although most studies stated that females were more likely to experience anosmia due to COVID-19 compared to males, the relationship between anosmia and gender in patients with CIVID-19 has not been clarified.

Here, we present a case with COVID-19 infection as a sole symptom of the disease.

## OBSERVATION

A 21-year-old nursing student complained a sudden loss of smell after a short time participating in the frontline of COVID-19 as health care worker. His main work during COVID-19 battle campagna was to do the rhinopharyngal specimen for COVID-19 antigen detecting test and RT-PCR. He denied having fever or sore throat. He also denied any dry cough or difficulty breathing. He had not experienced any recent tiredness or diarrhea. He did not reported another additional symptom such as a loss of taste.

In his recent medical history, he had recent contact with people who came to the healthcare unit for doing COVID-19 test to diagnosis of COVID-19 infection.

In addition to a recent medical history of anosmia, the patient had not any recognized health problem in the past and excluded any medications. He also denied any ENT (ear-nose-throat) interventions recently. The patient is a non-smoker and does not use any illicit drugs.

The physical examination reveals a 21-year-old man in no acute respiratory distress syndrome. His temperature was 37.0°C. His pulse was 80 beats/min, and his blood pressure was 110/60 mm Hg. A pulse oximetry examination revealed a room air saturation of 97%. Examination of the lungs showed no crackles nor rhonchi or wheezing. Examination of the cardiovascular system was unremarkable, as was the abdominal examination. Examination of the skin was also unremarkable for the pathologic process. ENT examination revealed any abnormal sign or symptom such as polyps or nasal septum deviation. There was only a severe anosmia which was recognized as the sole symptom in this patient.

Portable chest x-ray was obtained and did not reveal any effusions or infiltrates. A complete blood cell count showed an decreased white blood cell count of 4.5 x $10^3$/µL (reference range: 6.0 – 8.0 x $10^3$/µL) and predominant with low level of lymphocyte: 23.9% vs 25 – 30% of normal value. There were any significant microcytic or hypochromic anaemia (with a haemoglobin of 14.0 g/dL (reference range: 12.0 – 17.0 g/dL); a mean corpuscular volume (MCV) of 83.7 fL, and a mean corpuscular haemoglobin (MCH) of 28.1 pg/cell *(Table 1)*.

**TABLE 1. Complete blood count charaterictics.**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| WBC | : 4.5 | - $10^3$/µL | < 6-8 > | LYM% (W-SCR) | : 23.9 | L- % | < 25-30 > |
| RBC | : 4.98 | + $10^6$/µL | < 3.8-4.2 > | MXD% (W-LCR) | : 15.8 | L % | < 1-20 > |
| HGB | : 14 | g/dL | < 12-17 > | NEUT% (W-MCR) | : 60.3 | % | < 57-70 > |
| HCT | : 41.7 | - % | < 42-49 > | LYM# (W-SCC) | : 1.1 | L- $10^3$/µL | < 1.2-2.9 > |
| MCV | : 83.7 | fL | < 80-102 > | MXD# (W-MCC) | : 0.7 | L $10^3$/µL | < 0.2-1.2 > |
| MCH | : 28.1 | pg | < 26-38 > | NEUT# (W-LCC) | : 2.7 | $10^3$/µL | < 2.5-5.8 > |
| MCHC | : 33.6 | g/dL | < 28-37 > | RDW_SD | : 40.3 | fL | < 37-54 > |
| PLT | : 190 | - $10^3$/µL | < 200-400 > | P-LCR (PCT) | : 15 | % | < 11-43 > |
| PDW | : 10 | fL | < 9-17 > | MPV | : 8.4 | - fL | < 9-13 > |

*WBC: white blood cells; RBC: red blood cells.*

The result of RT-PCR /COVID-19 at the moment of diagnosis of anosmia (T0) was positive with Ct value for N-gene of 18.65 and for ORF1a of 19.45 *(Figure 1)*.

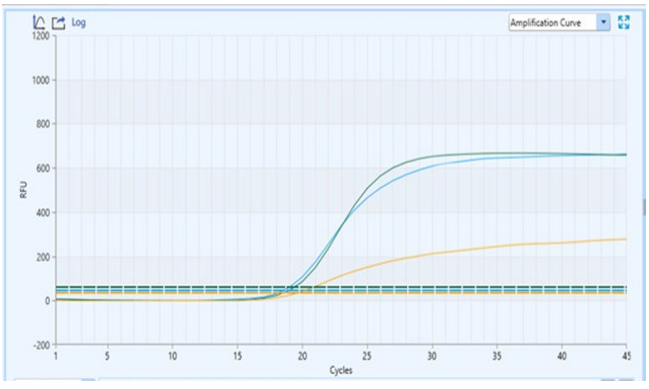


**FIGURE 1.** ***RT-PCR result of presented case report at T0 (admission day).***

The patient received his treatment including nasal Betadine spray (1 buff x 3 times/day), nasal corticosteroid spray (Budesonide: 1 buff each nostril x 3 times / day), Ivermective 200mcg x 2 times / day x 5 days; antiviral therapy (Fapivirapir 400 mg / day x 5 days); Xarelto 20 mg x 5 day). There was no side effect of combined treatment complained by patient. Anosmia was improved after T1 and recovered totally at T2.

The patient had been discharged after 2 weeks of treatment within RT-PCR /COVID-19 was negative after the first week (T1) and second week (T2). He has continued his treatment with nasal corticosteroid (Budesonide) and retrain olfactory system with eucalyptus and menthol odour.

## DISCUSSION

Anosmia is a specific symptom of COVID-19, a coronavirus family SARS-CoV-2. It has been associated with a large number of COVID-19 cases, even in the absence of other common symptoms such as fever, sore throat, dry cough, difficulty breathing, tiredness, diarrhoea. In addition, changes in taste are also commonly associated with smell loss in COVID-19.

However, this case report shows that anosmia may be presented as a single symptom of COVID-19 infection. Therefore, some countries have considered sudden smell loss as specific as the diagnosis value of RT-PCR test [10,11].

**Prevalence of anosmia in COVID-19 patients**

The prevalence of anosmia in patients with COVID-19 varies considerably and depends mainly on different cohort characteristics and demographics. In general, it has been demonstrated that the prevalence of anosmia is more than 50% of cases [8,9].

Interestingly, some studies have shown that anosmia usually associated with taste loss in COVID-19 and more common in young patients compared to older patients. However, it has been suggested that there are no differences between gender for having anosmia in patients with COVID-19 [12,13].

Some studies have shown the prevalence of anosmia is higher in Western countries in comparison to Asian countries [7,9]. It might be due to the lack of complete report of all symptoms, as well as the different viral variant or host genetic differences. The most recent systematic review on 30,264 patients demonstrated nearly 3-fold higher prevalence in olfaction and/or taste impairment in populations in Western countries than in populations in East Asia, and it was independent of age or disease severity [14].

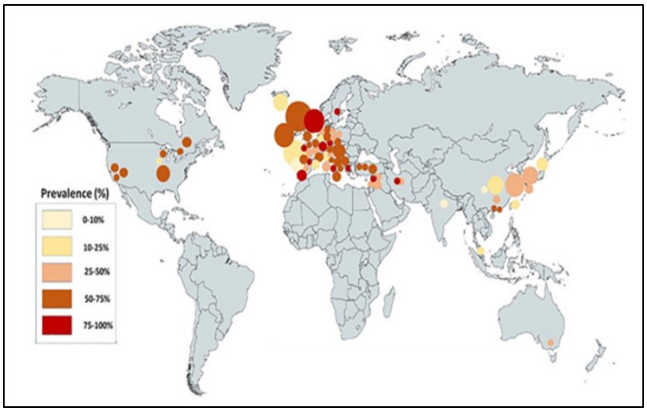


**FIGURE 2.** *Prevalence of chemosensory deficits in COVID -19 patients. World map based on 68 studies with a total of 30,264 patients* [14].

**Clinical characteristics of anosmia in COVID-19 patients**

In our case report, anosmia has been disappeared after ten day under local and systemic treatment. The patient has been recovered his smell ability before discharged from hospital. Previous studies also found out that anosmia for the majority of infected patients tends to be short-term and has a rapid recovery, though in some patients it can persist for much longer [15,16].

Therefore, people with a sudden anosmia should presume they are positive for COVID-19 in waiting the confirmation of RT-PCR result and start to do quarantining or self-isolating. The present case report also demonstrates that unlike anosmia due to colds, seasonal flu and other ENT causes where anosmia likely to be associated with running nose, blocked nose or sneezing, the sudden anosmia in COVID-19 may be directly related to SARS-CoV-2 infection within the nasal epithelium and olfactory neurons' damages without any other symptoms.

**Mechanism of anosmia in COVID-19**

The mechanisms underlying anosmia in COVID-19 have been fully explored during the pandemic. Some initial observations showed that although small percentage of people who do develop blocked nose or running nose (rhinorrhea) could account for hyposmia or even anosmia, the majority of COVID-19 patients who suffer from anosmia typically do not get nasal congestion (blocked nose) or rhinorrhea. Hence, other potential mechanisms have been clarified recently.

The hypothesis of anosmia related to the direct invasion of nasal olfactory neurons or infiltration of the neurons in the olfactory bulb by SARS-CoV-2 is unlikely because olfactory neurons do not express SARS-CoV-2 binding receptors such as ACE2 or TMPRSS2. Thus, the presence of SARS-CoV-2 in the brain might be via other pathways.

Although olfactory neurons do not express ACE2/TMPRSS2, another cell type (sustentacular cells) in the nose found in addition to olfactory neurons known as maintenance cells expresses for both ACE2 and TMPRSS2. These cells can support the olfactory nerve cells in the nose and can be destroyed during COVID-19 infection, leading to sensory dysfunction and sudden loss of sense of smell or anosmia [17]. In fact, when SARS-CoV-2 (COVID-19) binds to ACE2/TMPRSS2 on nasal sustentacular cells leading to cell death and loss of sensory cilia on olfactory receptor neurons. Therefore, odorants particles fail to bind to cilia neurons, explaining why anosmia being occurred in the early stage of COVID-19 infection [18-20].

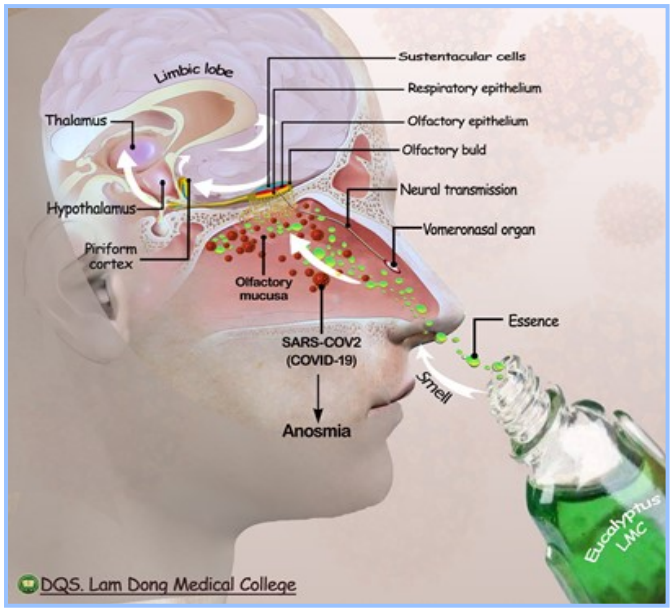


**FIGURE 3.** *Mechanism of anosmia in COVID-19 infection.*

Recently, French researchers [21] have just clarified the mechanisms involved in this anosmia in patients with COVID-19 and animal model. They found out that several chronological stages emerge in this loss of smell, including disappearance of the cilia allowing the reception of odorous molecules by the sensory neurons, presence of viruses in sensory neurons, disorganization of the olfactory epithelium linked to apoptosis, invasion of the olfactory bulb by the virus, and presence of neuroinflammation and viral RNA in several areas of the brain. The authors also showed that sensory neurons were infected with SARS-CoV-2 and the virus then spread to other nerve structures where it induced a strong inflammatory response. Infection of olfactory neurons could therefore constitute a gateway to the brain and explain why some patients develop various clinical manifestations, psychological or neurological diseases. This study has shown that the classic RT-PCR tests performed on nasopharyngeal swabs can be negative while the virus persists deep in the nasal cavities, in the olfactory epithelium. The diagnosis of SARS-CoV-2 by nasal brushing may then be considered to supplement the nasopharyngeal swab.

**Treatment of anosmia**

In our case report, the patient received combined treatment with antiviral and anti replication in association with local corticosteroid treatment. The patient's evolution and clinical status were better after one week and before discharged. His anosmia was recovered completely after two weeks under general treatment. Hence, it is suggests that COVID-19–related anosmia may improve spontaneously and a specific treatment which targets to neuroprotective effect may not be required. It might be considered for specific treatment if anosmia persists more than 2 or 4 weeks. However, the efficacy treatments for patients with COVID-19–related anosmia is still under investigation.

Therefore, the available treatment which aims to recover postinfectious anosmia may potentially be helpful for patients with COVID-19. Although previous systemic review has demonstrated the improvement of anosmia in patients with postinfectious OD after olfactory training [22], obviously, early therapy with olfactory training involving repeat and deliberate sniffing of an available or a scheme of odorants (lemon, menthol and eucalyptus) for 20 seconds each at least twice a day may be helpful (our patient done). Oral and intranasal corticosteroids might be used to treat an inflammatory response in patients with COVID-19- related anosmia. However, due to the safety concerns, the use of systemic corticosteroids for the routine management of acute COVID-19 is not recommended. It is likely that the initiation of intranasal corticosteroid treatment might benefit in these patients; hence, for patients who were using intranasal steroids before developing COVID-19 for their allergic rhinitis or nasal polyps, this treatment should be continued. Moreover, other treatment have been proposed to use as adjuvant therapies for patients with anosmia including intranasal vitamin A, which aims to promote olfactory neurogenesis, and systemic omega-3, which may act through neuroregenerative or anti-inflammatory response [22,23]. However, patients with COVID-19-related anosmia should continue the general prevention during convalescence and post discharged period [24].

## CONCLUSION

Acute anosmia is a common symptom of COVID-19 which may occur as a sole symptom. Unlike other ENT conditions such as alergic rhinitis, septal deviation or nasal polyps where anosmia is usually a result of nasal congestion, in COVID-19, some affected patients do not have nasal congestion. However, related-COVID-19 anosmia may be recovered totally with an adequate treatment. Hence, anosmia could be considered as a clinical marker of COVID-19 infection during SARS-COV2 pandemic.

## CONFLIT OF INTERESTS

*The authors declare no conflict of interest.*

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