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# A case of olfactory neuroblastoma that presented with olfactory dysfunction after a COVID-19 diagnosis

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#### ABSTRACT

*Background:* Olfactory dysfunction is associated with conditions such as respiratory tract infections, trauma, sinonasal diseases, and neurodegenerative diseases. During the coronavirus disease 2019 pandemic, there was an increase in patients complaining of olfactory dysfunctions. Many studies have reported that olfactory dysfunction is associated with coronavirus disease 2019 and that the prognosis is usually favorable.

*Case presentation:* Recently, we experienced a patient with olfactory dysfunction, which was aggravated after a coronavirus disease 2019 diagnosis. The patient had no other medical history, and their nasal endoscopic examination demonstrated no abnormal lesions. Through a psychophysical olfactory function test, the patient was diagnosed with anosmia. A paranasal sinus computed tomography demonstrated sclerotic bony changes in the cribriform plate area. A paranasal sinus magnetic resonance image study found an approximately 3.5 cm-sized olfactory neuroblastoma in the anterior cranial fossa.

*Conclusions:* We suggest clinicians remember the possibility of underlying intracranial lesions in patients with olfactory dysfunction even during the coronavirus disease 2019 pandemic and understand the guidelines of magnetic resonance imaging when evaluating olfactory dysfunction patients. Furthermore, we recommend that clinicians pay attention to the history of olfactory dysfunction before the symptoms progress and making a coronavirus disease 2019 diagnosis.

#### 1. Introduction

Olfaction has many important roles, including maintaining good nutritional health, pleasure sensation, interpersonal behaviors, and identifying dangerous compounds, such as expired food or smoke [[1]]. Olfactory dysfunction is the impairment of olfaction and can be classified as qualitative or quantitative. Quantitative olfactory dysfunction refers to a diminished function of smell and can be categorized into hyposmia or anosmia. Qualitative olfactory dysfunction refers to an altered sense of smell and can be further specified into parosmia or phantosmia [[1]].

Various conditions have been found to be associated with olfactory dysfunction. Viral infections in the respiratory tract, rhinitis, medications, chronic rhinosinusitis with or without nasal polyps, trauma, and intracranial pathologies have all been reported to be possible causes of olfactory dysfunction. Furthermore, neurodegenerative diseases such as Alzheimer's and Parkinson's have been

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shown to be associated with olfactory dysfunction [[2]]. Since the coronavirus disease 2019 (COVID-19) pandemic, the symptoms of olfactory dysfunction have become more common, and a larger portion of the general public has become aware of these symptoms.

A large body of evidence has now demonstrated that the loss of smell is one of the most common symptoms of COVID-19, and the loss of smell may be the only presenting feature of patients with COVID-19 [ [3]]. Regarding the progress and recovery of the olfactory dysfunction, more than 60 % of the patients recovered olfactory dysfunction; however, some remained hyposmic or anosmic even six months after recovering from a COVID-19 infection [ [4]]. Therefore, it is likely that the patients who subjectively complain of olfactory dysfunction induced by COVID-19 are often regarded as having COVID-19-associated olfactory dysfunction, and the potential possibility of underlying intracranial pathologies is less emphasized. In this case report, we report the case of a patient affected by olfactory dysfunction, which was subjectively recognized after a COVID-19 diagnosis. Although the patient was suspected of suffering from COVID-19-associated olfactory dysfunction, the symptoms were due to an underlying intracranial pathology, an olfactory neuroblastoma.

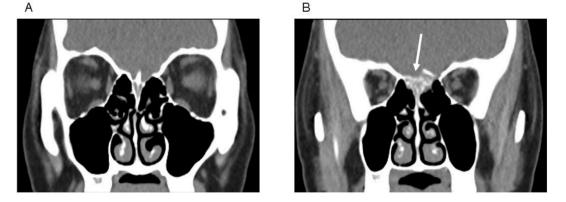
#### 2. Case report

A 45-year-old female presented to our facility with olfactory dysfunction, which was aggravated after a diagnosis of COVID-19. The patient stated that they could not exactly remember when the olfactory dysfunction started. However, after the diagnosis of COVID-19 (one month before visiting our clinic), the patient recognized that their olfactory function was much worse. The patient said that the olfactory dysfunction was quantitative olfactory dysfunction, which is a loss of olfactory; however, they did not have any gustatory dysfunction symptoms. Except for the olfactory dysfunction, the patient had no other rhinologic symptoms, such as rhinorrhea, nasal obstruction, or headaches. The patient had no other notable medical history. A nasal exam using a 0° rigid endoscopy revealed normal findings and no nasal occupying lesion in either nasal cavity. We performed an olfactory function test, developed and validated as a culture-friendly psychophysical olfactory function test (Yonsei Olfactory Function test (YOF)) [ [5]], and a paranasal sinus computed tomography (PNS CT). The YOF test is a validated conventional psychophysical olfactory function at which 2-phenylethyl alcohol is correctly identified four consecutive times, and the discrimination score is the sum of the number of correct answers when selecting the unique odorant among three odorants (2 identical, 1 different). The identification (TDI) score is calculated by adding the threshold, discrimination, and identification scores. Possible TDI scores range from 1 to 36.

Based on the YOF olfactory function test results, the patient's TDI score was 8, corresponding to the total loss of smell, and the patient was diagnosed as having anosmia. The patient did not have other qualitative dysfunctions, such as phantosmia. The PNS CT demonstrated no definite space-occupying lesions in either sinonasal cavity (Fig. 1A). There were no polyps, sinusitis, or mucosal thickening in the sinuses. However, we found a bony sclerotic change with soft tissue density in the cribriform plate (Fig. 1B). We suspected that there could be a space-occupying lesion in the anterior skull base and a paranasal sinus magnetic resonance image (PNS MRI) exam was performed. The PNS MRI images showed an enhanced lesion measuring about 3.5 cm on the anterior cranial fossa (Fig. 2A and B). Based on the PNS CT and PNS MRI images and the olfactory function test, the patient was diagnosed with an olfactory neuroblastoma and was referred to another institute for surgical treatment.

#### 3. Discussion

Olfactory neuroblastoma, also known as an olfactory sensory neuroepithelial tumor, is a malignant nasal cavity tumor originating from the neuroectoderm. The incidence of olfactory neuroblastomas has been estimated to account for 2-3 % of all malignant intranasal tumors [[6,7]]. Olfactory neuroblastomas arise from the olfactory neuroepithelium, which extends from the roof of the nose



**Fig. 1.** PNS CT images of the patient. (A) The coronal CT image demonstrates no definite paranasal sinus lesions that might affect olfactory function. (B) The coronal CT image shows a sclerotic bony change with soft tissue density in the cribriform plate. The arrow indicates the sclerotic bony lesion.

Fig. 2. PNS MRI images of the patient. (A) The T1-enhanced coronal image shows a mass lesion in the base of the anterior cranial fossa. (B) The T2 coronal image demonstrates a mass in the anterior cranial fossa that measured about 3.5 cm. Arrows indicate the mass lesion in the anterior cranial fossa.

to the area of the superior turbinates, a portion of the nasal septum, and can extend into the cribriform plate of the ethmoid sinuses [ [8]]. The most common symptoms of olfactory neuroblastomas are nasal obstruction and recurrent epistaxis. Other symptoms include headache, facial pain, sinusitis, and anosmia. Unilateral symptoms are more common than bilateral symptoms. Since most of these symptoms are similar to those of benign sinonasal diseases, diagnosis of olfactory neuroblastoma is sometimes missed and only diagnosed once it has reached an advanced stage [[8]]. More advanced stages of olfactory neuroblastomas present with symptoms beyond the nose and paranasal sinuses, such as epiphora, diplopia, proptosis, and decreased visual acuity [[9]].

In our patient, the olfactory dysfunction, described as anosmia, was the only symptom. During the COVID-19 pandemic, olfactory dysfunction symptoms were encountered more often in the clinical field. Localized inflammation of the olfactory clefts by SARS-CoV-2 infections, SARS-CoV-2 infections of the supporting cells and pericytes, and release of inflammatory cytokines have been suggested as possible mechanisms [ [10]].

In many cases, olfactory dysfunction symptoms were subjectively recognized by the patient after a COVID-19 diagnosis. It has been reported that there are inconsistencies between subjective olfactory dysfunction symptoms and psychophysical test results [ [11]]. In addition, the prognosis of patients with olfactory dysfunction caused by COVID-19 has been reported to be favorable. Therefore, clinicians have recommended that patients with subjective olfactory dysfunctions take a wait-and-see approach instead of having an active evaluation. However, our case has taught us that olfactory dysfunction should be carefully evaluated even during the COVID-19 pandemic and that there is a possibility of underlying pathologies other than COVID-19, including olfactory neuroblastoma, like in our case, that should be considered (Supplementary Table 1).

The clinical diagnosis of olfactory neuroblastoma is primarily dependent on imaging. Several different types of masses or tumors, such as meningioma, osteoma, and fibrous dysplasia, can occur in the anterior skull region. Among them, olfactory neuroblastomas typically arise from the olfactory nerve and extend into the anterior skull base. Therefore, the most characteristic findings of an imaging study are a mass extending across the cribriform plate and bony erosions of the cribriform plate (such as in our case), orbit, and paranasal sinuses. In addition, a homogenous mass with necrotic non-enhancing areas on CT images is another typical finding of olfactory neuroblastomas. A PNS MRI exam can help differentiate the tumor from obstructed secretions in the paranasal sinuses, determine meningeal and extradural invasion, and identify the extent of perineural involvement. Although PNS CT is superior to PNS MRI in evaluating bony structures, soft tissue boundaries between tumors are more accurately delineated with a PNS MRI, especially in cases of an intracranial extension where only a PNS MRI can define the extension of the tumor [ [6]].

Screening patients with olfactory dysfunction by a PNS MRI has a low diagnostic yield when diagnosing olfactory neuroblastomas or intracranial masses that affect the olfactory pathway [1]]. For example, among 280 MRI scans performed on patients with olfactory dysfunction, only two cases with an intracranial mass were identified [1]]. Currently, the British Rhinological Society guidelines advise that an MRI scan should be performed if the patient presents with isolated anosmia for more than three months, does not have a COVID-19 infection, and has a normal nasal endoscopic examination [12]]. However, in our case, although the symptoms of olfactory dysfunction were recognized after a COVID-19 infection, the olfactory dysfunction could have been associated with underlying intracranial pathologies, such as olfactory neuroblastomas. However, the clinical characteristic of this case was that the

patient said that their subjective olfactory function was affected even before the COVID-19 diagnosis. Therefore, we hypothesized that a mild olfactory dysfunction was present before the COVID-19 diagnosis and was a neglected symptom by the patient until the COVID-19 diagnosis, when the COVID-19 infection aggravated the olfactory dysfunction, which then became recognizable by the patient.

We suggest that clinicians should collect more sophisticated and complete histories regarding olfactory dysfunction symptoms before and after a COVID-19 diagnosis. If the olfactory dysfunction was associated with upper respiratory tract infection symptoms, we suggest that clinicians should evaluate the PNS CT images and carefully review the ethmoid roof area. A thorough medical history and an early PNS MRI evaluation should be considered in cases where the olfactory dysfunction was present before the COVID-19 diagnosis and not associated with upper respiratory tract infection symptoms.

#### 4. Patient consent statement

Written informed consent was obtained from the patient.

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#### Data availability statement

The data are not publicly available since they contain information that could compromise the privacy of the research participant. Data will be made available on request.

#### CRediT authorship contribution statement

**Kyung Soo Kim:** Investigation, Data curation. **Hyun Jin Min:** Writing – review & editing, Writing – original draft, Validation, Funding acquisition.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e22311.

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#### Abbreviations

Coronavirus disease 2019:: COVID-19 Yonsei Olfactory Function test: YOF Paranasal sinus computed tomography: PNS CT Threshold-discrimination-identification: TDI Paranasal sinus magnetic resonance image: PNS MRI