

The impact of ENT manifestation in COVID-19 patients

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ABSTRACT

The pandemic with the new coronavirus – SARS-CoV-2 – has caused extraordinary changes in our way of life. Infection with this virus has caused a huge number of diseases worldwide. After healing from this infection, many patients continued to show symptoms at a distance after the infection itself.

SARS-CoV-2 virus infection is mainly manifested by symptoms related to the lower respiratory tract, such as fever, cough, dyspnea and chest pressure, which could rapidly evolve to acute respiratory distress syndrome (ARDS). However, COVID-19 also causes various symptoms related to the upper respiratory tract, including nasal congestion, neck pain and olfactory dysfunction.

We aim to review, analyze and compare small-looking research studies. Studies show what the changes in ENT are in COVID-19 pandemic disease, how these symptoms influence the course of the disease and how much immunodepressed the patient this virus. It was found that this virus leaves a very precarious immune system and leaves serious consequences in terms of activating some pathologies and symptoms. We also intend to present an atypical case of a patient infected with the SARS-CoV-2 virus that showed a multitude of ENT manifestations both during the acute state and after healing.

Keywords: ENT, COVID-19 disease, SARS-CoV-2, Otorhinolaryngological manifestations

INTRODUCTION

The 2019 coronavirus disease (COVID-19) is one of the most severe diseases caused by the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1]. SARS-CoV-2 virus infection has medical complications for all medical and surgical specialties. When the first case of the COVID-19 infection was reported, many of the ENT surgeons asked a series of questions related to the problems that the pandemic posed to the medical act.

COVID-19 belongs to the SARS-related coronavirus species that led to previous epidemics in the last

two decades such as SARS-CoV in 2002–2003 in China [14] and Middle East Respiratory Syndrome (MERS-CoV) in 2012–2013 in Arabia Saudi [15]. SARS-CoV-2 virus disease has a broad symptomatology (with classic symptoms of an infectious disease of the upper and lower respiratory tract such as fever, cough, fatigue, dyspnea and headache and non-classical symptoms such as abnormalities of smell and taste [16]). It is a disease with different symptoms from case to case, and most of the time the symptoms persist for a long time. The characteristics of the disease differ according to ethnicity, geographic location,

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age of the patient and the form of the virus [7-9]. The otolaryngological symptoms encountered in patients infected with the SARS-CoV-2 virus are anosmia, ageusia, dysphonia, dysphagia, deafness, which may accompany other specific symptoms of COVID-19 [10]. This disease can also cause other symptoms related to the upper respiratory tract, such as nasal congestion, sore throat and smell dysfunction [17]. There is no information classified in specialized articles about the manifestations of the ears, nose, throat, in the disease with SARS-CoV-2 infection. Unfortunately, there are not many previous studies related to the effects of ENT manifestations on positive COVID-19 patients [18]. The aim of the current paper was to identify and discuss the different ENT manifestations that have been reported in positive patients with COVID-19 in the reviewed and published literature [18].

OBJECTIVE

The purpose of this paper is to review and choose the most common ORL manifestations in patients infected with the SARS-CoV-2 virus found in the literature and to determine the impact of these manifestations on the health of people suffering from COVID-19 disease.

MATERIALS AND METHODS

This is a study that presents retrospective literature research for ENT manifestations in patients infected with the SARS-CoV-2 virus. We performed a systematic search of PubMed, Nature, Science Direct, Elsevier, The Lancet, Thieme databases using keywords: "ENT", "Manifestations", "COVID-19", "virus SARS-CoV-2", "Clinical", "Ear, nose, throat", "patients" from the beginning of the 2020 pandemic until March 2023.

The patients' characteristics, history, ENT clinical examination, paraclinical investigations, treatment details, results and their evolution were collected and entered into the study.

RESULTS

The most ENT manifestations reported in recent studies were sore throat at 29%, nasal congestion 26%, nasal obstruction 23%, sneezing 26%, vertigo syndrome 25%, headache 24%, olfactory and gustatory dysfunction at 20%, rhinorrhea 20%, upper respiratory tract infection 12% and enlarged tonsils 8% [19].

From the studies researched so far, it is found that the severity of the disease of COVID-19 in patients who presented ENT symptoms is as follows: 20% of patients had mild cases, 8% of patients had

moderate cases and 5% of patients had severe cases, with no significant difference in the severity of COVID-19 between patients who had ENT manifestations and those who did not [19].

Most of the patients had no history of ENT disease and only 33% of patients had a history of ENT disease [19].

A large part of the cases were admitted to the Intensive Care Unit, and the rest were admitted to the hospital or outpatient [19]. Many patients with severe complications, some of them dying, had pre-existing complications, had morbid obesity, liver disease, very poor immunity, smokers or hypertension [19]. Most of the patients who died of SARS-CoV-2 virus infection were between 49 and 59 years old, in percentage 40%, between 60 and 65 years old in percentage 20%, and over >70 years old in percentage 20% [19]. None of the patients who died had serious ENT complications that would disrupt the vital functions of people with COVID-19 [19]. Comorbidities such as coronary artery disease, hypertension, diabetes, severe kidney disease, cirrhosis were monitored in these cases with ENT manifestations. The mortality rate in this case was 11% [20]. Patients infected with the SARS-CoV-2 virus reported through a questionnaire that ENT conditions persisted up to one month after healing [20]. Anosmia, hyposmia and dysgeusia have been reported in more than 30% of cases as post-COVID symptoms and one month after healing [20]. ENT treatment in patients infected with the SARS-CoV-2 virus: Most of the patients required symptomatic, antibiotic and immune boosting treatment [20]. They were given antibiotic, doses of antiviral, steroids and low molecular weight heparin. Patients received paracetamol and algocalmin for fever and headache, gargle and analgesics for sore throat [20]. Patients who experienced changes in smell and nasal congestion, with muco-purulent secretions, were treated with nasal sprays to decongest, clean and reduce inflammation [20]. Patients also underwent supportive treatment with vitamin C, Vitamin D, magnesium and vitamin complex [20].

DISCUSSION

ENT manifestations of COVID patients

The first incubation site for viral replication of COVID-19 is in the nasal cavity; 12% of patients infected with the SARS-CoV-2 virus are urgently present with nasal diseases such as rhinorrhea, nasal congestion, nasal obstruction, anosmia or hyposmia [21]. COVID-19 is characterized by a variety of specific and non-specific symptoms such as fever, cough, shortness of breath, fatigue, and other symptoms. myalgia, rhinorrhea and impairment of the sense of smell and taste [27].

In the advanced stages of the disease, there were also symptoms of pneumonia, acute respiratory distress syndrome (ARDS), respiratory failure [22-24]

In recent research studies it has been shown that the most common presentation in emergency rooms was sore throat, cough and nasal congestion. Patients also experienced shortness of breath, strong and heavy headache, fatigue, muscle pain, rhinorrhea and hyposmia or anosmia. The number of patients who had changes in taste and smell was small [27]. Most patients have experienced marked fatigue, generalized body pain, anxiety, anorexia and headache [27]. In Dagur et al.'s report [25] the common symptoms of COVID-19 are intense fever, fatigue, and dry cough. The symptoms have been investigated by meta-analyses conducted by Krajewska and colab. [26] who have observed that in Chinese studies, fever and dry cough symptoms have been common, while in Australian studies, rhinorrhea and dyspnea were frequently observed [27]. Research studies in South Korea, Italy, China and Germany have shown that hyposmia and anosmia are common symptoms [27].

RHINOLOGICAL MANIFESTATIONS OF COVID-19

During this period in several countries it was discovered that patients with SARS-CoV-2 virus infection have long-lasting olfactory and gustatory dysfunctions. The world medical organizations to combat infectious diseases have introduced these symptoms as characteristic of the disease in the COVID-positive patient guide [28]. Olfactory dysfunctions act through obstruction of the olfactory mucosa, infection of the supporting sustentacular cells, in which ACE-2 receptors are found, and through damage produced at the level of olfactory sensory cells with the help of a neuropilin-1 receptor or at the level of the olfactory bulb [29,30]. Studies by authors such as Xu et al [31] reported that ACE-2 receptors are detached in the epithelial cells of the tongue, thus the virus can penetrate through the oral mucosa [46]. Other authors demonstrated through experimental studies on a group of mice that there can be no such expression of ACE-2 in the taste buds, but that a significant distribution is found in the basal part of the filiform papillae [31]. There is a possibility that the mechanism of taste dysfunction caused by SARS-CoV-2 virus infection occurs through the direct eradication of taste receptors where the pathogen enters the epithelial cells and associated inflammation occurs [46]. Olfactory and gustatory dysfunctions appear early during the evolution of the COVID-19 disease and can appear as single symptoms or symptoms associated with other manifestations of the SARS-CoV-2 virus infection [46]. These dysfunctions appear more frequently in

COVID-19 than in other viral diseases of upper respiratory tract infections. Olfactory and gustatory dysfunctions are classified as quantitative such as hyposmia, hypogeusia, anosmia or ageusia or qualitative as dysgeusia, parosmia or phantosmia. All these symptoms are quickly treated, but some may persist for a longer time, even after resolution of the respiratory manifestations [32]. SARS-CoV-2 virus infection most often acts in the chemosensory regions [46]. Nasal obstruction, rhinorrhea, sneezing are ENT manifestations of a rhinological nature that appear in the COVID-19 disease, but not so dominantly [46]. Patients infected with SARS-CoV-2 virus who are known to have chronic diseases such as diabetes, hypertension or heart problems are prone to the dangers of developing complications such as rhinocerebral mucormycosis [46].

OTOLOGICAL MANIFESTATIONS OF COVID-19

Otological manifestations in positive COVID-19 patients are sudden loss of sensorineural hearing, tinnitus, vertigo, dizziness, otalgia, cranial nerve paralysis. They can be classified as either single or multiple symptoms and either alone or accompanied by other disease-specific effects with SARS-CoV-2 virus infection [35,48]. Many patients from different countries have complained of dizziness during infection or after healing [46]. Previous studies in China and beyond have demonstrated that dizziness was the main neurological manifestation of the disease [36]. Dizziness is caused by neuroinvasive factors of infection with the SARS-CoV-2 virus [46]. Several mechanisms have been described by which the disease COVID-19 affects neural tissues: the virus transposes to the nervous tissues through the blood, which, in turn, binds to ACE-2 receptors that are present in the capillary endothelium and which results in hypoxia, direct invasion and through immune-mediated action [37,38]. Hearing deficit in COVID-19 disease can be both transmission and sensorineural [46]. Conductive hearing loss is largely due to dysfunction of the Eustachian tube. The virus manages to act brutally in this area, and direct invasion of the middle ear is an immediately possible condition [46]. Through this mechanism, sensorineural deafness is formed in the COVID-19 disease. Sensorineural deafness caused by COVID-19 [39,40,48] has been shown to be difficult to explain. For the first time, there were only a small number of studies that presented themselves as case reports or a small number of cases [46]. Second, there were studies that found that there was no change in the prevalence of sensorineural deafness between the pre-pandemic and pandemic periods [41]. Studies have been reported in Italy showing that there was a significantly higher mean pure and vestibular

tone involvement in these patients during the COVID-19 period compared to pre-pandemic [41]. More studies are needed to explore the role of the virus in the mechanism of producing sensorineural deafness [46]. Ear conditions during the COVID-19 infection should be much better studied in order to understand the effect that the virus produces at the ear level and to exclude or confirm the disease in order to be able to better control the otological manifestations caused by the SARS-CoV2 virus infection [46].

LARINGOLOGICAL MANIFESTATIONS OF COVID-19

COVID-19 disease acts directly on the tissues of the upper respiratory and digestive tract through ACE-2 or transmembrane protease receptors [42], which will accelerate various manifestations such as dysgeusia, sore throat, hoarseness, dysphagia and odinophagia [46]. Other conditions encountered with SARS-CoV-2 virus infection are acute laryngitis, acute epiglottitis or croup in infants [43,44]. Acute laryngitis is not so common in SARS-CoV-2 virus infection but also once the studies performed are beneficial for the early diagnosis of the disease, isolation and control of infections, prevention of unfavorable development of infection and correct treatment of airway obstruction [47].

Research studies show that neck symptoms are the most common manifestations in COVID-19 patients [46]. Dysphonia and dysphagia, which are specific symptoms of COVID-19, are considered by some authors and researchers to be symptoms induced by treatment against the SARS-CoV-2 virus after healing or during therapeutic conduct, especially in patients requiring respiratory support [47].

Studies in Italy and the Lombardy region showed that the most common symptoms were fever (56%), cough (60%) and fatigue (70%), while upper respiratory symptoms were nasal congestion (41%), sore throat (30%), odor and loss of taste sensation (65%) [48]. This study was conducted using the Sino-Nasal outcome test questionnaire test-22 (SNOT-22).

Physiopathological, for the olfactory and gustative dysfunction of SARS-CoV-2 virus infection, the following cause is criminalized: The tropism of SARS-CoV-2 virus that reaches olfactory cells by signal between spike protein and ACE 2 protein on the lining of the nasal fossa epithelium [47]. The virus can enter the olfactory neuronal receptor that affects and destroys it. And the migration of this virus to the olfactory bulb and its multiplication at this level until it penetrates the central nervous system through the channels in the cells that cover the olfactory bulb. At this level the virus produces major imbalances, thus destroying the physiological process of smell and taste and the appearance of hyposmia, anosmia or dysgeusia [50].

Patients with SARS-CoV-2 virus infection did not experience eye problems such as blurred vision, subconjunctival hemorrhage, eyelid bruising, conjunctival scars, keratitis [48-51]. COVID-19 disease could be diagnosed by the existence of RT-PCR test taken from the fornix of the lower eyelid, which helps to tighten tears and conjunctival secretions in the eye [50-52].

SARS-CoV-2 virus has also been detected in saliva at the onset of the disease through saliva collected from the opening of the salivary gland duct for this reason, the virus can be transmitted to a person who has close physical contact with the infected patient, or also the virus can be transmitted through surfaces contaminated by saliva particles infected with SARS-CoV-2 virus. The epithelial cells of ACE-2 positive salivary glands have been found to be the entry gate for SARS-CoV-2 virus [53].

CASE REPORT

A 48-year-old male patient known to have high blood pressure was presented to the emergency room for symptoms specific to SARS-CoV-2 virus infection, with respiratory distress, cough, sore throat, fever, anosmia, ageusia, expectoration, nasal obstruction and rhinorrhea.

The patient is hospitalized at the Constanta Infectious Diseases Hospital, where he receives specialized treatment in the ATI department. The patient is intubated for severe respiratory failure, he is being treated according to the guidelines for SARS-CoV-2 virus infection.

After healing, the patient remains with otorhinolaryngological symptoms such as anosmia, ageusia, xerostomia, severe dysphagia, nasal obstruction, cough, cacosmia, rhinorrhea. The patient cannot eat meat, dairy, feels tired, lethargic and depressed. He loses weight and has olfactory hallucinations. His mental condition is critical, with a severe depression DASS-21 score.

When conducting a computer Tomograph examination, chronic sinusitis is observed at the level of the maxillary, ethmoidal and frontal sinuses with bone lysis.

The patient is thoroughly examined with the carrying out of additional investigations for the diagnosis of osteomyelitis. It is decided multidisciplinary therapeutic conduct for the treatment of osteomyelitis. After carrying out a drug treatment with antibiotics, exploratory and drainage surgery is decided.

Intraoperatively, massive bone destruction is observed at the ethmoidal level. Surgical drainage of abscesses was performed, constituted by curettage and lavage, resection of devitalized bone tissue and its plasty.

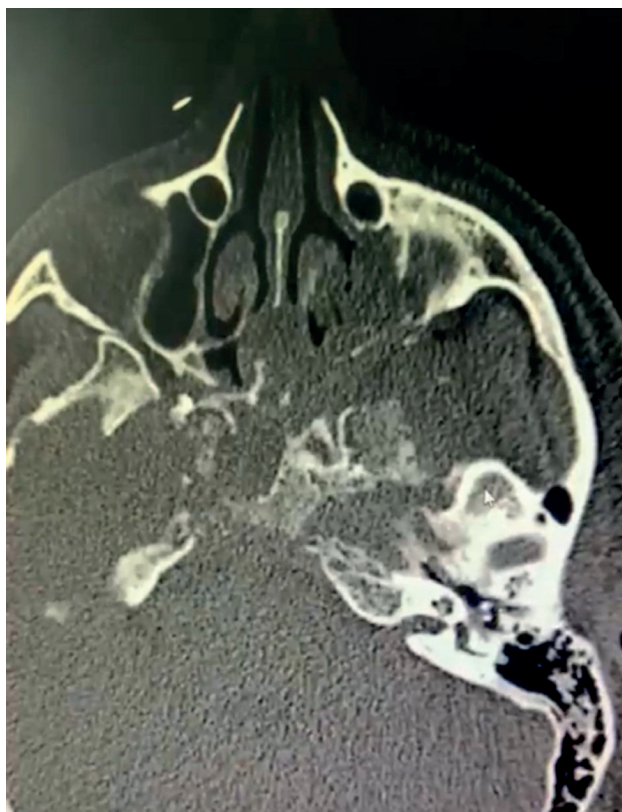


FIGURE 1. Chronic sinusitis and osteolysis at the ethmoid level, skull base, a Post-Covid patient, see native skull CT examination, “Alexandru Gafencu” Military Emergency Hospital Constanta, 2021, own source

Two weeks after surgery, the patient remains with anosmia, ageusia, cacosmia, xerostomia, severe dysphagia and some induced symptoms.

SARS-CoV-2 virus infection was found to cause a compromised immune system. People with a weak-ened immune system are at a higher risk of develop-ing osteomyelitis.

CONCLUSION

This study is presented through the collection of clinical, observational data, Investigations and treatment have led to the conclusion that a multi-disciplinary study is needed to analyze the mechanisms of the effects of the SARS-CoV-2 virus on the anatomical and histological structures at the upper

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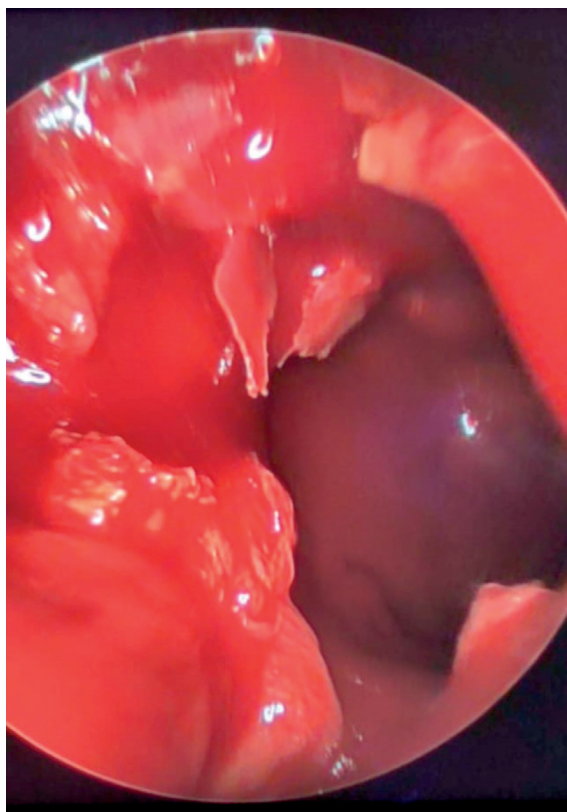


FIGURE 2. Chronic sinusitis, in a Post-Covid patient, intraoperative view, ethmoidectomy with view of skull base osteolysis, “Alexandru Gafencu” Military Emergency Hospital Constanta, 2021 own source

airway level leading to the establishment of these ENT manifestations in COVID-19 disease. It must be analyzed which are the most persistent ENT manifestations and how seriously it affects the patient in this area of the nose, ear and throat.

Further investigation of these complications will increase the context in which SARS-CoV-2 disrupts upper airway defense mechanisms.

It turns out that the SARS-CoV-2 virus infection leaves not only neurological and cardiovascular consequences, but also consequences in the ENT sphere.

In conclusion, the most common ENT manifestations of SARS-CoV-2 virus infection are sore throat, nasal congestion, nasal obstruction, olfactory and gustatory dysfunction, and headache.

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