



Full Length Article

Sudden and persistent dysphonia within the framework of COVID-19: The case report of a nurse



Rodolfo Buselli^{a,1}, Martina Corsi^{a,*}, Gabriele Necciari^a, Piero Pistolesi^b, Sigrid Baldanzi^a,
Martina Chiumiento^a, Elena Del Lupo^a, Paolo Del Guerra^b, Alfonso Cristaudo^a

^a Occupational Health Department, Azienda Ospedaliero-Universitaria Pisana, 56124, Pisa, PI, Italy

^b Department of Public Health, Azienda USL Toscana Centro, 50053, Empol, FI, Italy

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ABSTRACT

In December 2019, clusters of atypical pneumonia with unknown etiology emerged in the city of Wuhan in China. In early January 2020, the Center for Disease Control in China announced that it was identified a new coronavirus, first tentatively named 2019-nCoV and officially named SARS-CoV-2 by the International Committee on Taxonomy of Viruses. On February 11, 2020 the WHO identified the disease caused by SARS-CoV-2 as COVID-19 (CORonaVirus Disease-19 based on the year of appearance). Although only a few months have passed since the beginning of this pandemic, numerous studies, case reports, reviews by leading international scientific and medical journals have been published. However, given the unpredictability of virus behaviour and the still limited knowledge about it, many aspects of the infection are still little known. A recent epidemiological study has shown the presence of dysphonia in some patients with COVID-19, with a minority reporting aphonia during the clinical course of the disease. This case study draws attention on a 50-year-old female nurse presented with a history of fatigue resulting from minor exertion and persistent dysphonia at the Occupational Health Department of a major University Hospital in central Italy. The patient had a history of COVID-19 infection, which lasted about two months with pulmonary and extrapulmonary symptoms. After two RT-PCR negativities for SARS-CoV-2, dysphonia and fatigue due to minor exertion persisted. The patient, following the persistence of the symptomatology, was subject to numerous specialist examinations, which showed no organic alterations. Based on her clinical and instrumental history, we hypothesized a psychogenetic dysphonia related to COVID-19. This case report highlights the importance of personalized medicine with long-term follow-up and robust psychological support in patients who tested positive for COVID-19 and in particular in the categories at greatest risk of both contagion and adverse physical and mental outcomes like health care workers.

1. Introduction

Healthcare systems worldwide are facing the pandemic of the severe acute respiratory coronavirus 2 (SARS-COV-2) and its associated disease, named coronavirus disease 19 (COVID-19). This virus is a new human pathogen, and currently, there are no specific treatment options. COVID-19 mostly affects the respiratory system, ranging from mild flu-like symptoms to severe pneumonia, but extrarespiratory multisystemic involvement has also been reported (Zhu et al., 2020).

Human Coronaviruses (HCoVs) commonly share viral structures and infection mechanisms, together with the potential for host Central Nervous System (CNS) invasion (Wu et al., 2020). The exact route by which

HCoVs enter the CNS remains a topic of active investigation. Tissue distribution of host receptor angiotensin-converting enzyme 2 (ACE2) may not be solely sufficient to fully describe viral tropism and other mechanisms (such as axonal transport) are likely to be involved (Baig et al., 2020). The intranasal administration of HCoVs resulted in the rapid invasion of viral particles into the brain, possibly through the olfactory bulb via the trans-synaptic route bringing to anosmia or hyposmia and ageusia or dysgeusia as concomitant symptoms of COVID-19 infection (Freni et al., 2020).

In a recent epidemiological study the occurrence of dysphonia in some COVID-19 patients was observed, with a minority reporting aphonia over the clinical course of the disease. In particular more than 20

* Corresponding author.

E-mail address: dott.martinacorsi@gmail.com (M. Corsi).

¹ These authors contributed equally to the Paper.

percent of dysphonic symptoms were observed, particularly in female patients, among a total study comprising 700 patients. The severity of dysphonia was significantly associated with the severity of dysphagia. A significant positive association was found also between dysphonia and cough (Lechien et al., 2020).

Dysphonia may be related to laryngeal involvement by the airway inflammatory process and may be caused by vocal fold edema or inflammation. However, the etiology of dysphonia in COVID-19 patients needs to be investigated. An ongoing study conducted at the Anatomy Department of University of Mons observed that vocal folds were associated with a high expression of angiotensin-converting enzyme 2 (ACE2), which is the COVID-19 receptor (Lechien et al., 2020). Studies about the expression of ACE2 receptor by laryngeal cells would provide interesting findings to clarify the pathogenesis of dysphonia in patients affected by COVID-19 (Li et al., 2020).

Nevertheless, sudden dysphonia could also be linked to the psychopathological strain generated by COVID-19, especially in vulnerable subjects (Colizzi et al., 2020). Psychogenic dysphonia is, in fact, defined as psychogenic disturbances of voice and speech quality without the existence of primary organic changes in the larynx (Kraszewska et al., 2019). Human psyche has a significant impact on the course of verbal communication, affecting the quality of voice and speech. Emotional condition significantly influences the process of voice production, the functioning of respiratory-phonatory-articulation mechanism and suprasegmental elements of speech.

Psychogenic dysphonia most often occurs between 30 and 50 years of age in subjects with a dysregulated emotional system, mainly in women (Baker, 2003). Due to the influence of various emotions, negative and positive, the process of producing voice and the functioning of the respiratory-phonatory-articulatory mechanism are subject to change. Long-term disturbances of mental emotional and psychosocial balance, caused by anxiety, stress, depression, traumatic experiences, personality conflict or disturbances in social contacts are an important risk factor for the occurrence of voice quality disorders with psychogenic background (Helena et al., 2014).

In this regard, adverse mental health impact has been reported in patients affected by COVID-19, which could either be related to the social strain or to the eventual direct effect of the virus, which in other HCoV infections have been proven to promote the onset of psychiatric symptoms. In addition to the social strain, it is well known, in fact, that viral infections may be associated with psychiatric symptoms due to activation of a powerful immune-inflammatory response (Orsini et al., 2020). There is a link between mood disorders and inflammatory cytokines levels, including tumour necrosis factor- α (TNF α), interleukins (IL-1, IL-6) and others. According to this theory, the proinflammatory cytokines responsible for the acute phase response act on the brain to induce psychiatric symptoms. One key player in this action of cytokines in the brain is an enzyme known as indoleamine 2,3 dioxigenase (IDO) that degrades tryptophan, an essential amino acid that is the limiting factor for the synthesis of serotonin. An elevation in IDO activity is associated with alterations in brain serotonin neurotransmission and with the development of depressive-like behaviours (Henry et al., 2020).

In a more holistic approach to the phenomena, SARS-CoV-2 has recently been implicated in the onset of psychosis, mood disorders, post-traumatic stress disorders and suicide (Gunnell et al., 2020). Outbreaks of COVID-19 can elicit peculiar psychogenic reactions in the general population and particularly in specific vulnerable populations like health care workers (Buselli et al., 2020a). Increased workload, physical exhaustion, inadequate personal equipment, nosocomial transmission, and the need to make ethically difficult decisions on the rationing of care may have dramatic effects on the physical and mental well-being of health care professionals. Their resilience can be further compromised by isolation and loss of social support, risk or infections of friends and relatives as well as drastic, often unsettling changes in the ways of working (Pappa et al., 2020).

Despite daily global updates, general knowledge of COVID-19

remains unclear. In the broad sweep of available data, evidence on SARS-CoV-2 are limited. Reliable and up-to-date answers to immediate clinical questions can be difficult and time-consuming particularly regarding clinical presentations and treatment strategies. (Holmes et al., 2020; Smith et al., 2020).

Consistently with these observations, the aim of this article is to analyze a case of sudden and prolonged dysphonia in a female nurse affected by COVID-19 in both a physical and psychiatric perspective.

2. Case report

2.1. Socio-demographic and clinical details

The patient is a married 50-year-old female who works as a nurse at ASL (Azienda Sanitaria Locale) in Central Italy. She lives with her husband and two children. She referred to our outpatient clinic in July 2020 reporting fatigue resulting from minor exertion efforts and persistent dysphonia. She started with dry cough, asthenia, myalgia and diarrhoea on March 19, 2020. The following day, the patient developed fever (axillary temperature of 38°), dyspnea and headache. As a suspected case of Covid-19, she was tested for SARS-CoV-2. After a reverse transcriptase polymerase chain reaction (RT-PCR) assay was performed, she tested positive for SARS-CoV-2. On day 3, the fever disappeared, while the other symptoms reoccurred cyclically for about 48 days, coughing remaining the most common symptom. As she was undergoing home quarantine, she began taking hydroxychloroquine and azithromycin. After two negative RT-PCR, on May 7 and 9, she was declared clinically cured. After the apparent resolution of the symptoms, fatigue began to appear as a result of minor exertion and especially dysphonia, with considerable breathlessness just a few seconds after the beginning of speech. This symptomatology forced the patient to undertake a complex diagnostic procedure. The patient underwent the following specialist examinations: pneumology examination, chest CT scan, neurological specialist examination with brain scan, cardiology specialist examination with echocardiography and pulmonary ultrasound and ENT specialist examination. All the specialist exams showed no alterations, as a result of which a psychogenic background began to be hypothesized. See figure.

2.2. Psychiatric evaluation

The psychiatrist who performed the clinical evaluation belongs to a multidisciplinary group of an Occupational Medicine Unit which is directed by an occupational physician. The whole team has specific experience in work-related stress and emergency management.

The psychopathological presentation revealed a personological profile characterized by a cyclothymic-anxious temperament with hypersensitivity to stressful life events, interpersonal sensitivity and elements of both panic-agoraphobic and obsessive-compulsive spectrum. She reported negative family history for psychiatric disorders.

At the age of 30, the patient developed important anxiety symptoms characterized mainly by general tension and gastro-enteric somatizations highly participated on the emotional level. As a result, the patient turned to a psychiatrist and began a psychopharmacological therapy with Selective serotonin reuptake inhibitors (SSRIs) antidepressants (sertraline) for a short period (few months) with little clinical benefit and consequent spontaneous resolution of the clinical picture. Subsequently, the patient presented a sufficient psycho-affective balance and discrete general personal functioning although there remained a somatic-neurological symptomatology characterized by vertigo and nausea, recently classified in the context of a migraine disorder with aura, and treated for about two years with anticonvulsant therapy (topiramate) with consequent improvement of the symptomatology. In recent months, following a period of positivity for SARS-CoV-2 (COVID-19) characterized by asthenia and cough, the patient had a recurrence of a reactive anxious symptomatology developed a persistent dysphonic picture for which she carried out specialistic examinations and instrumental checks both with

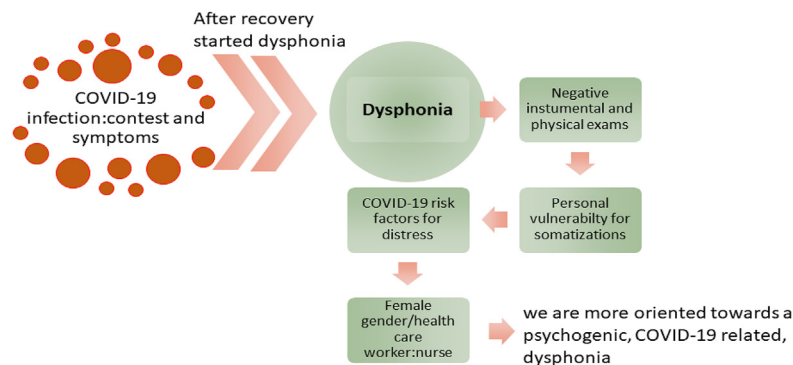
negative results, or in any case not proportional to the clinical symptoms reported.

At current clinical observation, the patient is accessible to intrapsychic experiences. She appears lucid, alert, mnesic and normal-oriented in the classic parameters. Mimicry and gestures appear slightly coerced and suffering. Speech is compromised by the dysphonic picture with evident phonatory fatigue and reported wheezing. The affective dimension is marked by a certain degree of demoralization in association with a marked state of internal tension with the expression of experiences of frustration in relation to the gradual loss of autonomy and the impotence of the current situation. Pervasive thoughts regarding the patient's own health problems persist. Pervasive thoughts

et al., 2020).

From a social perspective, there are other problems that can contribute to poor psychological outcomes. Children are at home relatives might become ill which puts on further stress and sense of guilt on health care personnel. In addition, there might be economic and work-related worries. All these factors may contribute to psychic disorders (Joos, 2020).

It is also noteworthy that the patient tested positive for COVID-19 and this may have further contributed to a vicious circle of stress. In this regard, the evidence regarding serious clinical and sometimes fatal outcome as well as the repeated exposure to media reports of unprecedented circumstances requiring new medical strategies may lead to un-



3. Discussion

At the current moment, too little is known about SARS-COV-2 and its related disease, COVID-19, to be able to make an adequate differential diagnosis between a physical or psychogenic dysphonia.

Nevertheless, all instrumental exams performed by the patient were negative for a real physical dysfunction, on the contrary she certainly presents some risk factors for psychological distress which could direct clinical diagnosis more towards the psychiatric side. See figure of clinical case presentation set out above.

The patient is a female nurse who tested positive for SARS-COV-2 and suffered from common symptoms of COVID-19. A recent meta-analysis of 13 cross-sectional studies evidenced how health care workers and in particular female nurses presented high levels of distress during the pandemic (Pappa et al., 2020). This is probably due to the fact that due to their closer contact with patients they may be more exposed to moral injury pertaining to suffering, death and ethical dilemmas. Furthermore, there is literature agreement that women with trauma exposure exhibit greater sensitivity and lower tolerance to negative emotions than men. (Liu et al., 2020; Carmassi et al., 2020).

In this regard there are many facets of distress during a pandemic. According to literature from SARS or Ebola epidemics, the onset of a sudden and immediately life-threatening illness could lead to exceptional levels of pressure on healthcare workers: increased workload, physical pressure, isolation and loss of social support, inadequate protective measures, professional viral transmission, and unprecedented ethical concerns on the rationing of care may have important consequences on their personal physical and mental well-being (Wu et al., 2009). All these factors may lead to secondary traumatization (ST). ST is, in fact, similar to post-traumatic stress symptoms but results from knowledge of traumatic events suffered by others and the consequent stress. It is the emotional residue or strain of exposure to working with those suffering from the consequences of traumatic events. In contrast to burnout which generally emerges over time, it has a more rapid onset (Ruiz-Fernández

intended overconcerns. Evidence suggests that such preoccupations may degenerate in heightened anxiety and stress responses with downstream effects on health, on turn resulting in misplaced health-protective and help-seeking behaviours (Garfin et al., 2020).

These observations are corroborated by the fact that the patient also presented a history of psychiatric vulnerability for somatic symptoms closely related to work distress and with the need of a psychopharmacological therapy.

In literature, somatization is, in fact, considered closely linked with post-traumatic symptomatology in relation to complex trauma (Aragona et al., 2010). While there is solid evidence with regard to the frequent co-occurrence of trauma-related mental and somatic health problems, the nature of this relationship is still poorly understood. Psychological, behavioural, and biological factors, as well as the complex interactions between these factors, serve as possible mechanisms through which traumas may be associated with physical health (Carmassi et al., 2020; Buselli et al., 2020b). Somatic presentations may occur as a result of a number of mechanisms, including 1) trauma-independent somatic disorders; 2) traumatic injuries and tissue damage sustained in the course of the initial traumatic event; 4) autonomic, neuroendocrine, and immunologic dysregulation resulting from exposure to stress; 5) genetic and epigenetic predispositions; 6) somatoform disorders, particularly dissociative or conversion disorders associated with elevated stress levels (Morina et al., 2017).

In this regard, we argue that the patient may suffer from dysphonia mainly of a psychosomatic origin that could benefit from antidepressants with anxiolytic power. Psychopharmacological therapy could also have the purpose of further helping the differential diagnosis through the observation of the therapeutic response. Obviously, a careful longitudinal analysis is necessary for a real understanding of the phenomena without underestimating the possibility of a possible laryngotracheal or systemic muscle impairment.

This case report highlights the importance of personalized medicine with long-term follow-up and good psychological support in patients who tested positive for COVID-19 and in particular in the categories at greatest risk of both contagion and adverse physical and mental outcomes like health care workers.

Declaration of competing interest

Authors declare no conflict of interest.

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