

Anosmia and COVID-19 in south Lombardy: description of the first cases series in Europe

Marco Capelli , Patrizia Gatti 

ENT Columbus Clinic Center, Milano, Italy

Cite this article as: Capelli M, Gatti P. Anosmia and COVID-19 in south Lombardy: description of the first cases series in Europe. B-ENT 2020; 16(1): 86-90.

ABSTRACT

Objective: The Basso Lodigiano is located in southern Lombardy. The capital of this district is the city of Codogno where on February 21, 2020, the first case of COVID-19 (Corona Virus Disease 2019) was diagnosed in Italy. The etiological agent is known to be a new coronavirus called SARS-Cov-2 (Severe Acute Respiratory Syndrome – Coronavirus – 2). Even asymptomatic or paucisymptomatic patients can transmit the virus and contribute to the expansion of the infection. From 21 February 2020, we have noticed a significant increase of anosmia cases in the population of Codogno and we believe there may be a relationship with the SARS-Cov 2 infection.

Methods: In the period between 21 February and 15 March 2020, we described 27 patients, living in Codogno, with anosmia. We calculated the incidence of the anosmia symptom in our patients in the period following the first diagnosis of COVID-19 in Italy (February 21, 2020/ March 15, 2020) and then compared it to the incidences relating to the same period of the years 2019 and 2018 and to the incidences in other periods from 1 January 2018. We then analysed the results through test χ^2 in order to verify a statistical significance in the results.

Results: We observed a statistically significant increase in the incidence of the anosmia symptom in the period between 21 February and 15 March of 2020 compared to the incidence of the same symptom in other periods

Conclusion: The interpretation of the results leads us to argue that anosmia may be a symptom related to SARS-Cov2 infection. This symptom could be significant in paucisymptomatic patients who represent a potential viral transmission reservoir. In this regard, in this age of pandemic, when doctors observe patients with anosmia, they should consider SARS-Cov 2 infection in the differential diagnosis.

Keywords: Anosmia, coronavirus epidemic, neurotropism, SARS-Cov 2, world pandemic.

Introduction

On February 21, 2020, the first case of COVID-19 (CO-Corona VI-virus D-disease 2019, the name that WHO has attributed to the new coronavirus disease) in Italy was diagnosed at the Codogno Hospital. The causative agent is a new Coronavirus defined by the International Committee on Taxonomy of Viruses SARS-Cov 2 (Severe Acute Respiratory Syndrome – Coronavirus – 2) (1). It is the third large-scale epidemic of the 21st century related to Coronavirus infection after SARS-Cov (Severe Acute Respiratory Syndrome – Coronavirus) in 2002 and MERS-Cov (Middle East Respiratory Syndrome – Coronavirus) in 2012 (2).

Chan JF et al. (3) confirmed human to human transmission of the virus through respiratory droplets, and the transmissibility by fecal-oral route has been hypothesized (4). These modes of transmission make the expansion of the disease very rapid (5, 6). Compared to previous Coronavirus epidemics, COVID-19

is more easily transmitted. In fact, from November 2019 to February 2020 there were 75199 cases recorded. SARS had affected 8098 patients from November 2002 to July 2003, MERS had affected 2496 people from April to November 2012. The mortality rate of COVID-19 seems to be currently lower (2.67%) than the other 2 epidemics (9.60% and 34.40% respectively) (5).

Compared to the known coronaviruses which generally involved an incubation of 2-4 days, SARS-Cov 2 has a longer incubation time (1-14 days) (5, 6). COVID-19 has several clinical manifestations. More often it appears with an aspecific picture characterized by fever, asthenia, malaise and cough. Compared to other Coronaviruses, SARS-Cov2 would appear to affect the upper respiratory tract less. In some cases, gastrointestinal disorders are reported. Older and debilitated people are more exposed to the infection and its complications and can develop ARDS (Acute Respiratory Distress Syndrome) and multiple-organ failure (7).

Corresponding Author: Marco Capelli; info@otorinocremona.it

Received: March 19, 2020 **Accepted:** April 24, 2020

Available online at www.b-ent.be



CC BY 4.0: Copyright@Author(s), "Content of this journal is licensed under a Creative Commons Attribution 4.0 International License."

In our opinion the disease that we are therefore going to face presents some critical points. The first is represented by the danger of the disease, the second is linked to its extreme diffusion favoured by the numerous interpersonal and globalized contacts that modern society imposes. The third critical point, according to the "Diagnosis and treatment scheme for novel coronavirus pneumonia trial 6th edition" is given by the potential contagiousness of asymptomatic and paucisymptomatic subjects, which in our opinion could represent the portion of the population least sensitive to the problem of viral spread and the consequent containment of the infection (5).

In this study, we propose Anosmia as a frequent, but little considered symptom in SARS-Cov 2 infections, in order to hope for a scrupulous observation of the rules of contagion containment even in subjects only affected by this disorder.

Methods

We conducted a retrospective study analyzing data expressed by patients in the anamnestic report. We have obtained informed consent from all patients for the use of these data and all data have been used completely anonymously in accordance with current legislation on privacy. Our study respects the principles of the Helsinki Declaration. The study focusing attention on patients with anosmia in the south of Lombardy in the 3 weeks following the detection of the first case of COVID-19 in Italy. We chose a retrospective study because it has the advantage of providing a relatively rapid result since at the beginning of the study the time required for the events to happen had already elapsed.

Codogno (home of the first Italian diagnosis COVID-19) and other 11 municipalities are considered an epidemic outbreak. These municipalities after February 21 were literally isolated by government authorities in order to contain the infection and for this reason some drastic measures were taken including prohibiting entry and transit and any professional activity deemed non-essential, including that of Medical Centers.

Between 21 February and 15 March 2020, we provided telephone consultations to 40 patients who asked for advice on ENT problems. We observed an increase in requests for ENT opinion for the onset of hypo-anosmia (27 patients). We then calculated the incidence of the symptom in the 3 weeks following the first case of COVID-19 and compared it with the incidence of the anosmia symptom in the first weeks of the

year (from January 1 to February 20, 2020). We then compared these 2 incidences with those of similar periods for 2019 and 2018 using our database.

We used the Chi-square test to compare the incidences observed in the different periods studied from January 01, 2018 to March 15, 2020 and demonstrate with statistical significance an increase in cases of Anosmia in COVID-19 periods.

Results

We observed a sample of 27 patients suffering from anosmia in the period between February 21, 2020 and March 15, 2020 (Table 1). The observed people are made up of 17 females and 10 males with an average age of 44 years. The average female age observed is of 41 years, the male age of 49. All patients reported total loss of olfactory function. 10 cases have presented fever along with anosmia.

Table 1. Clinical characteristics of the 27 patients observed affected by anosmia. Anosmia and COVID-19: description of a cases series that occurred in Codogno area

Patient	Age	Gender	Anosmia	Fever	Comorbidity
1	53	F	Yes	No	No
2	27	F	Yes	No	Diabetes
3	68	M	Yes	No	No
4	30	M	Yes	Yes	No
5	45	F	Yes	No	No
6	20	M	Yes	No	Allergy
7	74	M	Yes	Yes	No
8	30	F	Yes	No	No
9	71	M	Yes	Yes	No
10	30	F	Yes	Yes	No
11	39	F	Yes	No	No
12	40	M	Yes	No	No
13	48	F	Yes	Yes	No
14	30	F	Yes	No	No
15	43	F	Yes	No	No
16	53	F	Yes	No	LES
17	36	F	Yes	Yes	No
18	35	F	Yes	Yes	No
19	59	F	Yes	Yes	No
20	48	F	Yes	No	No
21	46	M	Yes	No	No
22	42	F	Yes	No	No
23	57	M	Yes	No	No
24	51	F	Yes	Yes	No
25	18	M	Yes	No	No
26	67	M	Yes	No	Allergy
27	29	F	Yes	Yes	No

Main Points:

- The COVID-19 pandemic represents a global health problem with very important health and economic implications with easy transmissibility that would be possible also by paucisymptomatic subjects
- The need to contain the spread of the epidemic leads us to know the various symptomatic forms of the disease
- In our opinion, anosmia represents a possible symptom of COVID-19 to be taken into consideration when patients affected by respiratory infections face these months
- We describe the first cases series of anosmia in Europe that occurred in the area of the first European epidemic outbreak

Table 2. Incidence of anosmia calculated in different periods from January 1, 2018 to March 15, 20. Anosmia and COVID-19: description of a cases series that occurred in the Codogno area

Year	Time lapse	Patients visited	Anosmia cases	Incidence
2018	1-1/31-12	1221	25	2%
	1-1/20-2	213	6	2,80%
	21-2/15-3	115	4	3,50%
2019	1-1/31-12	1198	30	2,50%
	1-1/20-2	210	7	3,30%
	21-2/15-3	107	3	2,80%
2020	1-1/15-3	227	33	14,50%
	1-1/20-2	187	6	3,20%
	21-2/15-3	40	27	67,50%

Table 3. Observed frequency of cases of anosmia in different time intervals. Anosmia and COVID-19: description of a cases series that occurred in the Codogno area

Year	Time lapse	Without anosmia cases	Anosmia cases	Total Patients
2018	1-1/20-2	207	6	213
	21-2/15-3	111	4	115
2019	1-1/20-2	203	7	210
	21-2/15-3	104	3	107
2020	1-1/20-2	181	6	187
	21-2/15-3	13	27	40

Table 4. Theoretical frequency of anosmia cases that we would expect in the various periods observed (it is observed that the number of cases expected in the period February 21/March 15, 2020 is much lower than that occurred). Anosmia and COVID-19: description of a cases series that occurred in the Codogno area

Years	Time lapse	Without anosmia cases	Anosmia Cases	Total pazients
2018	1-1/20-2	206	7	213
	21-2/15-3	100	15	115
2019	1-1/20-2	203	7	210
	21-2/15-3	93	14	107
2020	1-1/20-2	181	6	187
	21-2/15-3	35	5	40

As shown in Table 2 we calculated the incidences of the anosmia symptom for the whole of 2018 (2%), 2019 (2.5%) and in the first months of 2020. We noticed a significant increase in the incidence in 2020 (14.5%). We then analyzed shorter periods of time and compared them. We observed that from 01-1 to 20-2 of 2018 (2.8%), 2019 (3.3) and 2020 (3.2%) the incidences are similar when compared with those relating to the whole of 2018 and 2019 as well as those of the period 20-2 / 15-3 of 2018 (3.5%) and of 2019 (2.8%). The incidence of Anosmia in the 3 weeks from 21-02 to 15-3, 2020 increases dramatically (67.5%).

We calculated the observed frequencies (Table 3) and the theoretical frequencies (Table 4) and we noticed a net increase in the observed cases [27] in the period 21-2 / 15-3, 2020 compared to those expected [5] in the same period.

We performed χ^2 tests to demonstrate the statistical significance of the increase in cases of anosmia compared to healthy people in the period of the COVID-19 epidemic. We set a significance level of 0.05. Comparing the theoretical χ^2 test (0.103) with the χ^2 tests calculated for the periods 01-1 / 20-2 and 21-2 / 15-3 we observe a significant difference over the years in the incidence of anosmia in the period 21-2 / 15-3 while we observe no significant difference in the periods 01-01 / 20-2 in the incidence of anosmia.

Discussion

On February 21 in the town of Codogno the first case of COVID-19 was found in Italy. The patient is a 38-year-old young man with bilateral interstitial pneumonia and ARDS. Since that day, the cases in Codogno area have multiplied exponentially. Swabs were initially available for diagnostics but af-

ter a few days only patients with severe respiratory syndromes could undergo this test to detect positivity for SARS-Cov 2. We therefore have a large slice of the population potentially affected by COVID-19 in asymptomatic or paucisintomatic form remained unknown but able to transmit the virus (5).

Casella et al. (7) distinguish several clinical manifestations from COVID-19. They identify a mild form (which occurs in about 80% of cases and is not associated with pneumonia), a severe form (characterized by dyspnea, tachypnea and saturation in $O_2 \leq 93\%$), and a critical phase characterized by respiratory failure and septic shock with dysfunction or organ failure (which occurs in about 5% of cases).

We have observed during the consultancy activity provided in these weeks an important increase in cases of anosmia in Codogno area. In particular, out of 40 patients evaluated 27 had this symptom. Patients reported loss of olfactory function for some hours or days not associated with obstructive symptoms such as nasal congestion or muco-purulent rhinorrhea. In some cases, there was a slight rise in temperature. We collected the clinical data in Table 1.

From a clinical point of view, they all seemed to be types of anosmia associated with sudden sensorineural deficit of I cranial nerve and in presence of an ongoing viral epidemic we suspected a possible association with SARS-Cov2. This hypothesis is in agreement with the results of Ling Mao et al. (8) which describes various neurological manifestations from COVID-19; he distinguishes them into 3 categories. Those with central involvement are dizziness, ataxia, headache, and convulsions, those with peripheral involvement such as Anosmia and those with neuromuscular interest.

The virus would reach the structures of the peripheral nervous system by hematogenous and retrograde sensorineural pathway and when it arrived it would recognize the ACE2 (Angiotensin-Converting Enzyme 2) receptor, also present in numerous organs in addition to the central nervous system. This receptor would also be recognized by SARS-Cov and MERS-Cov (9). Also, Yan-Choo et al. (10) underlines the neuroinvasive potential of SARS-Cov 2. The etiopathogenetic role of ACE2 receptors would also be described in myocardial complications according to reports from Ying Ying Zheng et al. (11)

With this work we do not only want to show the observational results relating to the increase in cases of anosmia in the 3 weeks following the detection of the first case of COVID-19 in the population of the Codogno area (from February 21, 2020 to March 15, 2020), but also lay the foundations for further studies aimed at demonstrating the hypothesis of an association between Anosmia and SARS-Cov2 infection (12, 13).

In our experience, anosmia represents a rare reason for requesting an ENT visit. In the last year (2019), anosmia cases have been 30 out of a total of 1198 patients visited. In 2018, out of a total of 1221 patients, only 25 had complained of anosmia. The incidence in both cases stands at a value of 2%. A similar incidence was recorded in the first weeks of the year (from 1 January to 20 February 2020).

Starting from 21 February and therefore in the midst of the COVID-19 crisis, we found 27 out of a total of 40 patients undergoing ENT counseling, suffering from anosmia with an incidence of 67,5%. We also calculated the incidence of anosmia in the periods from January 1 to February 20 of 2019 and 2018 with results of 3,3% and 2,8% respectively and the incidence of the periods from February 21 to March 15 of 2019 (2,8%) and 2018 (3,5%).

The calculations we performed showed a statistically significant difference over the years in the incidence of anosmia in the period 21-2 / 15-3 while we do not observe the significant difference in the periods 01-01 / 20-02 in the incidence of anosmia. This trend also seems confirmed by the data collected by Walker et al. (14)

Interpretation of these results, in view of the COVID-19 epidemic, appears to indicate a strong association between anosmia and SARS-Cov2 infection.

At the moment one of the main weapons against SARS-Cov 2 would seem to be the containment of contagion through isolation. However, there is a significant criticality linked to the possibility of transmitting the virus by those asymptomatic or paucisymptomatic patients (5). For these, in fact, there is currently no diagnostic assessment using a swab. It is therefore essential for the effective containment of the infection to identify the clinical pictures associated with the infection as early as possible.

Normally the symptoms listed in the clinical picture of COVID-19 are on the one hand those of the classic upper respiratory virus (nasal congestion, sneezing, pharyngodynia, dry cough) typical of paucisymptomatic forms and on the other those related to the involvement of the lower respiratory tract such as productive cough, dyspnea up to multi-organ involvement and septic shock (5, 7).

We recall that the correlation between anosmia and SARS-Cov 2 for our patients is only hypothetical but, based on the data collected and analyzed, we consider it very plausible.

According to Gane et al. (15) we believe that in the age of COVID-19 pandemic when observing patients with anosmia doctors should consider SARS-Cov 2 infection in the differential diagnosis and if further studies prove this thesis we could reasonably resort to use of the swab also in the numerous hyposmic or anosmic subjects for early diagnosis of SARS-Cov2 infection (16).

Other studies will have to clarify our hypothesis in order to easily identify an infected and contagious subpopulation and consequently contain the expansion of the virus more effectively.

Conclusion

The SARS-Cov 2 infection represents a worldwide emergency due to an exponential spread and a sometimes very severe associated clinical picture that can lead to respiratory failure and death. Patients with fever and cough can be recognized as infected by swab and placed in isolation in case of positivity. However, there is a slice of asymptomatic or paucisymptomatic population affected by COVID-19 which represents a large

risk of contagion for the healthy population. In this regard, we suspect that anosmia represents an important and frequent symptom in the paucisymptomatic forms of COVID-19. In our opinion, in this age of pandemic, when we observe patients with anosmia, doctors should consider SARS-Cov 2 infection in the differential diagnosis.

Acknowledgements: The authors would like also to thank Ornella Ponzoni for her valuable support and Dr. Matilde Grecchi, for her contribution to the statistical analysis and data presentation.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.C., P.G.; Design – M.C., P.G.; Supervision – M.C.; Resources– M.C., P.G.; Materials - M.C.,P.G.; Data Collection and/or Processing – M.C., P.G.; Analysis and/or Interpretation – M.C., M.G.; Literature Search - M.C., P.G.; Writing Manuscript – M.C., O.P.; Critical Review – M.C.,

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

- Gorbalenya AE, Baker SC, Baric RS, et al. Severe acute respiratory syndrome-related coronavirus: the species and its viruses – a statement of the coronavirus study group. [\[CrossRef\]](#)
- Guo YR, Cao QD, Hong ZS, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Mil Med Res* 2020. 13; 7 :11. [\[CrossRef\]](#)
- Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020 15; 395: 514-23. [\[CrossRef\]](#)
- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA* 2020 Feb 7. [Epub Ahead of Print] [\[CrossRef\]](#)
- Deng SQ, Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. *J Clin Med* 2020 Feb 20; 9: e575. [\[CrossRef\]](#)
- Habibzadeh P, Stoneman EK. The Novel Coronavirus: A Bird's Eye View. *Int J Occup Environ Med* 2020; 11: 65-71. [\[CrossRef\]](#)
- Casella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). *StatPearls Publishing; Treasure Island (FL), StatPearls [Internet]* 2020 Jan-2020 Mar 8.
- Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; e201127. [Epub Ahead of Print] [\[CrossRef\]](#)
- Zhao Y, Zhao Z, Wang Y, et al. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov. *bioRxiv* 2020, Jan 26. [Epub Ahead of Print] [\[CrossRef\]](#)
- Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. *J Med Virol* 2020 Feb 27. [Epub Ahead of Print] [\[CrossRef\]](#)
- Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol* 2020 Mar 5. [Epub Ahead of Print] [\[CrossRef\]](#)
- Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. *Rhinology* 2020 Apr 11. [Epub Ahead of Print] [\[CrossRef\]](#)
- Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms. *Int Forum Allergy Rhinol* 2020 Apr 12. [Epub Ahead of Print] [\[CrossRef\]](#)
- Walker A, Hopkins C, Surda P. The use of google trends to investigate the loss of smell related searches during COVID-19. *Int Forum Allergy Rhinol* 2020 Apr 11. [Epub Ahead of Print] [\[CrossRef\]](#)
- Gane SB, Kelly C, Hopkins C. Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome? *Rhinology* 2020 Apr 2. [Epub Ahead of Print] [\[CrossRef\]](#)
- Lechien JR, Chiesa-Estomba CM, De Siati DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol* 2020 Apr 6. [Epub Ahead of Print] [\[CrossRef\]](#)