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SHORT COMMUNICATION

Ageusia and anosmia, a common sign of COVID-19? A case series from four countries

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Abstract

Over the course of the pandemic due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), multiple new clinical manifestations, as the consequence of the tropism of the virus, have been recognized. That includes now the neurological manifestations and conditions, such as headache, encephalitis, as well as olfactory and taste disorders. We present a series of ten cases of RT-PCR-confirmed SARS-CoV-2-infected patients diagnosed with viral-associated olfactory and taste loss from four different countries.

Keywords Anosmia · Ageusia · Clinical manifestations · Neurological · SARS-CoV-2 · COVID-19

Introduction

As the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues to evolve, novel signs and symptoms continue to emerge and expand the clinical manifestations of coronavirus disease 2019 (COVID-19) (Rodriguez-Morales et al. 2020a). This includes an ever-increasing number of reports linking the virus to a number of presumed neurological disorders (Paniz-Mondolfi et al. 2020).

The spectrum of neurological manifestations includes headache (Rodriguez-Morales et al. 2020b), encephalitis, Guillain-Barre syndrome (Zhao et al. 2020), as well as olfactory and taste dysfunction (Ollarves-Carrero et al. 2020). Despite recognition of these symptoms, there is still a lack of reports,

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delving deeply into the clinical and pathophysiological aspects of SARS-CoV-2-related anosmia and ageusia. Herein, we present a series of ten cases of RT-PCR-confirmed SARS-CoV-2-infected patients diagnosed with viral-associated olfactory and taste loss from four different countries. Of these, nine patients presented with ageusia and eight with anosmia, with seven of them presenting overlapping anosmia/ageusia persisting for a range of 4 to 25 days.

Cases

The median age of these COVID-19 patients was 48 years old, seven females and three males (Table 1). Patients 1 and 3 were related, as well as patients 5 and 6. Four patients were from Germany, three from the USA, two from Venezuela, and one from Bolivia. Eight referred cough as the most common presenting symptom, with only five presenting fever. Other symptoms included dyspnea, generalized weakness, headache, diarrhea, dehydration, polyarthralgia, nausea, and vomiting (Table 1). Patients 1, 4, and 7 required hospitalization for 17, 15, and 10 days, respectively. Notably, ageusia and anosmia were among the most common signs found in all patients with a median time of presentation at 2 days after onset of symptoms for ageusia and 3 days for anosmia.

Anosmia was the debuting clinical sign in three patients, of whom two presented with olfactory loss at day 1, and one (patient 7), 2 days previous to the onset of symptoms. Ageusia was also an early sign, presenting between days 1 and 2 in five patients and between days 4 and 5 in three. Late-onset anosmia (day 7) and ageusia (day 10) was observed in patient 10. Ageusia persisted for a median of 8 days (ranging 4 to 25) and anosmia for a mean of 11 days (5 to 25). In two patients, co-infection with the influenza virus was assessed, resulting negative by RT-PCR in patients 1 and 4 (Table 1). Patient 1 had repeated positive RT-PCR testing for SARS-CoV-2 at days 6, 10, 11, and 17 of disease.

Discussion

Our results, from four very different countries in Europe, North and South America, are consistent with those found by other groups were postviral olfactory loss presents more commonly in women, with a female-to-male ratio of 2:1 and typically over 50 years of age (Seiden 2004). Concurrent affectation of the sense of taste suggests that most probably ageusia in these patients is secondary to a diminished taste perception as a consequence of anosmia. However, sensorineural impairment due to direct viral injury cannot be entirely excluded (Elterman et al. 2014; Rahban et al. 2015).

Recent data suggest that smell and taste disorders may be significantly more frequent among COVID-19 patients than influenza patients (Hopkins et al. 2020; Lechner et al. 2020; Lee et al. 2020; Moein et al. 2020; Reinhard et al. 2020; Tong et al. 2020). As we observed in our patients, deficits in olfactory and taste function were usually of acute onset and at early stages of the disease, presenting for most cases as the initial clinical manifestation throughout the first days (Beltran-Corbellini et al. 2020). In a recent case-control study with 17 patients with smell and taste disorders, the mean duration of symptoms was 7.5 days (Beltran-Corbellini et al. 2020). To date, despite the massive ongoing pandemic affecting over 9.18 million people worldwide, as of June 23, 2020, there is limited information regarding the real prevalence of ageusia, anosmia, and other sensorineural related disorders associated to SARS-CoV-2 infection from Latin America. Olfactory and taste dysfunction has been reported as a clinical manifestation of a wide range of viral infections, particularly those causing upper respiratory tract infections (Seiden 2004).

However, these symptoms are usually attributed as conductive or obstructive signs due to mucosal edema and not as direct sensorineural noxa by the virus, leading to substantial underreporting in a high proportion of patients (Seiden 2004). Multiple viruses are known to use the olfactory nerve as a shortcut into the central nervous systems, including the influenza virus, which can also lead to long-term olfactory disorders in some cases (Ollarves-Carrero et al. 2020; van Riel et al. 2015). Rhinovirus, respiratory syncytial virus, paramyxovirus, adenovirus, echovirus, and enterovirus have also been linked to cytopathic damage of the olfactory epithelium (Seiden 2004). Hypogeusia, dysgeusia, hyposmia, and dysosmia associated with COVID-19 require more detailed studies to understand their pathophysiology, but especially their clinical course and potential long-term implications (Ollarves-Carrero et al. 2020).

As the pandemic continues to expand, early detection and screening for suspicious cases, based on broader clinical findings, would be a useful aid to diagnosis, besides rRT-PCR confirmation; particularly in resource depleted settings such as Latin America were numerous regions are already reaching concerning epidemic proportions (Cimerman et al. 2020). Despite some reports, anosmia is not frequent in the context of common cold and flu. The typical flu or viral upper respiratory tract infection can cause changes in smell usually secondary to nasal congestion, but that does not appear to be the case with COVID-19. Our patients did not have any significant nasal congestion or obstruction. An increase in smell and taste disorders, in the context of the ongoing COVID-19 pandemic in Latin America, makes this case series of relevance.

We endorse the assessment of smell and taste disorders, such as ageusia and anosmia, as a critical component of the anamnesis and as a helpful diagnostic clue for COVID-19. Early recognition of these signs, along with flu-like symptoms, may aid in supporting individuals' self-isolation in the current epidemic context (Beltran-Corbellini et al. 2020). Finally, as a consequence of this, multiple national guidelines are considering both of these cardinal clinical signs as part of the constellation of findings

Table 1 Summary of clinical features of the patients infected with SARS-CoV-2

	Patient									
	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Country	Germany	Germany	Germany	Germany	USA	USA	Venezuela	Venezuela	Bolivia	USA
Age (years)	86	51	50	66	38	45	44	61	32	39
Sex	F	M	F	M	F	M	F	F	F	F
Relationship	Mother-in-law of P3	–	Daughter-in-law of P1	–	Wife of P6	Husband of P5	–	–	–	–
Occupation	Housewife	Carpenter	Housewife	Retired	Unemployed Colombian veterinarian	Dialysis Hospital cleaning and disinfection company manager	Housewife	Engineer	Government employee	Physician
Chronic medical illness	Coronary bypass 13 years ago, breast cancer 24 years ago	None	None	None	None	None	Systemic lupus erythematosus (SLE)	Type 2 diabetes mellitus	None	Adult Still's disease
Symptoms started, date	18-Mar-20	14-Mar-20	23-Mar-20	23-Mar-20	18-Mar-20	10-Mar-20	11-Apr-20	09-Mar-20	21-Mar-20	7-Apr-20
Interval between symptom onset and consultation (days)	1	2	1	4	2	2	1	2	12	0
Consultation date	19-Mar-20	16-Mar-20	24-Mar-20	27-Mar-20	20-Mar-20	12-Mar-20	12-Apr-20	11-Mar-20	2-Apr-20	7-Apr-20
Presenting symptoms and signs										
Fever	–	–	–	D1	–	D1	D2	D2	–	D3
Cough	D1	D1	D1	D1	D1	D2	D1	D1	–	–
Malaise	D1	–	–	–	D3	D1	D1	D1	D1	–
Dyspnea	–	D1	D1	–	D2	–	–	D1	–	–
Generalized weakness	–	–	–	–	–	D1	D1	D2	–	D3
Headache	–	–	–	–	D3	–	D1	D1	–	–
Diarrhea	–	–	–	–	D3	D1	–	–	–	D21
Polyarthralgia	–	–	D5	–	–	–	D2	–	–	–
Dehydrated	D3	–	–	–	–	–	–	–	–	–
Ageusia	**D2–D7, 5 days**	**D1–D5, 5 days**	**D5–D7, 22 days**	**D1–D11, 11 days**	**D5–D16, 11 days**	**D4–D29, 25 days**	**D2–D8, 7 days**	**D2–D5, 4 days**	–	**D10–D18, 8 days**
Anosmia	–	–	**D5–D7, 22 days**	**D1–D11, 11 days**	**D5–D16, 11 days**	**D4–D29, 25 days**	**2D(POS)–D4 then D7-D14, 13 days**	**D1–D5, 5 days**	**D1–D7, 7 days**	**D7–D15, 8 days**
Hospitalized	Yes	No	No	Yes	No	No	Yes	No	No	No
Discharged at day	17	–	–	15	–	–	10	–	–	–
Body temperature (°C)	36.9	37.0	37.0	39.0	37.0	37.9	37.3	37.0	37.0	38.6
Systolic blood pressure (mmHg) at income	125	105	110	120	N/A	N/A	120	110	N/A	N/A
Dyastolic blood pressure (mmHg) at income	80	70	70	80	N/A	N/A	85	70	N/A	N/A
Cardiac frequency (bpm)	91	72	70	60	N/A	N/A	81	75	N/A	N/A
Oximetry saturation (%)	98	N/A	N/A	92	N/A	N/A	97	98	N/A	93–94
White blood cell count ($\times 10^9$ cells/L); (normal range 3.9–9.9)	5.08	N/A	N/A	6.75	N/A	N/A	5.05	6.70	N/A	N/A
	508	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 1 (continued)

	Patient									
	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Lymphocyte count ($\times 10^9$ cells/L); (normal range 1.1–3.6)										
Platelet count ($\times 10^9$ cells/L); (normal range 162–341)	140	N/A	N/A	259	N/A	N/A	130	140	N/A	N/A
D-dimer (μg/mL) (normal range 0.0–0.5)	1.48	N/A	N/A	0.88	N/A	N/A	N/A	N/A	N/A	0.64
Ferritin (ng/mL) (normal range 12–150)	312	N/A	N/A	1288	N/A	N/A	240	190	N/A	N/A
Fibrinogen (g/dL) (normal range 2.0–4·0)	370	N/A	N/A	1000	N/A	N/A	N/A	N/A	N/A	N/A
C-reactive protein (mg/L) (normal range 0.0–5.0)	33	N/A	N/A	71.2	N/A	N/A	43	35	N/A	55
Aspartate aminotransferase (U/L) (normal range 0.0–32.0)	53	N/A	N/A	230	N/A	N/A	N/A	N/A	N/A	N/A
Potassium (mmol/L) (normal range 3.5–5.1)	2.8	N/A	N/A	4.5	N/A	N/A	N/A	N/A	N/A	N/A
Serum chloride (mmol/L) (normal 98–107)	95	N/A	N/A	96	N/A	N/A	N/A	N/A	N/A	N/A
Lactate dehydrogenase (U/L) (normal range 135–214)	376	N/A	N/A	414	N/A	N/A	N/A	N/A	N/A	N/A
IL-6 (pg/mL) (normal < 7)	7.3	N/A	N/A	29.7 (D5), 49.4 (D6), 14.4 (D10)	N/A	N/A	N/A	N/A	N/A	N/A
RT-PCR for Influenza viruses	Negative	N/A	N/A	Negative	N/A	N/A	N/A	N/A	N/A	N/A
RT-PCR for SARS-CoV-2	Positive, D6, D10, D11, D17	Positive	Positive	Positive	Positive	Positive	Positive, D3	Positive, D2	Positive	Positive
Antibodies, anti-SARS-CoV-2 (OD ratio) (normal < 8)										
IgG	13.93 (D11), 14.54 (D17)	8.04 (D23)	N/A	14.74 (D10), 12.17 (D18)	N/A	N/A	N/A	N/A	N/A	N/A
IgA	8.0 (D11), 12.3 (D17)	8.19 (D23)	N/A	40.21 (D10), 38.58 (D18)	N/A	N/A	N/A	N/A	N/A	N/A

Written consent was obtained from all the patients

F female, *M* male, *P1* patient 1, *P2* patient 2, *P3* patient 3, *P4* patient 4, *P5* patient 5, *P6* patient 6, *D* day of the disease, – negative, *N/A* not assessed, *IL-6* interleukin 6, *RT-PCR* reverse-transcriptase polymerase chain reaction, *SARS-CoV-2* severe acute respiratory syndrome coronavirus 2, *2D(POS)* 2 days before the onset of symptoms

defining COVID-19. The Centers for Disease Control (CDC) in the USA now recognizes these as early symptoms for screening purposes (CDC 2020). In Latin America, these findings have already been even included in Chile and Colombia, also as COVID-19 suspicion criteria (Gutiérrez et al. 2020). In these countries, no cases of ageusia and anosmia have been reported to date associated with COVID-19.

Author contributions JAVG, AJRM, APM conceived the report. JAVG, AJRM, APM, DW, RS, JPEA, collected data, analyzed, and interpreted clinical data. AJRM wrote the first draft. AGRM, DKBA, performed a review of the literature. All authors approved the subsequent draft versions. All authors approved the final submitted version.

Data Availability Copy of the clinical data of the patients is available.

Compliance with ethical standards

Written consent from all the patients was obtained. Written consent from the patient was obtained for publication.

Conflict of interest We declare that we have no competing interests, except JM and MPTT; they are the patients 5 and 10 of this case series.

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