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LETTER

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The manifestation of oral mucositis in COVID-19 patients: A case-series

Dear Editor,

We have read with great interest the correspondence of Kahraman et al (2020) on the emergence of oral mucosal changes adjacent to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; hereby we demonstrate the characteristics of 13 laboratory-confirmed coronavirus disease (COVID-19) patients with oral mucositis according to the CARE guidelines.[1,2]

The referenced patients sought care at our department from April to August 2020 due to generalized pain and soreness within the oral cavity related mainly to nonkeratinized mucosa without a specific cause (Table 1). All included patients had previously undergone polymerase chain reaction (PCR) testing for SARS-CoV-2, which confirmed their infection with a mean cycle threshold (Ct) value of 18.46 ± 3.8 (12-26). Their mean age was 51.08 ± 8.79 (34-62) years old, and eight of them (62.5%) were females. Regarding their COVID-19 symptoms, two patients (15.4%) had persistent fever, four (30.8%) had ageusia, and two (15.4%) had anosmia. The majority of them (69.2%) had a mild course of SARS-CoV-2 infection and were prescribed paracetamol (PCM); contrarily, four patients experienced a moderate course of infection—two patients (15.4%) were prescribed chloroquine and other two (15.4%) were prescribed dexamethasone.[3]

The mean onset of mucositis emergence was 0.85 ± 0.8 (0-2) days calculated since the day of PCR testing, while its mean duration was 8.62 ± 3.07 (7-14) days. An 11-item numerical rating scale (NRS) was used to evaluate the manifested intraoral pain where "0" denotes "no pain" and "10" denotes "pain as bad as you can imagine."[4] The mean score of pain intensity was 5.08 ± 2.36.[3-9] On intraoral examination, sporadic erythema with minor irritations was found all over the mouth (53.8%), on the buccal mucosa (30.8%), palate (15.4%), and gingiva (7.7%). Depapillation of the tongue was observed in all cases with a tendency to be more localized at the borders (Figure 1).

While nine patients (69.2%) were prescribed "Magic mouthwash" containing lidocaine 1%, chlorhexidine 2%, and prednisolone 20 mg in 100 mL, four patients (30.8%) were prescribed PCM to relieve their symptoms of mucositis. Mann-Whitney test yielded a statistically significant difference favoring "Magic mouthwash" in reducing the duration of mucositis, U (N_{Magic} = 9, N_{PCM} = 4) = 4.5, z = −2.85, P = .034.

Inferential statistics revealed that COVID-19 severity was significantly associated with duration of mucositis and its pain (H = 5.76 and 9.29; P = .016 and .002, respectively). Ageusia was also significantly associated with Ct value, mucositis duration, and onset (U = 2, 4.5, and 1.5; P = .013, .034, and .018, respectively).

Our findings support the suggested role of oral mucosa in providing an entry for SARS-CoV-2 due to the high expression of angiotensin-converting enzyme II (ACE2) receptors.[5] According to Sonis theory, oral mucositis is primarily initiated by oxidative stress and the formation of reactive oxygen species (ROS) in response to somatotoxic doses of nonsurgical oncologic treatment.[6] The excessive production of ROS in the mucosal tissues of severely ill COVID-19 patients may explain the significant direct association observed in our cases between severity of COVID-19 and mucositis duration and pain intensity.[7] Secondary infections and drug reactions cannot be ruled out entirely, especially with severely ill patients due to immune dysregulation.[8] In addition, oral mucosal changes were consistently observed in children with pediatric multisystem inflammatory syndrome temporally associated with SARS-COV-2 (PIMS-TS), which is suggested to be linked to IgG antibody-mediated enhancement.[9]

In conclusion, oral mucositis may occur in COVID-19 patients either as a direct manifestation of cellular damage triggered by SARS-CoV-2 or as an opportunistic infection due to immune dysregulation. This case-series warrants larger epidemiologic studies to verify the etiology and prevalence of oral mucositis among COVID-19 patients.

PATIENT CONSENT

All patients agreed to use their clinical and laboratory results for academic purposes while concealing their identifying personal data.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Abanoub Riad: Writing-original draft. Islam Kassem: Data curation; Investigation. Mai Badrah: Formal analysis. Miloslav Klugar: Supervision; Writing-review & editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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TABLE 1 Demographic, clinical, and laboratory characteristics of COVID-19 patients with oral mucositis

No	Gender	Age	Comorbidities	Smoking	Hygiene	Ct	Fever	Ageusia	Anosmia	Severity	COVID-19-MED	Pain	Location	Onset	Duration	Mucositis-MED
1	Female	50	Diabetes	Yes	Fair	16	Yes	Yes	Yes	Moderate	Dexamethasone	8	All over the mouth	0	14	Paracetamol
2	Male	34	Hypertension & Diabetes	No	Fair	18	No	No	No	Mild	Paracetamol	3	Palate and buccal mucosa	1	7	Magic MW
3	Female	56	N/A	No	Good	24	No	No	No	Mild	Paracetamol	6	Hard and soft palate	1	7	Magic MW
4	Male	62	N/A	No	Poor	26	No	No	No	Mild	Paracetamol	3	All over the mouth	2	7	Magic MW
5	Female	45	Asthma	No	Poor	19	No	No	No	Mild	Paracetamol	3	All over the mouth	1	7	Magic MW
6	Female	57	N/A	Yes	Good	20	No	No	No	Mild	Paracetamol	4	Buccal mucosa	0	7	Magic MW
7	Male	49	N/A	No	Poor	18	No	Yes	No	Mild	Paracetamol	3	All over the mouth	0	7	Magic MW
8	Female	39	Hypertension	No	Fair	13	No	Yes	Yes	Moderate	Chloroquine	9	All over the mouth	0	14	Paracetamol
9	Male	46	N/A	No	Good	17	No	No	No	Mild	Paracetamol	3	Buccal mucosa	2	7	Magic MW
10	Female	62	N/A	No	Good	18	No	No	No	Mild	Paracetamol	4	All over the mouth	1	7	Magic MW
11	Male	55	Diabetes	No	Fair	19	No	No	No	Moderate	Dexamethasone	8	Gingiva	2	7	Paracetamol
12	Female	61	N/A	No	Good	12	Yes	Yes	No	Moderate	Chloroquine	8	Buccal mucosa	0	14	Paracetamol
13	Female	48	Asthma	Yes	Fair	20	No	No	No	Mild	Paracetamol	4	All over the mouth	1	7	Magic MW

Abbreviations: Ct, Cycle threshold value of polymerase chain reaction (PCR) test for SARS-CoV-2; COVID-19-MED, medication prescribed for COVID-19; mucositis-MED, Medication prescribed for mucositis.

FIGURE 1 Mucositis in palate of a laboratory-confirmed COVID-19 patient

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