LETTER TO THE EDITOR



Oral erosions and petechiae during SARS-CoV-2 infection

To the Editor.

An increasing number of reports have been written regarding cutaneous manifestations during the coronavirus disease-2019 (COVID-19), 1-3 though knowledge of the possible oral manifestations is still poor. This may be due to a lack of intraoral examinations, which may be caused by limited availability of the recommended protective measures and the use of telemedical consultations for SARS-CoV-2 infections. We describe a patient presenting with cutaneous and oral lesions associated with a SARS-CoV-2 infection.

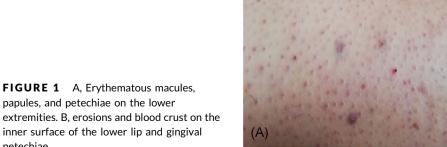
A previously healthy 19-year-old woman presented to the Emergency Department with a seven-day history of intermittent fever and sore throat. She had started taking oral cefixime (400 mg per day) 3 days earlier. She also reported a sudden onset of fatigue, hyposmia, and asymptomatic cutaneous and oropharyngeal lesions that started 2 days before admission. On admission, she was afebrile and her vital signs (blood pressure, beats/minute, oxygen saturation) were normal. Physical examination revealed erythematous macules, papules and petechiae on the lower extremities (Figure 1A); erosions, ulcerations, and blood crusts on the inner surface of the lips (Figure 1B) and palatal and gingival petechiae. Chest radiograph and pulmonary ultrasound were normal. A complete blood cell count revealed increased white cells (12 000/mm³, 60% of lymphocytes), aspartate aminotransferase (200 U/L), alanine aminotransferase (140 U/L), lactic dehydrogenase (LDH) (300 mU/mL) and severe thrombocytopenia (platelet count 2000/mm³). Hemoglobin and C-reactive protein levels were normal. Real-time reverse transcriptase-polymerase chain reaction (PCR) from a nasopharyngeal swab was positive for SARS-CoV-2. Antibiotic therapy was discontinued

and intravenous immune globulins (400 mg/kg) and methylprednisolone (1 mg/kg) was administered for 5 days.

On day 5, the systemic symptoms regressed, though some maculopapular lesions were still present on the legs; the platelet count had increased to 98 000/mm³, and aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase returned to normal ranges. On day 10, the complete blood count was normal (white cells 9000/mm3 with 40% of lymphocytes; platelet count 152,000/mm³) and skin and mucosal lesions disappeared.

In the literature, the prevalence of cutaneous findings in SARS-CoV-2 patients ranges from 0,2%¹ to 20,4%.² Skin lesions are heterogeneous and divided into acral erythematous-edematous chilblain-like lesions, maculopapular, vesicular and urticarial eruptions.3 Petechial eruptions are sporadically reported,4 while oropharyngeal lesions have been described in only seven patients to date (Table 1).5-8 They were all adult patients (mean age 57 years), often affected by diabetes and hypertension, presenting with painful oropharyngeal lesions in the form of ulcers (5 cases), 5,6,8 blisters and gingivitis (1 case),⁵ palatal petechiae, erythema and pustules (1 case). Histological analysis, performed in three cases revealed inflammatory infiltrates and focal necrosis-hemorrhages in the lamina propria, and in one case, small vessel obliteration with thrombi. In these three cases, infections with herpes simplex virus (HSV)1/2 were excluded through in-situ hybridization and PCR on the lesion tissue.^{6,8}

Compared to the previously reported cases, 5-8 our patient was younger and without comorbidities. Notably, the oral lesions in our patient were painless, heterogeneous in morphology, and associated





papules, and petechiae on the lower extremities. B, erosions and blood crust on the inner surface of the lower lip and gingival petechiae

TABLE 1 Clinical, laboratory, and histological findings of COVID-19 patients manifesting oropharyngeal lesions

Time of resolution of the oropharyngeal lesions				
Time of resolution or ophar lesions	10 d	1 wk	3d	% × ×
Associated skin Treatment of the lesions	Valacyclovir 500 mg three times/daily for 10 d, topical chlorhexidine and hyaluronic acid.	Topical antiseptic mouthwash.	Hyaluronic acid and chlorhexidine mouthwash. prednisolone 30 mg per day	Dexamethasone, dipyrone
Associated skin lesions	None	None	Rash under her breasts, back and genital area	Petechia-like and vesicobul- lous lesions
Histology of oropharyngeal lesions	Present Not performed	Present Not performed	Present Not performed	Present Severe vacuolization of the epithelium, inflammatory inflitrate and focal necrosishemorthages in the lamina propria, superficial-deep small vessels obliteration with evident thrombi. HHV-1, HHV-2, CMV, treponema pallidum and EBV in-situ hybridization negative.
Pain	Present	Present	resent	Present
Latency time from the onset of symptoms	No other symptoms	No other symptoms	30 d	Not reported
Oropharyngeal lesions	Orange-colored ulcers with an erythematous halo on the hard palate (resembling herpetic stomatitis)	Pinpoint yellowish ulcers with an erythematous halo on the hard palate	Blisters in the internal lip mucosa, desquamative gingivitis	Ulcerated lesion, reddish macules of different sizes scattered along the hard palate, tongue, and lips
Systemic signs and symptoms	Asthenia, fever, hyposmia, dysgeusia, enlarge- ment of neck lymph nodes	None	Fever, diarrhea	Fever, cough, shortness of breath
SARS- CoV-2 infection	Suspected	Suspected	Confirmed	Confirmed
Patient's age	99	28	65	2
Patient's sex	Σ	Σ	ш	Σ
Authors	Martin Carreras- Presas et al ⁵	Martin Carreras- Presas et al ⁵	Martin Carreras- Presas et al ⁵	Soares et al ⁶

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						Latency time		-			Time of
Authors	Patient's sex	Patient's age	SARS- CoV-2 infection	Systemic signs and symptoms	Oropharyngeal lesions	from the onset of symptoms	Pain	Histology of oropharyngeal lesions	Associated skin lesions	Associated skin Treatment of the lesions oropharyngeal lesions	resolution of the oropharyngeal lesions
Cebeci Kahraman et al ⁷	Σ	51	Confirmed	Fever, fatigue, severe dry cough, sore throat, hyposmia, disgeusya	Oropharynx erythema, hard palate petechiae, soft palate pustules	10 d	Present	Present Not performed	Not reported	None	7 d
Ansari et al ⁸	ш	99	Confirmed	Fever, shortness of breath	Hard palate ulcers	5 d	Present	Present Edema with mucosal desquamation, granulation and ulceration under the mucosa; invasion of mononuclear cells with large and glassy nuclei	Not reported	Topycal mixture of diphenhydramine, dexamethasone, tetracycline, and lidocaine	7 d
Ansari et al ⁸	Σ	75	Confirmed	Shortness of breath, dysphasia	Ulcer with a red background on the anterior tongue	7 d	Present	Present Edema with mucosal desquamation, granulation and ulceration under the mucosa; invasion of mononuclear cells with large and glassy nuclei	Not reported	Topycal mixture of diphenhydramine, dexamethasone, tetracycline, and lidocaine	у р <u>г</u>
Our case	ш	19	Confirmed	Confirmed Intermittent fever, fatigue, hyposmia	Erosions, ulcerations and blood crust in the inner surface of the lips and palatal and gingival petechiae	7 d	Absent	Absent Not performed	Macules, papules and petechiae on the lower extremities	Intravenous immune globulins (400 mg/ kg) and methylpredniso- lone (1 mg/kg)	5 d

with severe thrombocytopenia that was probably of crucial importance in determining the onset of her cutaneous and mucosal petechiae. Conversely, the oral erosions might have been caused by direct viral vascular and mucosal damage, as SARS-CoV-2 uses the host protein angiotensin-converting enzyme-2 (largely expressed in vessels, nasal and oral mucosa) to gain intracellular entry.¹

Mild thrombocytopenia (50 000–150 000 platelets/mm³) is commonly found in viral infections and has been described in 36% of COVID-19 patients. Its pathogenesis is multifactorial: the hyper-inflammatory state and cytokine storm induced by the viral infection induces a prothrombotic state with endothelial and platelet activation and consumption. The reduced platelet production may be influenced by a direct viral insult to the bone marrow and the use of antibiotics, antivirals, and other agents may further reduce the platelet count. Therefore, we ascribed, at least for the petechial component, the cutaneous and mucosal lesions of our patient to her severe thrombocytopenia, triggered by the SARS-CoV-2 infection and potentially worsened by the cefixime treatment. Indeed, drug-induced thrombocytopenia by cephalosporins has already been described. 11,12

Our case deserves attention for several reasons: the severe thrombocytopenia, uncommon until the later stages of COVID-19,¹⁰ the maculopapular-petechial eruption, a rarely reported cutaneous manifestation, and, importantly, the presence of erosions and blood crusts on the inner mucosa of the lips and gingival-oropharyngeal petechiae. Such mucosal lesions have never been described during a SARS-CoV-2 infection.

In conclusion, the intraoral examination should always be performed in patients with suspected or confirmed SARS-CoV-2 infection. Detection of mucosal lesions, with or without cutaneous manifestations, could represent a sign of potentially life-threatening conditions such as severe thrombocytopenia, even in patients with apparently mild COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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