

Superficial mucocèles as a sequel to Stevens-Johnson syndrome during treatment of cutaneous squamous cell carcinoma with cemiplimab: A case report and review of literature

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Abstract. Superficial mucocèles (SM) are small, benign, translucent vesicles, which develop in the oral mucosa, mainly on the lower lip, due to a rupture of minor salivary gland ducts and the extravasation of saliva. The use of immune checkpoint blockade treatment may lead to dermatologic immune-related adverse events in 40-50% of patients and with severe dermatologic immune adverse events of Common Terminology Criteria for Adverse Events of grade G3-G4 in 1-2% of patients. The present study described the case of a patient with squamous cell carcinoma treated with cemiplimab with the adverse effect of Stevens-Johnson syndrome. The patient developed multiple SM, which made it challenging for the patient to speak and eat. Ablative treatment using a plasma device (Plasma IQ) and electrocoagulation were used to remove all lesions, which achieved a precise and timely therapeutic effect without any remainder of scarring. Through the publication of the present case report and literature review, the present article aimed to enhance the understanding of this condition, providing valuable diagnostic and therapeutic information about the

spectrum of mucosal involvement among drug-related toxicities of current oncological treatment.

Introduction

Superficial mucocèles (SM) are small, translucent, intra- or subepithelial vesicles affecting the oral mucosa. Their formation typically results from injuries or chronic and recurrent inflammation. These lesions tend to be recurrent and cause discomfort to the patients (1). Cemiplimab is a highly potent human monoclonal antibody that targets programmed death 1 (PD-1) (2). Cemiplimab treatment is available under the national drug program 'B.125 Treatment of patients with advanced squamous cell carcinoma of the skin with cemiplimab' for the treatment of patients with metastatic or locally advanced squamous cell carcinoma of the skin, who are not eligible for radical surgery or radiotherapy. To the best of our knowledge, previously published literature reviews have detailed a total of 99 cases of Stevens-Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN) after immunotherapy (3-58). The present manuscript reported the case of an adult male diagnosed with squamous cell carcinoma and treated with cemiplimab, who developed SJS, which led to SM after 5 weeks of SJS diagnosis. To enhance the current understanding of the occurrence of these rare adverse effects, a review of the literature was conducted, which focused on the incidence of oral mucositis (OM) and the development of severe adverse effects such as SJS/TEN, during oncological treatments. The present report aimed to offer valuable insights to be used by clinicians for the effective understanding and management of this uncommon condition. Table I presents definitions of different forms of oral mucosal damage during oncological treatment.

Methods

The present report focused on various types of anticancer therapies and their associated side effects. The Medline database (<http://www.ncbi.nlm.nih.gov/pubmed>) was searched using the following search terms: 'atezolizumab' or 'avelumab'

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Abbreviations: SM, superficial mucocèles; OM, oral mucositis; ICIs, immune checkpoint inhibitors; CTCAE, Common Terminology Criteria for Adverse Events; RECIST, Response Evaluation Criteria in Solid Tumours; SJS, Stevens-Johnson Syndrome; TEN, toxic epidermal necrolysis; PD1, programmed cell death protein 1; OM, oral mucositis

Key words: adverse drug reaction, superficial mucocèles, Stevens-Johnson syndrome, toxic epidermal necrolysis, anticancer therapies, cemiplimab

or ‘camrelizumab’ or ‘cemiplimab’ or ‘dostarlimab’ or ‘durvalumab’ or ‘ipilimumab’ or ‘nivolumab’ or ‘pembrolizumab’ or ‘penpulimab’ or ‘relatlimab’ or ‘retifanlimab’ or ‘serplulimab’ or ‘sintilimab’ or ‘tislezumab’ or ‘toripalimab’ or ‘tremelimumab’ or ‘EGFR inhibitor’ or ‘cetuximab’ or ‘panitumumab’ or ‘afatinib’ or ‘osimertinib’ or ‘vandetanib’ or ‘apatinib mesylate’ or ‘gefitinib’ or ‘erlotinib’ or ‘dacomitinib’ or ‘lapatinib’ or ‘angiogenesis inhibitors’ or ‘sorafenib’ or ‘sunitinib’ or ‘cabozantinib’ or ‘bevacizumab’ or ‘pazopanib’ or ‘axitinib’ or ‘lenalidomide’ or ‘BRAF inhibitor’ or ‘vemurafenib’ or ‘dabrafenib’ or ‘KIT and BCR-ABL inhibitors’ or ‘imatinib’ or ‘ALK inhibitors’ or ‘crizotinib’ or ‘rituximab’ or ‘bortezomib’ or ‘enfortumab vedotin’ or ‘brentuximab vedotin’ or ‘mTOR’ or ‘sirolimus’ or ‘everolimus’ or ‘temsirolimus’ or ‘alpelisib’ or ‘BTK inhibitor’ or ‘ibrutinib’ or ‘BCL2 inhibitor’ or ‘venetoclax’ and ‘Stevens Johnson syndrome’ or ‘SJS’ or ‘toxic epidermal necrolysis’ or ‘TEN’ or ‘oral mucositis’ or ‘stomatitis’ or ‘superficial mucoceles’. All relevant publications were selected and their references were further checked and researched for any additional undetected published cases (V.C, M.S, A.P). Primary case reports, case series, reviews and reports from clinical trials were included. A total of 8,379 potentially eligible articles were selected. Articles that were not written in English and did not contain the full manuscript were excluded, which left 7,812 studies. After the removal of irrelevant articles and duplicate manuscripts based on titles, abstracts and full articles, a total of 97 articles were included in the present review (V.C). A flowchart on the selection and evaluation of scientific articles is provided in Fig. S1.

Case report

A 56-year-old male undergoing immunotherapy for squamous cell carcinoma of the right lower leg with metastases to the lungs and right inguinal lymph nodes presented to the Department of Dermatology, Military Institute of Medicine-National Research Institute, Central Clinical Hospital Ministry of Defense in Warsaw in November 2023. At the time of referral to the Dermatology Clinic, the patient's cancer stage was assessed as stable disease according to the Response Evaluation Criteria in Solid Tumours (RECIST) (59). The patient had undertaken 16 courses of treatment with cemiplimab 350 mg every 3 weeks beginning in December 2022. The patient reported to the Dermatology Clinic due to blistering of the mucous membrane and epidermis throughout the lips and painful erosions of the oral mucosa (Fig. 1A). The severity of the OM was rated as G3 on the Common Terminology Criteria for Adverse Events (CTCAE) scale (Table II) (60). Furthermore, the presence of erythema multiforme (EM) lesions was observed on the palmar skin of the hands (Fig. 1B and C). The percentage of body surface area affected was estimated as 2%. The skin changes were accompanied by an increase in inflammatory markers: C-reactive protein (8.3 mg/dl; normal range, 0-0.5 mg/dl), procalcitonin (0.11 ng/ml; normal range, ≤0.046 ng/ml) and erythrocyte sedimentation rate (72 mm/h; normal range, 0-8 mm/h). Laboratory tests demonstrated no other abnormalities, such as elevations in liver enzymes or eosinophilia. Based on the clinical symptoms and following the exclusion of the potential influence of other drugs, the patient was diagnosed with SJS



Figure 1. Case presentation. (A) Extensive erosions in the mucous membrane of lips and tongue. (B) On the palmar surface of the hands there were lesions of erythema multiforme with the characteristic symptom of a shooting target. (C) Magnification of the bulls-eye-type lesions found on the palms.

Table I. Definitions of different forms of oral mucosal damage during oncological treatment.

Type of oral mucosal damage	Definition (Ref.)
Superficial mucocele	Small, translucent, tense, single or multiple subepithelial vesicles affecting the oral mucosa (8) with a predilection for the soft palate, retromolar pads and posterior buccal mucosa (1).
Mucocele	Mucocele is a common oral mucosal lesion resulting primarily from trauma to the minor salivary glands, the lower labial mucosa is more affected (8). They are located submucosal (1).
Mucositis	Oral mucositis is a severely debilitating condition characterized by erythema, edema and ulcerations of the oral mucosa (96).
Stomatitis	Inflammation of the mucous membranes of any of the structures in the mouth (97).

Table II. Clinical assessment scales for OM.

Scale	Grade 0	Grade I (mild)	Grade II (moderate)	Grade III (severe)	Grade IV (life-threatening)	Grade V (death)	(Refs.)
WHO	No OM	Erythema and soreness	Ulcers, able to eat solids	Ulcers, requires a liquid diet	Ulcers, alimentation not possible	NA	(96)
NCI-CTCAE	None	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain, interfering with oral intake	Life-threatening consequences; urgent intervention indicated	Death	(60)

NA, not applicable; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; WHO, World Health Organization; OM, oral mucositis.

induced by immunotherapy (G3 on the CTCAE scale). This adverse event developed 12 months after the initiation of cemiplimab as a sole complication of this treatment regime. Skin lesions were not preceded by pruritus, skin pain or rashes. During hospitalization, intravenous dexamethasone at a dose of 12 mg was administered and was gradually reduced after clinical improvement of the patient's symptoms was shown. Additional laboratory tests showed no circulating anti-nuclear antibodies or pemphigus/pemphigoid antibodies using indirect immunofluorescence tests. The histopathological examination was waived due to the typical clinical manifestation of SJS, such as targetoid skin lesions, classic oral mucosal involvement, the course of the disease and also partially due to the negative result obtained using indirect immunofluorescence (61) (cat. no. FA 1501-1005) with a dilution of 1:10 for anti-pemphigus and anti-pemphigoid antibodies on the substrates of the company Euroimmun Polska Sp. zo.o. using the TITERPLANE technique to standardize immunological analysis. The patient continued the treatment at home, which began with prednisone (30 mg/day) and the dose was gradually decreased over a 3-week period.

During a follow-up visit at 5 weeks after hospitalization, numerous whitish cysts, 2-4 mm in diameter, were found on the inner surface of the lower lip (Fig. 2A and B), and single cysts were present on the lateral surfaces of the cheek

mucosa. The lesions caused discomfort for the patient during speaking or eating. The videodermoscopic examination was performed with a Fotofinder.Universe 2.0.41.19 videodermoscope (FotoFinder Systems GmbH), having a magnification of 20x (Fig. 3) and showed nodular lesions with an opalescent surface, surrounded by a halo. Inside the lesion, hairpin vessels were arranged radially and polymorphic vessels on the periphery of lesions were observed. A punch biopsy was taken from persistent small erosions within the hypertrophic mucosal epithelium. A superficial stasis cyst, SM, was diagnosed based on histopathological examination (histopathology report no. 464/24) (Fig. 4A and B).

The Plasma IQ device (Berger & Kraft Medical) was used to treat the cysts. The procedure was performed under local anesthesia with 1% lignocaine solution. A satisfactory therapeutic and aesthetic outcome was achieved directly following the procedure (Fig. 5A). However, after 2 weeks, a number of lesions began to reoccur on the lower lip. The patient was treated with electrocoagulation, which was successful (Fig. 5B; the image was taken 2 weeks after electrocoagulation). Due to the diagnosis of SJS, the immunotherapy was permanently discontinued. From the SJS episode (November 2023) until the time of manuscript submission (October 2024), the patient remained under oncological supervision with 4-monthly follow-up and no further therapy was introduced due to the

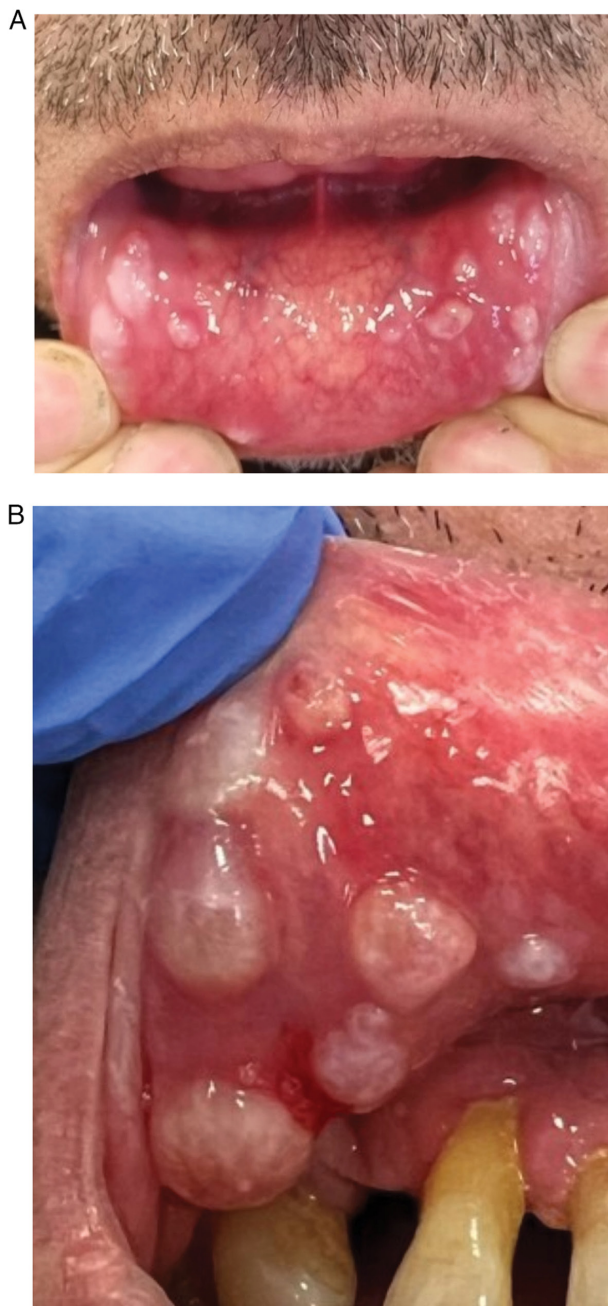


Figure 2. (A) Superficial cysts with an umbilical depression are visible on the inner surface of the lower lip 5 weeks after hospitalization. (B) Lower lip with superficial cysts 5 weeks after hospitalization.

partial response obtained according to the RECIST criteria. In case of disease progression, radiotherapy or surgical treatment should be recommended.

Literature review

The present literature review summarized all cases of SJS, TEN and SJS/TEN in patients undergoing cancer therapy reported to date (Table III). These are several rare side effects that can occur when using anticancer therapies and, to date, 99 cases of SJS/TEN have been described following immunotherapy (3-58). The clinical presentation of the disease is initially a morbilliform rash, followed by the development



Figure 3. Videodermoscopic presentation of SM 5 weeks after hospitalization: Pink, white and yellow-brown structureless background, and linear and hairpin vessels in a radial pattern. At the vertical surface of the SM's walls, the colour is red due to the perpendicular orientation of vessels. SM, superficial mucocoele.

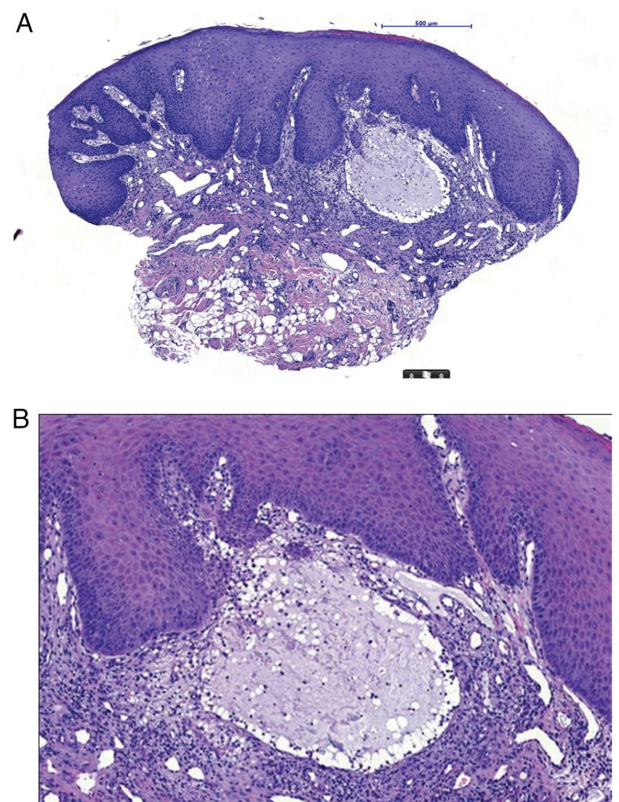


Figure 4. Histology. (A) Oral mucosa. Subepithelial extravasation of saliva (H&E; magnification, x100; scale bar, 500 μ m). (B) The mucosa of the oral cavity. Subepithelial extravasation of saliva accompanied by inflammatory infiltration (H&E; magnification, x200).

of targetoid lesions, epidermal detachment and mucous membrane ulcerations (62). The median time between the start of immune checkpoint inhibitor (ICI) therapy and the onset of SJS/TEN ranged from 1 day to 3 years. For patients with SJS, the median time to onset was 5.8 weeks and the average time was 13.8 weeks. For patients with TEN, the median time to onset was 4.0 weeks and the average time was 11.3 weeks. Several cases of TEN after termination of treatment have also been previously reported (3). Various possible mechanisms have been described to explain the induction of SJS/TEN in patients treated with ICIs. It has been suggested



Figure 5. (A) Clinical presentation directly after removing the superficial mucocele with a Plasma IQ device (Berger & Kraft Medical Sp. z o.o.). (B) 2 weeks after electrocoagulation with satisfactory result.

that cutaneous immune-related side effects may represent a pathogenic immune response against the microbiota. Another hypothesis suggests that ICI therapy increases the patient's sensitivity to other drugs or active agents (3). Histopathology of SJS/TEN-like reactions shows epidermal necrolysis associated with a change in the vacuolar interface, cleavage along the dermal-epidermal junction and subepidermal lymphocytes. Leukocytoclastic vasculitis may occur and infiltration of CD8+ T-lymphocytes, and increased programmed cell death ligand 1 (PD-L1) expression may be a response to lymphocyte overactivity induced by anti-PD1 drugs (62). Activated cytotoxic T-cells trigger apoptosis of PD-L1-expressing keratinocytes. In addition, ICI-induced SJS/TEN-like reactions show a similar gene expression profile to classic SJS/TEN (62). Type IVc hypersensitivity, as well as co-stimulatory factor amplification and regulatory T-cell dysfunction, may also be involved in the pathogenesis of SJS/TEN-like reactions (63). In addition, lower patient age was significantly associated with poorer outcomes for patients with extensive disease, which differs from standard TEN, where a patient age of >40 years is associated with higher mortality (3). Further drugs that cause SJS/TEN-like reactions are enfortumab vedotin (60 cases) (64) and imatinib (20 cases) (4). Severe cutaneous adverse reactions to enfortumab vedotin may result from the expression of

nectin-4 in epidermal keratinocytes and skin appendages (65). Isolated cases have been described with other drug therapies. The mortality rate for ICI-induced SJS was 4%, while it was 35% for ICI-induced TEN (3). The mortality rate of patients with SJS/TEN induced by targeted anticancer therapies and immunotherapies was 17.86% (5).

In addition, the present manuscript summarized the incidence of one of the most common adverse effects of anticancer therapy, which is OM or stomatitis, depending on the treatment administered (Table III). Factors such as smoking, age, female sex, poor oral hygiene and previous antineoplastic therapy may increase the risk of mucotoxicity (5,6). OM or stomatitis occurs commonly as a complication of head and neck radiochemotherapy - in 80-90% of patients (66,67), in 80% of patients treated with head and neck radiotherapy (68) and as a complication of hematopoietic stem cell transplantation/grraft vs. host disease in 60-85% of patients (67,69). In patients treated with chemotherapy, the development of OM is dependent on the type of tumor and the chemotherapeutic used and develops in 14.4-81.3% of these patients (7). OM or stomatitis are less frequently developed in patients who undergo targeted therapies, such as mTOR (30% of patients) (70), and is more common in patients treated with everolimus (67%) (6), angiogenesis inhibitors (7-29%) (71) and anti-EGFR therapy (15%) (67). In the anti-EGFR-treated group, it is significantly more common to experience these side effects when using tyrosine kinase inhibitors, such as dacomitinib and afatinib (40%), compared with monoclonal antibodies such as cetuximab (7%) and panitumumab (5%) (71). Furthermore, these serious adverse effects are rarely reported in patients treated with immunotherapy (1.5-5%), and severe OM was reported in just 0.2% of these patients (6,7). Mucosal involvement was reported in 65% of patients with ICI-induced TEN and was significantly associated with an increased risk of mortality (3). The median onset of mucositis after immunotherapy is 21 weeks (72). The pathogenesis of OM formation during ICI treatment has not yet been thoroughly investigated. The infiltration of normal tissues, including the oral mucosa, with activated T-cells catalyzes a local cellular immune response (6). Histopathological examination of OM during ICI treatment shows patchy or florid lichenoid interface dermatitis in the upper lamina propria and mainly a CD4/CD8-positive band-like T-cell infiltrate (70). Cases of mucous membrane pemphigoid and oral lichen planus-like reactions induced by immunotherapy have also been reported (72). To date, 3 cases of mucosal toxicity after vemurafenib treatment have been described in the literature, whereas no reports were found for patients treated with dabrafenib (73-75).

SM is a rare disease. Based on the review of the current literature, 10 patients (1.2%) developed SM after radiotherapy (76) and 26 patients developed SM during HSCT/GVHD (8,77-86). To date, just two cases of SM occurring after immunotherapy have been described in the literature (5,8). Of these cases, 1 patient was treated with pembrolizumab and initially developed lichenoid lesions in the oral cavity, followed by the occurrence of SM (8). The second patient was treated surgically, with chemotherapy, corticosteroids and radiotherapy before immunotherapy (5). To date, no case has been reported of a patient who developed SJS after immunotherapy, followed by SM, to the

Table III. Clinical findings of cases of OM/stomatitis, SJS, TEN and other abnormalities within the oral cavity revealed during anticancer therapies.

Oncological treatment	Prevalence of OM/stomatitis, %	SJS/TEN cases, n	Prevalence of others, %	(Refs.)
Immunotherapy: Atezolizumab, Avelumab, Camrelizumab, Cemiplimab, Dostarlimab, Durvalumab, Ipilimumab, Nivolumab, Pembrolizumab, Penpulimab, Relatlimab, Retifanlimab, Serplulimab, Sintilimab, Tislelizumab, Toripalimab, Tremelimumab	Mucositis 1.5-5	SJS, 51; TEN, 48	Xerostomia, 5; Dysgeusia, 3; Dysphagia, 2; Oropharyngeal/oral pain, 3; Oral candidiasis, 2; Angular cheilitis, 2	(3-58)
EGFR inhibitors: Cetuximab, Panitumumab, Afatinib, Osimertinib, Vandetanib, Apatinib mesylate, Gefitinib, Erlotinib, Dacomitinib, Lapatinib	Global eGFR inhibitors: Stomatitis, 15; Mucositis, 15 Mucositis: Erlotinib, 8-20; Gefitinib, 17-24; Dacomitinib, 40; Afatinib, 40; Cetuximab, 7; Panitumumab, 5; Lapatinib, 2-50	SJS, 4; SJS/TEN, 1; TEN, 8	Dysgeusia, 6-15 (Dacomitinib, Afatinib); Xerostomia, 8-14 (Dacomitinib)	(4,6,67,69,71)
Angiogenesis inhibitors: Sorafenib, Sunitinib, Cabozantinib, Bevacizumab, Pazopanib, Axitinib, Lenalidomide	Global angiogenetic inhibitors: Stomatitis, 7-29 Stomatitis: Sunitinib, 16.5-27; Cabozantinib, 22-29; Sorafenib, 7-19 Mucositis: Sorafenib, 5-33; Sunitinib, 5-32	Sunitinib: SJS, 1; SJS/TEN, 1 Sorafenib: SJS, 3; TEN, 1 Lenalidomide: TEN, 2	Dysgeusia: 20-49 (Sunitinib); 24-34 (Cabozantinib) Xerostomia: 5.2-23 (Sorafenib)	(4,6,71,98,99)
BRAF inhibitor: Vemurafenib	Vemurafenib: 3 cases	Vemurafenib: SJS, 1; TEN, 5	Main oral toxicities: - Mucosal hyperkeratotic lesions - Gingival hyperplasia - Secondary squamous cell carcinoma	(4,71,73-75)
KIT and BCR-ABL inhibitor: Imatinib	Stomatitis, 1.1	SJS, 19; TEN, 1	Oral lichenoid reaction, 16	(4,100)
ALK inhibitor: Crizotinib	Stomatitis, <15	TEN, 1	Dysgeusia, 11-26	(70,101,102)
Anti-CD20: Rituximab	Stomatitis common at ≥ 1	SJS, 3; SJS/TEN, 1; TEN, 1	Common at ≥ 1 Irritation or ulcers in the throat and mouth; Problems swallowing	(4,103)

Table III. Continued.

Oncological treatment	Prevalence of OM/ stomatitis, %	SJS/TEN cases, n	Prevalence of others, %	(Refs.)
Proteasome inhibitor: Bortezomib	Mucositis/stomatitis, 5.9 Stomatitis, very common (≥ 10)	TEN - 1	Mouth swelling, 11.8 Other common adverse effects ≥ 1 : Dyspepsia; Oropharyngeal pain; Oral ulceration; Dysphagia	(4,104,105)
Conjugate drugs: Auristatine E; Enfortumab vedotin (NECTIN 4); Brentuximab vedotin (CD 30)	Enfortumab vedotin: Stomatitis, 7 (n=21 cases)	Enfortumab vedotin: TEN, 26 SJS, 34 Brentuximab vedotin: TEN, 2	ND	(4,64,65)
mTOR inhibitors: Sirolimus Everolimus Temsirolimus	Global mTOR: Stomatitis, 25-55; Mucositis, 30 Everolimus: Stomatitis, 67	ND	Xerostomia, 6 (mTOR, Everolimus) Dysgeusia, 9-32 (Everolimus)	(6,70,71,106)
PI3K inhibitor: Alpelisib	Stomatitis, 25	SJS, 2	Mucosal dryness, 12.7	(107-109)
BTK inhibitor: Ibrutinib	Stomatitis, 11-17	SJS, <1	ND	(110,111)
BCL2 inhibitor: Venetoclax	Stomatitis - very common (≥ 10)	ND	ND	(112)

SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis; OM, oral mucositis; EGFR, Epidermal Growth Factor Receptor; ALK, anaplastic lymphoma kinase; mTOR, mammalian target of rapamycin; PI3K, phosphatidylinositol 3-kinase; BTK, Bruton tyrosine kinase; BCL2, B-cell leukemia/lymphoma 2 protein; ND, not determined.

best of our knowledge. Based on the currently available literature, it could be suggested that the chronic persistence of autoreactive lymphocytes and increased levels of pro-inflammatory cytokines in tissues after SJS may be responsible for intraepithelial blisters and cyst formation in vacuolar interface dermatitis and the development of SM, as a result of chronic inflammation. The true prevalence of SM remains undetermined, but is likely to be underreported. To the best of our knowledge, there have been no reports of patients developing SM when they were treated with other oncological therapies.

Discussion

OM is one of the adverse effects of anticancer therapy, typically manifesting as extensive erosions or ulcers of the oral cavity, accompanied by pain and causing difficulties swallowing, which can negatively affect the patient's quality of life (87). OM in patients treated with immunotherapy is often recurrent, severe or chronic, and may persist for months after discontinuation of the treatment. Immunotherapy may cause various types of side effects in the oral cavity, which include lichen planus, bullous lichen planus, bullous pemphigoid,

erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (3,8).

SM was first reported in 1988 by Eveson (88) as small, 1-4-mm, translucent, tense, subepithelial vesicles affecting the oral mucosa. It occurs more often in older, middle-aged females, mainly on the soft palate, retromolar pad, buccal mucosa, lower labial mucosa or floor of the mouth (1). Numerous cases of superficial mucous cysts have been described to be caused by inflammation, such as allergic stomatitis. A case of SM was also reported in a child with drug-induced SJS (1). A relationship has also been shown between SM and local and systemic inflammation, such as in cases of Sjogren's syndrome or systemic lupus erythematosus (8). Amy *et al* (5) reported two cases of superficial mucous cysts in patients treated with pembrolizumab. Of the cases, one of the patients had previously been treated with radiotherapy and chemotherapy. In both cases, these changes appeared secondary to inflammation in the oral mucosa. Heguedusch *et al* (8) described 16 cases of patients with superficial mucous cysts. In the majority of the patients, the cysts occurred as a complication after radiotherapy of the head and neck, whilst other patients developed cysts as a complication of graft-vs.-host disease. Furthermore, a previous report

detailed the case of a patient treated with pembrolizumab, who initially developed lichenoid lesions in the oral cavity, which was followed by the onset of SM (8).

Previous reports detailed the dermoscopy of classic mucocele, which was located deeper compared with the patient of the present study (89,90). Hence, the videodermoscopic image of SM presented in the current manuscript, to the best of our knowledge, was the first report of such a case and differs from an image of mucocele and other abnormalities of the oral mucosa. Mucoscopy is a safe, non-invasive method that helps to differentiate between various mucocutaneous disorders such as pemphigus vulgaris or lichen planus (91,92). A previous report by Rather *et al* (89) described mucoceles located submucosally, which were deeper compared with the intra- or subepithelial locations observed with SM. SM can be misdiagnosed as bullous lichen planus, recurrent aphthous stomatitis, pemphigus vulgaris, discoid lupus erythematosus, verrucae, mucous membrane pemphigoid or herpetic lesions (1,89). To date, no effective treatment protocol has been proposed for SM. In asymptomatic cases, observation is sufficient. In cases of functional impairment and irritation, it is necessary to remove the minor gland by surgical excision, laser vaporization with a neodymium-doped yttrium aluminum garnet laser, laser ablation using CO₂ or cryosurgery (1,93). Surgery is a more invasive and painful method, which causes discomfort to the patient, particularly those with multiple and recurrent lesions. In addition, a patient who has undergone severe adverse reactions may potentially be traumatized and subsequent oral procedures after extensive ulcerations may be emotionally challenging. Heguedusch *et al* (8) reported that topical clobetasol propionate at a dose of 0.05% was effective for the treatment of SM associated with GVHD, radio-induced mucositis, erythematous lupus and oral lichenoid lesion associated with pembrolizumab.

The patient in the present study was treated using dermo-surgical technology with Plasma IQ (Berger & Kraft Medical). The device is certified by the Food and Drug Administration for the removal and coagulation of skin lesions. During the treatment, plasma beams are precisely delivered to the skin using thin needle electrodes, generating microthermal zones that lead to the pyrolysis of tissues in the treatment area, without damaging the surrounding tissues. The recovery period and tissue regeneration after the procedure ranges from 5–7 days (94). In the present study, the plasma device and electrocoagulation were used because of their high efficacy and low risk of scarring. These devices are more cost-effective, readily available and comfortable to use in the oral cavity because of their small size in contrast to larger laser heads (95). The use of this method allows for achieving a satisfactory aesthetic outcome with a short recovery period. However, it was still necessary to treat the recurring lesions. The recurrence of SM may be the result of the lichenoid inflammation damaging the salivary gland ducts (1). SM recurrence could also be due to scar formation and the incomplete removal of adjoining minor salivary glands (91). In the present study, recurrence after 2 weeks was potentially associated with persistent chronic inflammation in the tissue. As a preventive measure, patients should be closely monitored after severe cutaneous adverse reactions and educated about possible side effects.

Immunotherapy is an increasingly common treatment method used in oncology; however, it is associated with the possibility of the occurrence of various types of acute immune-related toxicities. Cutaneous adverse events can occur both during or after the cessation of treatment. These complications may persist chronically in ~20% of patients. Therefore, knowledge of these complications is crucial for effective patient care, early diagnosis, selection of adequate treatment and further dermatological supervision. The main concern for the management of these patients is to manage symptoms effectively to allow the patients to continue their oncological treatment. To the best of our knowledge, this is the first published report of SJS secondary to cemiplimab describing SM structures and the application of a plasma device for SM removal. Oral mucosal as an adverse effect is much more frequently reported during ICI treatment than during targeted therapies (6,67). The rapid development of oncology therapies and their use in a rising number of patients will increase the number of reported new complications that will require the advancement of new management methods.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MS, VC and AP conceptualized and designed the study and drafted the manuscript. MS, VC and AP participated in data collection and analysis. MS, VC, KP and WO interpreted the data and revised the manuscript. VC, AP, MS, PT and AC treated the patient. JK conducted the analysis of the pathological results. VC, AP, MS, JK, PT, AC and WO confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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