INTRODUCTION

Metastasis from distant organs, outside the head and neck region, accounts for about 1% of all malignancies of the oral cavity. In order of frequency, metastatic breast carcinomas to the oral cavity rank highest, followed by lung and kidney cancers. Metastasis develops in approximately one-third of renal cell carcinomas (RCC), and approximately one-half of these are distant metastases following an initial primary site diagnosis. Reports of metastatic renal cell carcinoma to the oral cavity presenting as first sign of disease are rare and indicate very poor prognosis. Here, we present a case of metastatic RCC to the left buccal mucosa of a 59-year-old woman, which represented the first sign of the disease.

CASE HISTORY

A 59-year-old woman presented at the University of Texas Health Science Center at Houston School of Dentistry clinic with the complaint of a swelling of the left buccal mucosa that was interfering with the fit of her dentures. The patient indicated that she noticed the lesion about three weeks prior to presentation. Past medical history was significant for hip and back pain, and a diagnosis of Guillain-Barre syndrome as a child. Furthermore, the patient's right kidney was removed along with a “benign” kidney mass in 2014. Intraoral examination revealed an edentulous patient with a pink-red, oval, ulcerated lesion with a white pseudomembranous surface measuring approximately 38 mm × 25 mm × 17 mm attached to the left buccal mucosa via a pedunculated stalk (Figure 1A). No regional lymphadenopathy was apparent, and a complete head and neck examination was otherwise unremarkable. Other remarkable findings included a significantly elevated blood pressure of 180/100 and a pulse rate of 90. At the time of presentation, the patient was not under the care of a physician.

DIFFERENTIAL DIAGNOSIS

Based on the clinical features of the lesion, the following differential diagnoses were generated: pyogenic granuloma, buccal...
fat pad herniation, traumatic ulcerative granuloma, squamous cell carcinoma, and metastatic disease. Subsequently, the patient was scheduled for surgical excision of the lesion, subject to adequate control of her blood pressure.

4  |  OUTCOME

At the time of surgery, 4 weeks after the initial presentation, the lesion had increased in size to approximately 50 mm × 30 mm × 25 mm (Figure 1B). A complete excision of the buccal mucosa lesion was achieved, following local anesthetic infiltration, and the specimen (Figure 1C) submitted for histopathologic examination. Histologic examination of the specimen revealed an ulcerated surface mucosa, showing organoid nests of polygonal cells partitioned by fibrovascular septa and delicate capillary-sized vascular channels, imparting an alveolus-like formation in areas (Figure 2). Tumor islands were infiltrative with prominent areas of central necrosis and hemorrhage. The malignant cells exhibited features of pleomorphism, hyperchromatism, prominent nucleoli, and increased and abnormal mitoses, with notable cytoplasmic clearing (clear cell morphology). Immunohistochemistry, with appropriate

**FIGURE 1** Clinical presentation of intraoral lesion. A, Initial presentation left buccal mucosal lesion with ulcerated and pseudomembranous surface attached to the buccal mucosa by pedunculated stalk. B, Presentation at time of surgery 4 wk later. C, Gross specimen following surgical removal

**FIGURE 2** Hematoxylin-and-eosin–stained histologic sections of excised specimen. A, Low power (4X) shows sheets of clear cells demarcated by thin fibrous septa and ulcerated surface. B, High power (40X) shows clear cells with pleomorphic renal cell carcinoma cells
positive and negative controls, was positive for AE1/AE3 and renal cell carcinoma (RCC) antigen (Figure 3). However, S-100 (not shown) showed punctate positivity, while Melan-A, myogenin, HMB-45, chromogranin were negative (not shown). The characteristic histopathologic features in combination with the immunohistochemistry findings confirmed a definitive diagnosis of metastatic RCC. The Table 1 summarizes the results of the immunohistochemistry panels investigated.

Following a histologic diagnosis, the patient was referred to a specialist hospital for further consultations and management. It was determined that the patient already had disseminated disease to distant organs, including metastasis to the brain. Unfortunately, the patient died from widely disseminated disease few months later.

| Tumor markers       | Immunohistochemistry result |
|---------------------|----------------------------|
| AE1/AE3             | +                           |
| S-100               | (+)                         |
| Melan-A             | -                           |
| HMB-45              | -                           |
| Myogenin            | -                           |
| Renal cell carcinomas | +                          |
| Chromogranin       | -                           |
| Synaptophysin       | -                           |

Note: Key: + = positive; (+) = punctate positive; and − = negative.

5 | DISCUSSION

A salient histopathologic feature of the present case is a distinct and dominant clear cell feature warranting consideration of a constellation of differential diagnosis of clear cell neoplasms of the oral cavity. These include primary and malignant neoplasms of the salivary glands such as mucoepidermoid carcinoma (MEC), clear cell oncocytoma, acinic cell carcinoma (ACC), epithelial myoepithelial carcinoma (EMC), clear cell...
The mechanism of RCC metastasis to the oral cavity is postulated to occur via arterial and paravertebral venous routes (Batson's plexus) rather than the lymphatic system, bypassing the filtration system and enabling the dissemination of tumor cells to the lung.\(^7\,18\,19\) Perhaps, this explains the concurrent metastasis to other distant secondary organs such as the lungs, brain, and liver in about two-thirds of the patients.\(^19\) Concurrent detection of metastatic RCC at multiple sites has been enhanced following the advent of imaging technologies such as computed tomography (CT), magnetic resonance imaging (MRI), and fluoro-2-deoxy-D-glucose positron emission tomography (FDG).\(^19\)

Cases of Guillain-Barre syndrome (an acute immune-mediated inflammatory peripheral neuropathy) developing in metastatic RCC patients treated with pazopanib and sunitinib malate have been reported.\(^21\,22\) In the present case, patient was diagnosed with Guillain-Barre syndrome as a child prior to a diagnosis of a kidney mass made in 2014 as an adult. Notably, there was no history of treatment with sunitinib, or related drugs, prior to the diagnosis of Guillain-Barre syndrome in the current case.

Although surgical excision of primary and metastatic lesions remains a standard procedure in the management of patients with RCC, there has been an increased insight into the molecular biology of RCC offering the potential for the development of new therapeutic strategies.\(^23\,24\) Unfortunately, surgical treatment of RCC patients remains a palliative measure as over 90% of patients die within one year of diagnosis.\(^3\,23\,24\)

In conclusion, metastatic RCC to the oral cavity, because of its rarity, presents a diagnostic oddity. In the present case, the oral tumor was the initial sign and presentation of the disease prompting further investigation into the primary source and location. Clinicians should therefore increase their index of suspicion for solid oral mucosal lesion to include the possibility, though very rare, of metastatic RCC that may clinically masquerade as local and benign epulides of the oral mucosa. Prompt excision of such lesion and submission of the specimen for histopathologic examination should constitute a routine practice.
CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTION
SP: involved in examination of patient and diagnosis, surgical treatment and follow-up of patient, and preparation of draft of the manuscript. JB: involved in examination of patient and diagnosis, surgical treatment and follow-up of patient, and preparation of draft of the manuscript. NN: involved in examination of patient and diagnosis, histopathologic diagnosis of surgical specimen, and preparation of draft of the manuscript. KO: involved in histopathologic diagnosis of surgical specimen, preparation of draft of the initial manuscript, review and correction of final manuscript, and submission of the manuscript.

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