An Extremely Rare Primary Intestinal-Type Mucinous Adenocarcinoma of Floor of Mouth Masquerade as Ranula

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Received: 28 January 2025

Accepted: 11 January 2026

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DOI 10.5001/omj.2030.01

Abstract

Background: Primary intestinal-type adenocarcinoma (ITAC) of the floor of mouth (FOM) is extremely rare, with only two cases reported worldwide to date. The two cases were described as malignant transformation of a congenital cyst at the FOM. Our presenting case is the first reported case of primary ITAC arising from the minor salivary gland of the FOM. Due to the rarity and submucosal growth characteristic, it might be misdiagnosed as a more common benign lesion like ranula. Case presentation: We present a case of primary ITAC arising from the minor salivary gland of the FOM, which masquerades as a ranula at the initial stage. Conclusion: The diagnosis is challenging, time-consuming and requires multiple modalities and multidisciplinary team approach. It is important to completely exclude metastatic adenocarcinoma, especially from the gastrointestinal tract, before concluding the final diagnosis of primary ITAC of FOM. Currently, there is no proper treatment guideline, and the majority are based on the previous reported case, the more common primary ITAC of sinonasal tract and oral cavity squamous cell carcinoma. The prognosis is yet to be defined due to the limited number of reported cases and the time of follow-up.

Keywords: adenocarcinoma, intestinal-type, floor of mouth, ranula

Introduction

Primary intestinal-type adenocarcinoma (ITAC) involving the oral cavity is extremely rare with only 19 cases reported worldwide to date.[1] Out of these, only 15 cases arose from the oral cavity subsites, and only two cases arose from the floor of the mouth. The two floor of mouth (FOM) cases were malignant transformation of a congenital sublingual teratoid cyst and lingual foregut duplication cyst, which appeared as a cystic lesion at the FOM on presentation.[2,3] Due to this rarity and location of the tumour, primary ITAC at FOM could be misdiagnosed as other more common lesion, like a ranula at the initial stage.

It is essential to thoroughly investigate and completely exclude the possibility of metastatic adenocarcinoma before labelling as primary ITAC of FOM. Although it is rare, accounting for only 1% of all oral cavity malignancies, the tumour could originate from the renal, hepatic, lung, endometrial, adrenal, thyroid, bone/soft tissue, and colorectal areas.[4,5]

Case report

A 41-year-old male with no medical illness presented with a six-month history of painless swelling of the FOM, associated with painless neck swelling and slurred speech for two months and dysphagia and shortness of breath for two weeks. The swelling of the FOM and neck was gradually increasing in size. Subsequently, the patient's tongue slowly deviated to left and speech became slurred. Dysphagia had progressively worsened, and the patient was able to tolerate the soft diet only for the past two weeks. The shortness of breath occurred when the

patient was lying down and on exertion. There was no history of trauma or surgery to the oral cavity, no fever or upper respiratory tract infection and no loss of appetite or loss of weight. He denied smoking, alcohol consumption or betel nut chewing and has no family history of malignancy.

Upon examination, the patient was in an upright position without any signs of respiratory distress. However, the patient was unable to lie flat for more than 10 minutes due to shortness of breath. The speech was slurred with the tongue deviated to the left side on tongue protrusion (Figure 1A) and reduced sensation at the left anterior 2/3 of the tongue. There was a smooth surface submucosal mass at the FOM causing significant displacement of the tongue superiorly and posteriorly (Figure 1B). The mass had a smooth surface, ill-defined margin, non-tender and firm in consistency upon palpation. The oropharynx was not visualised as obscured by the anterior 2/3 of the tongue. Neck examination revealed diffuse swelling at the left submandibular region with ill-defined margin, non-tender, firm in consistency, immobile and likely continuous with the FOM mass (Figure 1C). Flexible nasopharyngolaryngoscopy showed posterior displacement of the base of the tongue, causing partial obstruction of the oropharyngeal airway. Otherwise, laryngeal structures were normal. Other head and neck examinations were unremarkable.

A contrast enhanced computed tomography (CT) scan of neck was performed and showed a large, well-defined near-homogenous predominantly fluid density mass seen occupying the entire sublingual space arising from the left, measuring approximately 7.1cm x 6.6cm x 6.3cm (Figure 2). No enlarged cervical lymph node. The overall features are suggestive of a ranula causing airway narrowing.

Due to the high pre-operative suspicion for a simple ranula, where biopsy is non-diagnostic and risks spillage, a decision was made to proceed directly to excisional surgery. The patient underwent transcervical excision of the mass with keep in view of combined intra-oral approach if indicated. The surgery began with a left submandibulectomy, and the mass was exposed (Figure 3). Surprisingly, the mass was solid in nature, adhering to some extrinsic muscle of the tongue, and the tumour invaded the left hypoglossal nerve. After delineation from the surrounding muscles and soft tissues, the mass was successfully excised in total (Figure 4). The hypoglossal nerve was sacrificed. Postoperatively, the patient was able to lie flat without shortness of breath. However, the speech and swallowing were severely impaired due to immobile tongue. The speech and tongue movement were gradually improving and returned to baseline, while dysphagia was resolved after two months of aggressive rehabilitation by the speech and language therapist.

The histopathological examination revealed tumour tissue arranged in a colloid pattern with nests and glands of malignant cells suspended in the abundant pool of extracellular mucin (Figure 5). There was presence of dyscohesive signet-ring cells, and the malignant cells invading front have an infiltrative edge with involvement of adjacent skeletal muscle tissue. Immunohistochemistry (IHC) study revealed positivity for CK20, CDX2 and CK7 and negativity for P40, P63, TTF-1 and SMA. The overall histological features are suggestive of mucinous adenocarcinoma with intestinal differentiation and presence of positive margin and perineural invasion. The excised submandibular gland was negative for malignancy.

The patient was referred to the general surgery team to rule out primary malignancy from gastrointestinal tract (GIT). After thorough examination and investigation with whole body CT scan, positron emission tomography (PET) scan, oesophagogastroduodenoscopy, colonoscopy and biopsy, all results showed negative findings. Thus, the final diagnosis was FOM mucinous adenocarcinoma with intestinal differentiation without regional or distant metastasis (T4aN0M0 based on American Joint Committee on Cancer staging system). Subsequently, patient was referred to oncologist and planned for adjuvant concurrent chemoradiotherapy.

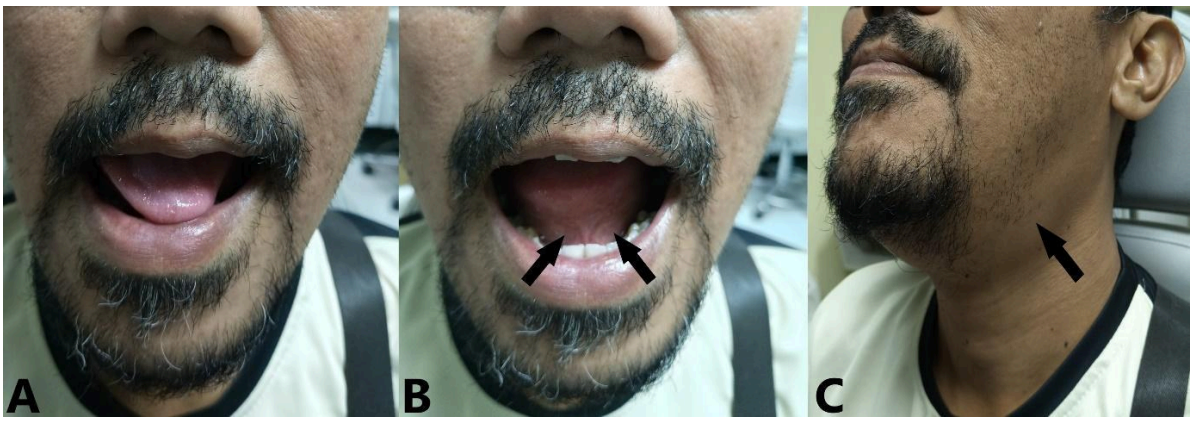

Figure 1: A. Tongue deviated to left side on tongue protrusion. B. Smooth surface submucosal mass at the floor of mouth causing significant displacement of the tongue superior and posteriorly. C. Diffused swelling at the left submandibular region likely continuous with the floor of mouth mass.

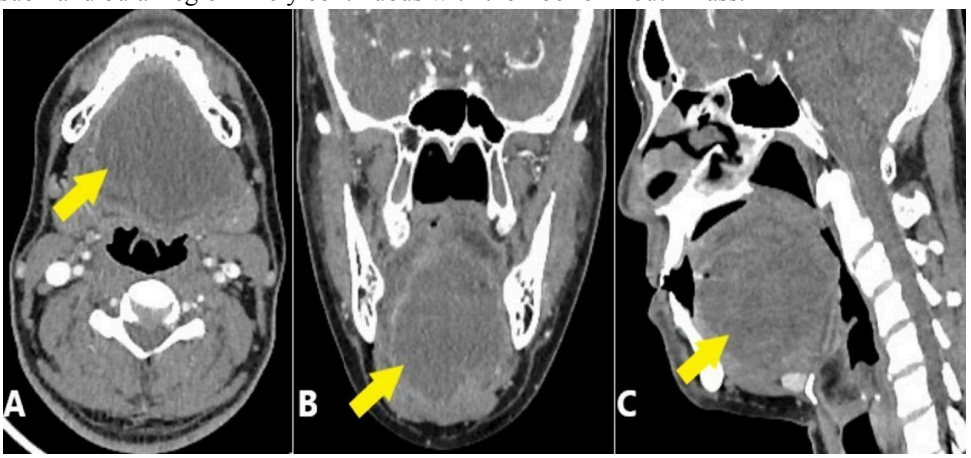

Figure 2: Contrasted computerized tomography (CT) scan of neck in axial (Figure A), coronal (Figure B) and sagittal (Figure C) views shows large well-defined near homogenous predominantly fluid density mass seen occupying the entire sublingual space and causing airway narrowing.

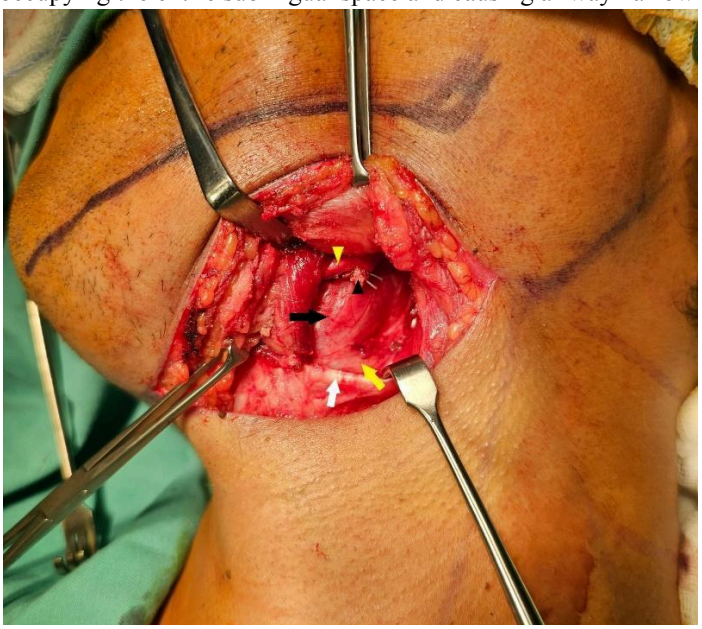

Figure 3: Mass (black arrow) immediately medial to left submandibular gland is exposed after submandibulectomy. The left hypoglossal nerve is invaded by the tumour. White arrow – posterior belly of digastric; yellow arrowhead – left lingual nerve; black arrowhead – stump of left submandibular ganglion.

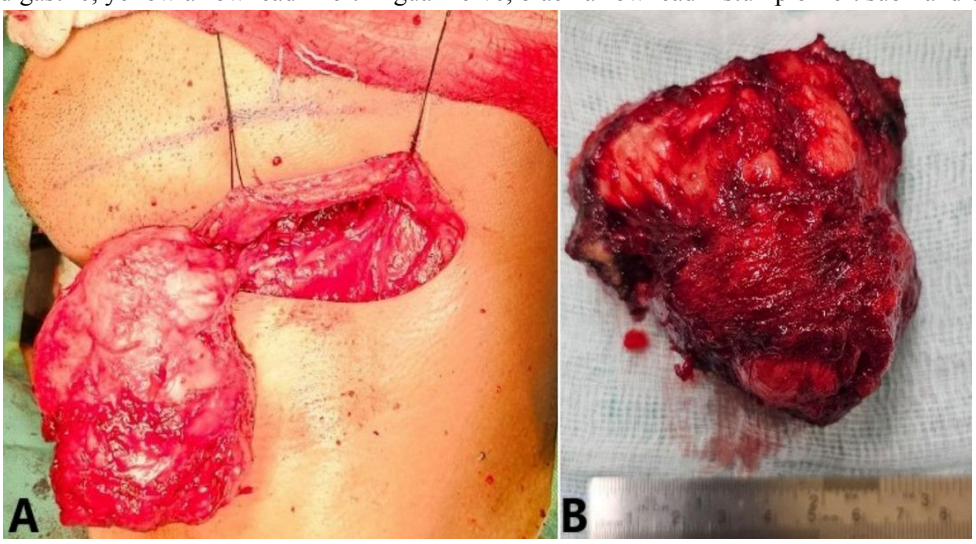

Figure 4: A. A solid mass is removed in total after delineation from the surrounding muscles and soft tissues. B. The mass removed adhered to some extrinsic muscle of the tongue.

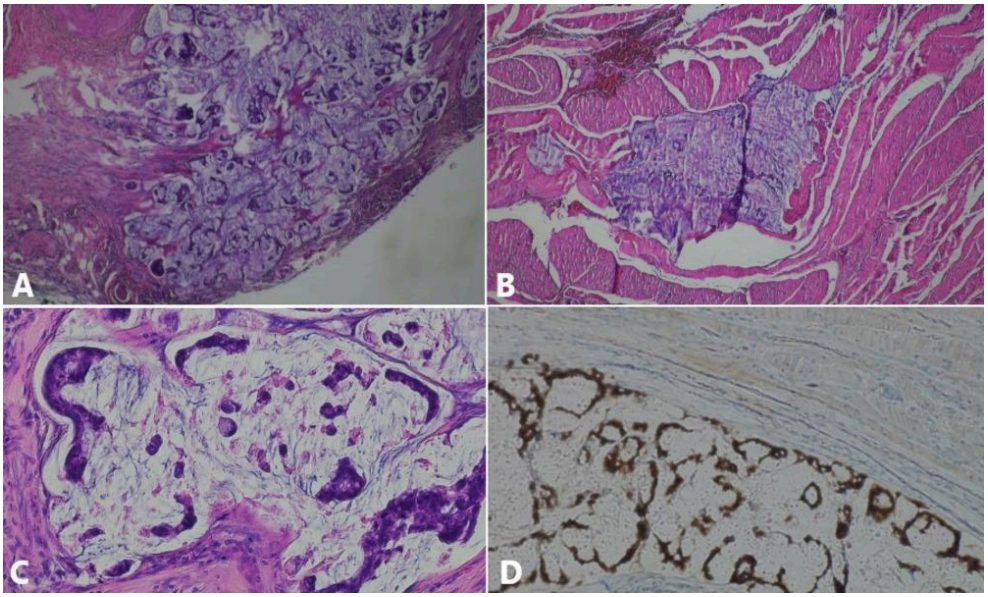

Figure 5: Nests and glands of malignant cells suspended in abundant pool of extracellular mucin (Figure A, H&E x200). Infiltrative focus of malignant cells within the bundles of skeletal muscle tissue (Figure B, H&E x200). Some of the cells have abundant intracytoplasmic mucin pushing the nuclei to the periphery imparting a signet ring cell morphology (Figure C, H&E x400). Nuclear reactivity for CDX2 immunostaining demonstrates evidence of intestinal differentiation (Figure D, x400).

Discussion

Primary ITAC of the head and neck is rare, and the sinonasal tract is reported as the majority site of involvement.[6] Oral cavity origin is extremely rare and most commonly involves the tongue.[1,4] Up to date, only two cases have been reported to originate from the FOM (Table 1).[1-3] However, both cases were different from our presenting case in terms of tissue origin. Agaimy *et al.* and Volchok *et al.* reported the primary ITAC of FOM arising from congenital cysts, namely sublingual teratoid cyst and lingual foregut duplication cyst,

respectively.[2,3] In the presenting case, we believed it originated from metaplasia of minor salivary glands based on the IHC staining features.

Primary head and neck ITAC are histologically similar to neoplastic intestinal mucosa, which categorised as a high-grade malignancy, often associated with regional and distant metastasis and a high recurrence rate.[7] Therefore, it is important to investigate fast, thoroughly and exclude possible metastasis, especially from GIT, before concluding as primary head and neck ITAC and introducing a treatment plan without delay. ITAC has been classified into five subtypes, namely papillary (18%), colonic (40%), solid (20%), mucinous, and mixed (approximately 20%).[7,8] This classification is clinically important in terms of prognosis, for example the papillary subtype is shown to be more indolent, while the solid and mucinous subtypes have poorer outcomes.[8]

The presenting symptoms are almost similar to other oral cavity malignancies, which typically involve disturbances in swallowing, speech and respiration. In addition, the FOM origin is more likely to have an early neurological deficit due to the proximity of the course of the hypoglossal and lingual nerves as seen in the presenting case. However, due to the growth characteristics of minor salivary gland tumours, which occur submucosally, they may resemble and misdiagnosed as benign lesions at the initial stage. The most common benign lesion of FOM is ranula, which also present with a submucosal lesion.[9] On the other hand, squamous cell carcinoma is the most common malignant lesion of FOM[9], but it usually occurs in the elderly and presents with an exophytic or ulcerative mass instead submucosal lesion. Other factors that may favour a benign lesion in the presenting case are the patient's age, absence of smoking, alcohol consumption and betel nut chewing, no constitutional symptoms, negative family history of malignancy and no palpable lymph node. Hypoglossal and lingual nerves palsy could be the only red flag sign of malignancy in this case, but they can occur in huge benign lesions, especially in confined spaces like FOM, due to nerve compression.

Ideally, imaging should be performed before biopsy or definitive treatment, to assess the origin and extension of the lesion, as well as signs of malignancy such as irregular margins, necrotic centres, bony erosion, and enlargement of cervical lymph nodes, to guide proper biopsy for representative tissue and planning of surgery. CT scan has the advantage of being readily available in most centres, with a short waiting time, a fast procedure, and better in bony delineation. Magnetic resonance imaging is usually only available in major tertiary centres with long waiting times, but it has the advantage of better soft tissue delineation. Both imaging modalities complement each other, but the CT scan is usually the first-line imaging in the majority of cases. The presenting case underwent a CT scan, and the findings were consistent with ranula due to the location and homogeneous fluid density mass. No biopsy was performed prior to the definitive surgery because the ranula content is usually non-diagnostic and it is difficult to obtain epithelial lining tissue for cytology or histopathology examinations.

Our surgery was started with a transcervical approach and submandibulectomy as it provides a better and wider surgical field and is easier to trace the hypoglossal and lingual nerves. After submandibulectomy, the mass was immediately medial to the submandibular gland, and was solid in nature, rather than cystic. However, we decided to proceed with excision as the mass was feasible for total excision without additional complication or morbidity. We believe this is the best decision at that moment because the mass can be excised in total for diagnosis and therapeutic purposes, thereby avoiding a second operation under general anaesthesia.

The IHC study is critical, especially in a complex or sporadic cases. In this presenting case, CK20, CDX2 and CK7 markers were positive. The CK20 and CDX2 are markers for GIT, and their positivity could be due to metastasis from GIT or intestinal differentiation in the tumour.[8] While CK7 may suggest for primary origin of the tumour from the salivary gland.[6,7,10] The presence of a signet ring suggests a mucinous subtype, which has been shown to have a poorer outcome. The combination of histopathology examination, IHC study, PET and CT scans, esophagogastroduodenoscopy, colonoscopy, and biopsy strongly suggests primary ITAC from the minor salivary gland of the FOM. With these findings and diagnosis, our presenting case becomes the first reported case of primary ITAC arising from the minor salivary gland of the FOM.

Currently, there are no guidelines on the treatment of primary ITAC of the oral cavity or FOM due to its rarity and non-specific nature of the disease.[10] The most commonly employed treatment is surgical excision, while post-operative adjuvant radiotherapy and chemotherapy are based on the histological features. The presence of positive a margin and perineural invasion as seen in the presenting case, could benefit from adjuvant concurrent radiotherapy and chemotherapy. This treatment strategy is similar to that used for more common squamous cell carcinoma of the oral cavity. The unavoidable morbidity associated with FOM malignancy and surgery is disturbance of swallowing and speech functions, mainly due to the proximity or involvement of the

hypoglossal nerve. The hypoglossal nerve innervates all muscles of the tongue, except the palatoglossus muscle, which is crucial for oral phase swallowing and articulation. Early referral to a speech language therapist and aggressive oral rehabilitation, even before the operation, is of paramount importance to minimise the complications. The prognosis remains undefined due to the limited number of reported cases and short follow-up period. A retrospective study of sinonasal adenocarcinoma showed no difference in prognosis between intestinal and non-intestinal subtypes of sinonasal adenocarcinoma.[11]

Table 1: Review of reported cases of floor of mouth intestinal-type adenocarcinoma

Author	Year	Age	Sex	Origin	Presentation	Pre-operative biopsy/ cytology	Pre-operative impression	IHC profile	Treatment
Agaimy et al (2)	2007	41-year-old	M	Sublingual teratoid cyst	Midline prelaryngeal mass since birth, dysphagia and dyspnoea for few weeks.	No	Median cervical cyst	Strong reactivity for EMA, pan-keratin (AE1/AE3), CK20 and CEA. Negative stain for CK7, CK14, S100 and TTF-1.	Excision via a combined oral and extra-oral approach and subsequent ipsilateral neck dissection.
Volchok et al (3)	2007	61-year-old	M	Lingual foregut duplication cyst	Progressive dysphagia, dry mouth, and changes of voice for 3 months.	No	Thyroglossal duct cyst or ranula.	NA	Transoral excision Postoperative concurrent chemotherapy and radiotherapy
Presenting case	2025	41-year-old	M	Minor salivary gland of the FOM	Painless swelling of FOM, neck swelling and slurred speech for 2 months and dysphagia and shortness of breath for 2 weeks.	No	Ranula	Positive for CK20, CDX2 and CK7 and negative for P40, P63, TTF-1 and SMA.	Transcervical excision Postoperative concurrent chemotherapy and radiotherapy

M: male; FOM: floor of mouth; IHC: immunohistochemistry; NA: not available.

Conclusion

Primary ITAC of FOM is extremely rare. Malignant transformation with intestinal differentiation of the minor salivary gland of FOM, which has been previously proposed as one of the theories of origin was demonstrated for the first time in this presenting case. It may be misdiagnosed as a benign lesion, such as a ranula, at initial

stage. The diagnosis is challenging and requires multiple modalities and a multidisciplinary team approach. The treatment guideline and prognosis are yet to be defined due to the very limited number of cases reported. With the emergence of histopathology and radiological expertise and technologies, we hope this disease entity will be more reported in the future.

Disclosure

The authors declared no conflicts of interest. Informed consent was obtained from the patient.

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