Published in final edited form as:

Hum Pathol. 2009 December ; 40(12): 1798–1802. doi:10.1016/j.humpath.2009.01.028.

Primary Colonic -Type Adenocarcinoma of the Base of the Tongue: a Previously Unreported Phenotype

Diana Bell, M.D.^a, Michael E. Kupferman, M.D.^b, Michelle D. Williams, M.D.^a, Asif Rashid, M.D.^a, and Adel K. El-Naggar, M.D., Ph.D.^{a,b}

^a Departments of Pathology, The University of Texas M.D. Anderson Cancer Center, Houston, TX

^b Department of Head and Neck Surgery, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Abstract

Primary lingual adenocarcinomas are rare and typically of salivary or seromucinous glands origin. Similarly, metastatic adenocarcinoma from distant primary sites to the tongue is an uncommon event, with only three cases from a colonic primary site reported. We present, for the first time, two primary colonic-type adenocarcinomas of the base of the tongue and discuss their putative origin and the clinicopathologic characteristics.

Keywords

Base of tongue; Primary adenocarcinoma; Intestinal-type; Metastatic carcinoma

INTRODUCTION

Primary lingual adenocarcinomas are rare and predominantly of salivary or seromucinous glands origin (1–5). Similarly, metastatic adenocarcinomas to the tongue are uncommon and comprise approximately 35% of all secondary tumors at this location (3,6–16). Of the latter, only three instances of colonic adenocarcinoma to the tongue have been reported (9,12,14).

We present, for the first time, two primary colonic-type adenocarcinomas of the base of the tongue and discuss their putative origin, clinicopathologic characteristics, and the differential diagnosis.

CASE REPORTS

Case #1

A 58-year-old male presented with recent oral bleeding and a tongue mass. The patient's significant medical history included hypertension and a long history of smoking. Physical examination revealed a firm mass occupying the base of the tongue with extension into the oral tongue (Fig 1). No lymphadenopathy was identified on examination. A biopsy was

Correspondence to: Adel K. El-Naggar, MD, PhD, Professor of Pathology and Head and Neck Surgery, Unit 85, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030 (anaggar@mdanderson.org)., Telephone: 713-792-3109; fax: 713-792-5532.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

taken and revealed colonic-type adenocarcinoma. Extensive examination (colonoscopy, PET/CT) failed to identify any gastrointestinal primary tumor. Induction chemotherapy was initiated, and after 6 weeks with no noticeable response the patient underwent total glossectomy and left neck dissection. On gross examination, the mass was 3 cm in size and centrally located in the submucosa of the base of tongue with extension into mobile tongue. The tumor showed a light-tan appearance and was firm with infiltrative ill-defined margins. Lymph node examination revealed microscopic metastatic carcinoma in only one level 3 lymph node. The postoperative course was uneventful and the patient has remained free of recurrence and metastasis to the last follow-up (13 months).

Case #2

A 58-year-old male presented with a history of bilateral neck adenopathy, macroglossia, pain, hoarseness, and slurred speech of one year's duration. The patient's significant medical history included hypertension and a long history of smoking. On physical examination an irregular ulcerated submucosal indurated mass in the base of the tongue and bilateral lymphadenopathy was noted. A biopsy of the tongue mucosa was taken and an adenocarcinoma with colonic features was diagnosed. A chest x-ray and CT-scan revealed multiple bilateral lung nodules. PET/CT scan and lower and upper gastrointestinal endoscopy showed no evidence of gastrointestinal primary tumors, and no other metastatic lesions were identified. Induction chemotherapy was initiated but due to progression of the disease at the primary site and regional nodes, the patient underwent total glossectomy and bilateral neck dissection. Grossly, a 4.5 cm firm and ill-defined mass was located in the base of tongue submucosa with extension in the anterior two thirds of the tongue (Fig. 2). Metastatic carcinoma to bilateral multilevel lymph nodes was found. The patient has remained free of recurrence and metastasis to the last follow-up (11 months) with excellent quality of life and return of function.

Methods

Immunohistochemistry (IHC)

Immunohistochemically, the following primary antibodies were used by the ABC-method: CDX2, CK7, CK20, and beta-catenin. Microsatellite instability status was also assessed by IHC for hMLH1, hMSH2, hMSH6, hPMS-2 mismatched repair proteins (17,18).

DNA analysis

DNA was isolated from paraffinized normal and tumor tissues using microdissection. The isolated DNA was of good purity, as judged by the fact that the A_{260}/A_{280} value of approximately 1.8. *K-ras* was amplified by polymerase chain reaction (PCR). The purified PCR products were applied to the fluorescent dye terminator cycle sequencing reaction (Perkin Elmer, Rodgau, Germany). Analysis of the product of the sequencing reaction was performed on an ABI Prism 310 sequencer (Applied Biosystems, Darmstadt, Germany). Nucleotide sequence alignment was performed with DNA Star software (DNASTAR, Inc, Madison, WI). All sequence reactions were performed in both directions and tested for concordance.

Results

a) Histopathology

Tumors in both patients were invasive well to moderately differentiated colonic-type adenocarcinomas (Figs. 3, 4). The colonic malignant epithelial cells forming tubular and glandular structures with intra-glandular necrosis were dominantly observed in both tumors, with a significant mucinous component found in the tumor from patient #2 (Fig. 4).

b) Immunohistochemistry

Both tumors manifested strong positive membranous/cytoplasmic staining for CK20 and beta-catenin, and nuclear staining for CDX2. CK7 staining was negative in carcinoma #2 (Fig. 4) and focally positive in tumor #1 (Fig. 3) (Table 1). Tumor cells in both cases showed nuclear staining for hMLH1, hMSH2, hMSH6, and hPMS-2 mismatch repair proteins.

c) *K-ras* Analysis

DNA sequencing of codons 12, 13, and 61 of the *K-ras* revealed no mutations.

DISCUSSION

We report a previously undocumented primary colonic-type adenocarcinoma of the base of the tongue in patients who had no prior or concurrent evidence of primary intestinal malignancy. The tumors were located in the submucosa of the base of the tongue and manifested histopathologic features and immunohistochemical profiles characteristic of primary colonic adenocarcinoma with a mucinous component. Interestingly, in both patients neck lymph node metastasis similar in distribution to those of primary base tongue carcinoma of squamous origin were found: the first patient had a single microscopic metastatic focus, while the second patient had widespread bilateral neck disease. The lack of primary colonic carcinoma and the anatomic restriction of metastasis to the neck lymph nodes supported the primary lingual origin of these tumors.

The primary clinical and pathologic issue in both cases was the exclusion of metastasis from a colonic primary site, especially with positive immunohistochemical staining for CK20 and CDX2 in both tumors. Moreover, all reported metastatic colonic carcinomas to the tongue were also submucosal and presented at a similar lingual location (Table 2). In contrast to our cases, all metastatic colon carcinoma to the tongue were preceded by colonic primary tumors (9,12,14). Taken together, the lack of colonic primary tumors and the selective metastasis to the neck nodes formed the basis for the primary lingual origin of our cases. Interestingly, the recent finding of an adenocarcinoma in a foregut duplication cyst of the floor of the mouth of a 61-year-old male may suggest an alternative origin for this phenotype (19). No evidence of a preexisting rudimentary cystic structure was found in our cases.

The histogenesis of both tumors is uncertain but an origin from a transformed minor salivary duct epithelium at this location is a likely possibility (20–25). This is supported by the IHC findings in both tumors and by studies of primary intestinal-type adenocarcinoma of the sinonasal tract where evidence of respiratory epithelium transformation to an intestinal phenotype have been noted in the adjacent non-neoplastic epithelium (18,26–29). The transdifferentiation of the respiratory to the intestinal type epithelium was associated with a reversal of the CK7/CK20 expression in the metaplastic epithelium which was maintained in the developing carcinoma (5,18,28). It is interesting, however, that similar primary phenotype in the lung manifested an immunoprofile consistent with primary adenocarcinoma and were negative for CK20 and CDX2 (30). These differences could be related to epigenetic differences between upper and lower respiratory epithelium.

Our analysis of the molecular alteration common to colonic adenocarcinoma in these tumors revealed a lack of alteration in the *K-ras* gene and hMLH1, hMSH2, hMSH6, hPMS-2 mismatch repair protein expression. Studies of similar tumors in the sinonasal tract have also shown infrequent alterations of these genes (18); only a single *K-ras* mutation was identified in one of the six tumors studied.

The small number of tumors analyzed, however, precludes any definitive conclusion on the involvement of these alterations tumors from extra-colonic. Although none of our patients developed either local or distant disease one year after surgery, the clinical outcome should be guarded.

Acknowledgments

Supported by: This work was supported in part by the Kenneth D. Müller Professorship, National Cancer Institute Specialized Program of Research Excellence (SPORE) grant in head and neck cancer and the National Cancer Institute grant CA-16672.

References

1. Franchi, A.; Santucci, M.; Wenig, B. Adenocarcinoma. In: Barnes, L.; Eveson, JW.; Reichart, P.; Sidransky, D., editors. Pathology and genetics of head and neck tumours. IARC Press; Lyon: 2005. p. 20-3. WHO classification of tumours
2. Goldblatt LI, Ellis GL. Salivary gland tumors of the tongue. Analysis of 55 new cases and review of the literature. *Cancer*. 1987; 60:74–81. [PubMed: 3034395]
3. Torres-Carranza E, Garcia-Perla A, Infante-Cossio P, et al. Airway obstruction due to metastatic renal cell carcinoma to the tongue. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006; 101:E76–8. [PubMed: 16504856]
4. Izumi K, Nakajima T, Maeda T, et al. Adenosquamous carcinoma of the tongue: report of a case with histochemical, immunohistochemical, and ultrastructural study and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998; 85:178–84. [PubMed: 9503453]
5. Michal M, Skalova A, Simpson RH, et al. Cribriform adenocarcinoma of the tongue: a hitherto unrecognized type of adenocarcinoma characteristically occurring in the tongue. *Histopathology*. 1999; 35:495–501. [PubMed: 10583573]
6. Zegarelli DJ, Tsukada Y, Pickren JW, et al. Metastatic tumor to the tongue. Report of twelve cases. *Oral Surg Oral Med Oral Pathol*. 1973; 35:202–11. [PubMed: 4513066]
7. Wang HY, Su CY, Lin JW, et al. Base of the tongue metastatic cancer from hepatocellular carcinoma: a case report. *Eur Arch Otorhinolaryngol*. 2004; 261:531–3. [PubMed: 14727125]
8. Shehab Z, Desousa S, Pahor AL. Metastasis in tongue from carcinoma of bronchus: a case report. *J Laryngol Otol*. 1994; 108:1099–101. [PubMed: 7861094]
9. Piattelli A. Lingual metastasis from a carcinoma of the colon. A case report and review of the literature. *Acta Stomatol Belg*. 1990; 87:257–64. [PubMed: 1966235]
10. Marioni G, Savastano M, Mattiello L, et al. Tongue base metastasis from neuroendocrine endometrial small cell carcinoma. *Am J Otolaryngol*. 2007; 28:284–7. [PubMed: 17606050]
11. Kurt M, Bulut N, Aksoy S, et al. Anterior tongue metastasis from lung cancer. *South Med J*. 2006; 99:784–5. [PubMed: 16866071]
12. Hatziotis JC, Constantinidou H, Papanayotou PH. Metastatic tumors of the oral soft tissues. Review of the literature and report of a case. *Oral Surg Oral Med Oral Pathol*. 1973; 36:544–50. [PubMed: 4580924]
13. Dominici A, Rizzo M, Travaglini F, et al. Non-functioning adrenal cortical carcinoma presenting with metastasis to the tongue. *J Oral Pathol Med*. 2003; 32:185–7. [PubMed: 12581389]
14. Davidson C. Chorionepithelion und Magenkrebs eine selten Verschmelzung zweier boesartiger Geschwulste. *Chaite-Ann*. 1905; 29:426–37.
15. Cochrane TJ, Cheng L, Crean S. Renal cell carcinoma: A rare metastasis to the tongue--a case report. *Dent Update*. 2006; 33:186–7. [PubMed: 16700276]
16. Baden E, Duvillard P, Micheau C. Metastatic papillary endometrial carcinoma of the tongue. Case report and review of the literature. *Arch Pathol Lab Med*. 1992; 116:965–8. [PubMed: 1524464]
17. McKinney CD, Mills SE, Franquemont DW. Sinonasal intestinal-type adenocarcinoma: immunohistochemical profile and comparison with colonic adenocarcinoma. *Mod Pathol*. 1995; 8:421–6. [PubMed: 7567943]

18. Yom SS, Rashid A, Rosenthal DI, et al. Genetic analysis of sinonasal adenocarcinoma phenotypes: distinct alterations of histogenetic significance. *Mod Pathol*. 2005; 18:315–9. [PubMed: 15492756]
19. Volchok J, Jaffer A, Cooper T, et al. Adenocarcinoma arising in a lingual foregut duplication cyst. *Arch Otolaryngol Head Neck Surg*. 2007; 133:717–9. [PubMed: 17638787]
20. Barnes L. Intestinal-type adenocarcinoma of the nasal cavity and paranasal sinuses. *Am J Surg Pathol*. 1986; 10:192–202. [PubMed: 3953940]
21. Choi HR, Sturgis EM, Rashid A, et al. Sinonasal adenocarcinoma: evidence for histogenetic divergence of the enteric and nonenteric phenotypes. *Hum Pathol*. 2003; 34:1101–7. [PubMed: 14652810]
22. Donhuijsen K, Hattenberger S, Schroeder HG. Nasal sinus carcinoma after wood dust exposure. Morphological spectrum of 100 cases. *Pathologe*. 2004; 25:14–20. [PubMed: 14767608]
23. Franquemont DW, Fechner RE, Mills SE. Histologic classification of sinonasal intestinal-type adenocarcinoma. *Am J Surg Pathol*. 1991; 15:368–75. [PubMed: 2006716]
24. Gnepp DR, Heffner DK. Mucosal origin of sinonasal tract adenomatous neoplasms. *Mod Pathol*. 1989; 2:365–71. [PubMed: 2548183]
25. Hopkin N, McNicoll W, Dalley VM, et al. Cancer of the paranasal sinuses and nasal cavities. Part I. Clinical features. *J Laryngol Otol*. 1984; 98:585–95. [PubMed: 6429261]
26. Bashir AA, Robinson RA, Benda JA, et al. Sinonasal adenocarcinoma: immunohistochemical marking and expression of oncoproteins. *Head Neck*. 2003; 25:763–71. [PubMed: 12953313]
27. Ariza M, Llorente JL, Alvarez-Marcas C, et al. Comparative genomic hybridization in primary sinonasal adenocarcinomas. *Cancer*. 2004; 100:335–41. [PubMed: 14716769]
28. Kennedy MT, Jordan RC, Berean KW, et al. Expression pattern of CK7, CK20, CDX-2, and villin in intestinal-type sinonasal adenocarcinoma. *J Clin Pathol*. 2004; 57:932–7. [PubMed: 15333652]
29. Korinth D, Pacyna-Gengelbach M, Deutschmann N, et al. Chromosomal imbalances in wood dust-related adenocarcinomas of the inner nose and their associations with pathological parameters. *J Pathol*. 2005; 207:207–15. [PubMed: 16041693]
30. Yousem SA. Pulmonary intestinal-type adenocarcinoma does not show enteric differentiation by immunohistochemical study. *Mod Pathol*. 2005; 18:816–21. [PubMed: 15605076]

Fig. 1.
CT of the neck with IV contrast showing an enhancing tongue mass (case #1).

Fig. 2.
The 4.5 cm firm tumor with ill-defined infiltrative boundaries was located in the submucosa (carcinoma #2).

Figs 3–4.

The carcinomas in both patients were a well to moderately differentiated colonic-type adenocarcinoma, with characteristic columnar malignant epithelial cells forming tubular and glandular structures, and with intra-glandular necrosis (Figs. 3, 4). The carcinomas of patient #2 exhibited considerable mucinous component (Fig. 4). Both carcinomas manifested strong positive staining for CK20 and CDX2 (Figs 3, 4). No CK7 staining was noted in carcinoma #2 (Fig 4) but in carcinoma #1 a focal staining was noted in tumor cells (Fig. 3).

Table 1

Immunomarkers in Invasive Intestinal-Type Adenocarcinoma of Tongue

Case #	CK7	CK20	CDX-2	β -Catenin
1	-*	+	+	+
2	-	+	+	+

* Focal positivity in few cells; -: Negative; +: Positive

Table 2

Clinicopathologic Features Intestinal-Type Adenocarcinoma in Tongue

Status	Age	Sex	Size (cm)	Site	Location	Time to mets	Disseminated disease
Metastasis							
Colon	54	M	2.5	LT	SM	3 months	UK
Rectum	68	M	2.5	BOT	SM	36 months	Yes
Colon	53	F	1.5	BOT	SM	7 months	Yes
Primary							
1	59	M	2.5	BOT	SM	Conc.	LN
2	59	M	3.5	BOT	SM	Conc.	LN, Lung

BOT: Base of Tongue; SM: Submucosal; LT: Lateral tongue; LN: Lymph node; UK: Unknown; Conc.: Concurrent