Basal cell adenocarcinoma of the buccal minor salivary gland with liver metastases

Si Chen, Shaodong Yang, Xinming Chen

From the *State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Department of Oral Implantology, School and Hospital of Stomatology, Wuhan University, Wuhan, China; †Department of Pathology, School and Hospital of Stomatology, Wuhan University, Wuhan, China

Correspondence: Xinming Chen · Department of Pathology, School and Hospital of Stomatology, Wuhan University, Wuhan, 430079, Hubei, China · T: (86)-27-87686375, F: (86)-27-87686375 · xmchen3011@126.com

Ann Saudi Med 2015; 35(4): 318-320
DOI: 10.5144/0256-4947.2015.318

Basal cell adenocarcinomas (BCACs) of salivary glands are rare malignant neoplasms that mostly affect the major salivary glands. They are generally considered low-grade carcinomas that are locally destructive and tend to recur, but only occasionally metastasize. Currently there are only a few reported cases of distant metastases from BCAC, and metastasis to the liver is not previously described. We report the first case of BCAC with histologically confirmed liver metastases. A 40-year-old man presented with a 2-month history of a painless swelling in the left buccal region. The lesion was completely resected, and the patient underwent postoperative radiotherapy. Permanent histology and immunohistochemical studies revealed a BCAC of the buccal minor salivary gland. After 14 months, two hepatic metastatic nodules were detected. The patient underwent a partial hepatectomy with adjuvant chemotherapy. No evidence of progressive disease or further recurrence was observed for 20 months after the hepatic metastasectomy. BCACs grow indolently and long-term survival can be expected. Surgery should be considered in selected patients as a therapeutic option in metastatic disease.
performed. The patient received adjuvant chemotherapy of 6 cycles using paclitaxel and carboplatin. No evidence of progressive disease or further recurrence was observed 20 months after the hepatic metastasectomy.

**PATHOLOGIC FINDINGS**

On gross pathologic examination, the resected tumor was solid, gray white and 1.5×1.5×1 cm in size. Microscopic examination of the specimen revealed an unencapsulated neoplasm consisting of basaloid cells with amphophilic cytoplasm and hyperchromatic to vesicular nuclei. The neoplasm showed solid growth patterns, often with peripheral palisading and a scanty hyalinized stroma. A membranous pattern was present focally, characterized by the production of eosinophilic hyalinized material both at the periphery and in the intercellular areas of the tumor nests. Focal areas of ductal structures and trabecular arrangement were also noted. Cytologic atypia was moderate, and areas of necrosis were focally evident. Mitoses were present (3 per 10 high power field). The tumor showed invasion of the adjacent minor salivary glands and soft tissues. At the periphery, a focus of vascular invasion was identified. Immunohistochemically, the tumor was diffusely positive for cytokeratin (CK) AE1/AE3, CK 34βE12, CK 5/6, and p63; focally positive for S100, and smooth muscle actin; negative for synaptophysin, and chromogranin. The Ki-67 labeling was 30%. The pathology of the two hepatic nodules was the same as that of the prior tumor of the cheek (Figure 2).

**DISCUSSION**

BCAC is an epithelial neoplasm that has cytological characteristics of basal cell adenoma but a morphologic growth pattern indicative of malignancy. It typically arises in individuals older than 60 years without gender predominance. It is most often found in the parotid gland, followed by the submandibular gland. Most BCACs probably develop de novo, but some arise by malignant transformation in basal cell adenomas. The tumor grows slowly and most patients are asymptomatic. Histologically, BCACs are characterized by a neoplasm composed of basaloid cells with 2 morphologic appearances: smaller cells with scant cytoplasm and dark nuclei, and polygonal cells with eosinophilic to amphophilic cytoplasm and pale basophilic nuclei. Four histomorphological architectural patterns (solid, membranous, tubular, and trabecular) have been described. While any combination of growth patterns may be seen in a single tumor, one usually predominates. The most common architectural pattern is a solid form.

Immunohistochemically, BCACs are uniformly reactive for cytokeratin. Positivity for carcinoembryonic antigen and epithelial membrane antigen has been noted in the majority of studied cases. The majority are also at least focally positive for smooth muscle actin, S-100, and vimentin, which demonstrate the presence of myoepithelial cells. However, the immunohistochemical profile of BCAC varies amongst cases and within different areas and architectural patterns of the same tumor. At the present time, none of the immunohistochemical reagents proved to be useful for confirmation of definite diagnosis of BCAC.

The major pathological differential diagnostic considerations for BCAC are basal cell adenoma, adenoid cystic carcinoma, basaloid squamous cell carcinoma and neuroendocrine carcinoma. The distinction between BCAC and basal cell adenoma is whether there is the presence of infiltrative and destructive growth and/or perineural or vascular invasion. The presence of a

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**Figure 1.** Computed tomography demonstrating two hypodense lesions in the right lobe of the liver (arrows).

**Figure 2.** Low power microphotograph showing the metastatic BCAC in the liver (hematoxylin-eosin stain, x20)
dual cell population composed of light and dark cells, absence of angular hyperchromatic cells and cribiform pattern helped distinguish them from adenoid cystic carcinoma. Also in favor of solid adenoid cystic carcinoma was a high mitotic index with necrosis. Basaloid squamous cell carcinoma shares some common microscopic features with BCAC, such as basaloid morphology, characteristic peripheral palisading of nuclei, foci of necrosis, and stromal hyalinization, but is characterized by extensive central necrosis and a higher histological grade. Unlike BCAC, basaloid squamous cell carcinoma shows squamous differentiation that involves the mucosal epithelium. Knowledge of tumor location may be useful, because basaloid squamous cell carcinoma has a predilection for the hypopharynx, base of the tongue, and supraglottic larynx, regions in which BCAC rarely occurs. Immunohistochemically, BCAC often shows reactivity for smooth muscle actin, S-100, and vimentin, but basaloid squamous cell carcinoma is negative for these. High-grade neuroendocrine carcinomas may have a basaloid pattern with peripheral palisading but exhibit mitotic activity, apoptosis, and necrosis beyond that seen in BCAC. Immunohistochemical examination of neuroendocrine markers is helpful in establishing a diagnosis of neuroendocrine carcinoma.10

Because of its rarity, there is limited data on the natural history of BCAC including its metastatic potential. It is generally considered a low-grade malignancy with favorable prognosis.2 In a group of 45 cases with available outcome data (median follow-up, 36 months; range, 5-192 months), only 4 patients (8%) subsequently developed positive cervical lymph nodes, 2 (4%) experienced distant metastases to the lungs and skin, and 1 (2%) died of local spread of tumor.9 Nagao et al reported 11 cases, with follow-up: 50% recurrent, none metastasized, and there were no deaths from tumor.9 In their review of the literature on BCAC of minor salivary glands, Parashar et al found a recurrence rate of 44% (8 of 18 patients), with 2 of 7 patients (12%) developing metastases to the regional lymph nodes.3 Furthermore, 2 of 17 patients (12%) died of disease. Distant metastases of BCAC are exceedingly rare with only five cases involving the lung, skin, mandible, hand, and brain reported.43 The present case is the first with metastasis to the liver and the first arising from minor salivary glands with distant metastasis.

Surgical excision with a wide margin to ensure complete removal has been suggested as the primary treatment for BCAC. Neck dissection is unnecessary unless there is definitive lymphadenopathy on clinical or radiologic examination. Radiotherapy has been proposed for diffusely infiltrative tumors or those with perineural or vascular invasion.3,5 In patients with metastatic disease, however, the potential therapeutic options are poorly defined. Watchful waiting, radiation therapy, palliative surgery, and systemic chemotherapy would be treatment options, but no standard palliative treatment modalities exist. Distant metastases are not necessarily inoperable. Ellis et al. described a patient with lung metastasis treated by lobectomy who was free of disease after 6 years.4 The present case showed an unusual presentation, with exclusive liver metastases 14 months after primary surgery. The patient underwent a partial hepatectomy with adjuvant chemotherapy. No evidence of progressive disease or further recurrence has been observed for 20 months after the hepatic metastasectomy.

In summary, this case highlights a rare manifestation of minor salivary gland BCAC metastatic to the liver. Unlike liver metastasis from other malignancies, BCACs grow indolently and long-term survival can be expected. Surgery could be considered in selected patients as a therapeutic option in metastatic disease.

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