Polymorphous low-grade adenocarcinoma of the epiglottis: A case report

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Abstract. Polymorphous low-grade adenocarcinoma is an uncommon malignant tumor derived from the terminal duct cells of the salivary glands. The present study described a rare case of polymorphous low-grade adenocarcinoma, T2N0M0 stage 2, in a 65-year-old man, who presented with a sore throat and painful dysphagia. Computed tomography revealed an infiltrative heterogenous enhancing mass involving the left aryepiglottic fold. He underwent a tumor removal with frozen section for evaluating the surgical margin. Subsequent supraglottic laryngectomy was performed. Polymorphous low-grade adenocarcinoma was diagnosed histologically, characterized by cytologic uniformly, morphologic diversity and an infiltrative growth pattern. Epiglottic cartilaginous invasion by the tumor is demonstrated. Clinical, radiological, endoscopic and pathological features with briefly reviewed relevant literatures are discussed. This is the first reported description in the literature, to the best of our knowledge, of an epiglottic polymorphous low-grade adenocarcinoma receiving successful supraglottic laryngectomy with 7 year disease free survival.

Introduction

Polymorphous low-grade adenocarcinoma (PLGA) is an uncommon malignant salivary gland tumor exhibiting cytologic uniformity, morphologic diversity, infiltrative growth pattern and low metastatic potential (1,2). The various appellations include terminal duct carcinoma and lobular carcinoma (1). PLGA originated from the reserve cells of the salivary gland and was introduced by the World Health Organization (WHO) as a new entity in 1990 (2). PLGA most commonly affects the minor salivary glands, primarily in the oral cavity, particularly the palate and buccal mucosa (1,2). Complete surgical excision with close evaluation of surgical margin remains the cornerstone of surgical management of PLGA. PLGA has a local recurrent rate of 9-17% and a regional metastatic rate of 9-15% (3). PLGA arising from the larynx is extremely rare and, to the best of our knowledge, only two cases have been previously reported (4,5) and primary epiglottic PLGA has never been reported. The present study reported a rare case of epiglottic PLGA in a 65-year-old male.

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Case report

Clinical summary. A 65-year-old Thai male patient living in Thailand was admitted to the faculty of Medicine, Ramathibodi Hospital (Bangkok, Thailand), due to intermittent sore throat and painful dysphagia for a duration of 3 months. The patient had an 8 year history of hypertension and dyslipidemia. The patient did not drink alcohol or smoke, and had no history of tuberculosis and cancer among the members of the families. Physical examination was significant for a solitary firm mass involving the left aryepiglottic fold. Laryngopharyngeal endoscopy revealed a bulging of the left epiglottis and left aryepiglottic fold by a submucosal mass measuring 2.1x2.3x1.2 cm. No abnormalities were observed in the nasopharynx, oropharynx and hypopharynx. No impairment of the laryngeal motion was observed and the cervical lymph node could not be palpated. Computed tomography (CT) revealed an infiltrative heterogeneous enhancing mass, which invaded the left-sided epiglottis and left aryepiglottic fold (Fig. 1). The patient underwent tumor removal with frozen section for evaluating the surgical margin. Subsequent supraglottic laryngectomy was performed. The definite diagnosis was T2N0M0 stage 2 PLGA. The patient recovered uneventfully and no additional therapy was administered. An improvement in the sore throat was also observed. At the 7 year follow-up, the patient remains well and exhibits no evidence of recurrence and systemic metastasis.

Pathological findings. The gross pathological specimen consisted of a supraglottic laryngectomy specimen showing a single polypoid submucosal lesion involving the left aryepiglottic

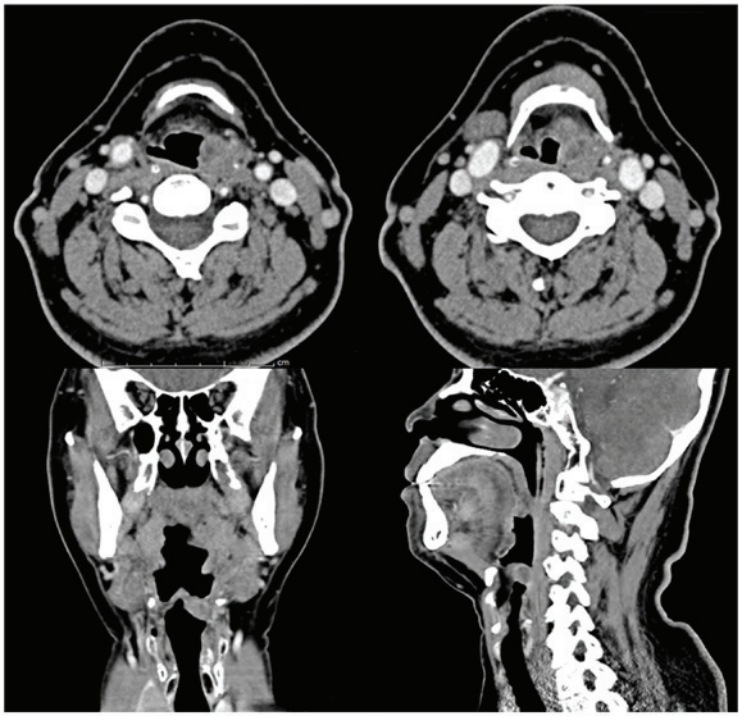

Figure 1. Computed tomography imaging study of the larynx and neck reveals an infiltrative heterogenous enhancing mass involving the left aryepiglottic fold extending to left pyriform sinus. An axial view is shown in the upper images, a coronal and a sagittal view is shown in the lower images.

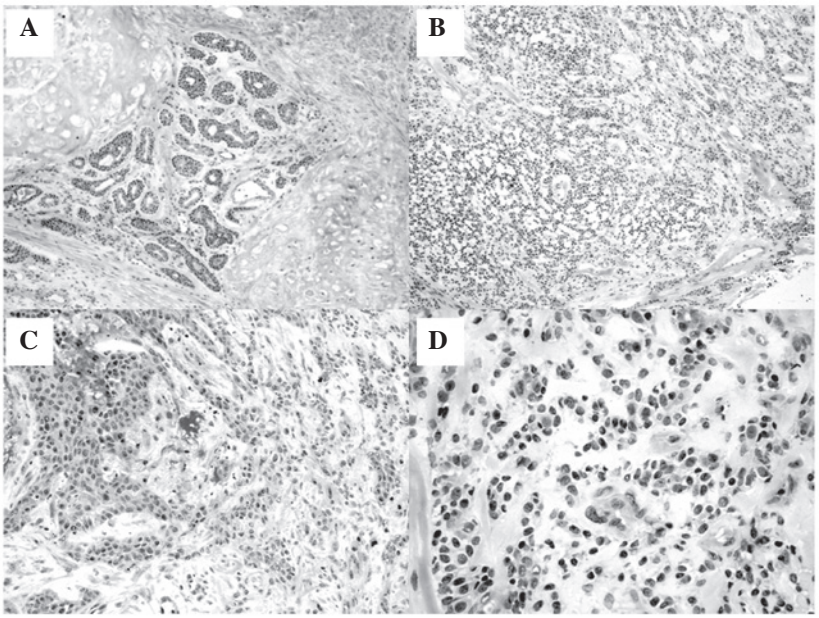

Figure 2. Light microscopy of a frozen sections of the epiglottis stained with hematoxylin and eosin revealed uniformity of cell type with variation in architectural patterns showing tubular (A) cribriform, (B) fascicular and (C) solid formations. The tumor exhibited invasive features into the epiglottic cartilage (A). The neoplastic cells (B) are small and uniform with bland round to oval basophilic nuclei, (C) inconspicuous nucleoli and (D) a moderate quantity of eosinophilic cytoplasm (magnification, x100).

fold with intact overlying laryngeal epiglottic mucosa. The lesion was an unencapsulated firm gray-tan-white mass measuring 2.2x2.3x1.2 cm. The sections of the left epiglottic mass revealed bland uniformity of cell type with variation in architectural patterns consisting of tubular, cribriform, solid and fascicular formations. The peripheral section of the tumor revealed invasive features into the epiglottic cartilage (Fig. 2). The neoplastic cells were small and uniform with bland, round to oval, basophilic nuclei, inconspicuous nucleoli and a moderate quantity of eosinophilic cytoplasm. Mitotic activity was inconspicuous. The stroma between the nests of tumor cells revealed hyalinized fibroconnective tissue without myoepithelial cell proliferation. Neither lymphovascular nor perineural invasion was detected. Immunohistochemical staining revealed that tumor cells were positive with epithelial cell markers, including cytokeratin (both AE1/AE3 and

cytokeratin 7) and epithelial membrane antigen (EMA), confirming the epithelial origin of the tumor. Tumor cells were also immunoreactive with antibodies against vimentin and CD117. Tumor cells were negative immunohistochemically for gross cystic disease fluid protein 15 (GCDFP15), estrogen receptor, progesterone receptor, androgen receptor, HER-2/neu (CD340), prostatic specific antigen (PSA), thyroid transcription factor 1 (TTF1), PAX8, napsin A, CD43 and smooth muscle actin, excluding metastatic mammary, prostatic, thyroid and pulmonary adenocarcinoma, as well as adenoid cystic carcinoma and salivary duct carcinoma. The proliferative index of the tumor cells, demonstrated by Ki67, ranged between 2 and 8% throughout the tumor, with a mean index of 5%.

Discussion

PLGA is an uncommon, low-grade malignant salivary gland neoplasm characterized by cytological uniformity, morphologic diversity, infiltrative growth pattern and low metastatic potential (1,2). PLGAs originate from the reserve cells exhibiting both luminal and myoepithelial differentiation of the ductal cells of the salivary glands (6). PLGA shows a female predilection of ~2:1 (1,3). The average age at presentation occurs principally during the fifth to seventh decade (1,3). The patients have an average age of 59 years with a range between 16 and 94 years (1). The tumors are usually found in the junction between the soft and hard palates, although cases with involvement of the major salivary glands and the minor salivary glands have been reported (3). The minor salivary glands are scattered throughout the upper respiratory tract, including laryngeal aryepiglottic fold, which may be a potential site for PLGA. PLGAs usually remain asymptomatic until they produce a mass effect causing a sore throat and airway obstruction. The routine initial laboratory investigations are non-contributory. The imaging procedures, including CT and magnetic resonance imaging may allow early recognition of PLGAs. Diagnosis is often delayed as a result of protean non-specific and diverse clinical manifestations at presentation, with resultant poor outcome resulting from advance local invasion and regional metastasis. The common metastatic sites include the lymph nodes and lungs (1,3,7). The tumor size range varies between 0.4 and 6 cm with an average size of 2.2 cm (8). The microscopic findings demonstrated uniform tumor cells exhibiting small to medium sized, oval pale nuclei and occasional nucleoli (1,3,8). Mitoses were uncommon. The morphological configurations included lobular, papillary, cribriform and trabeculae (1-3). Whorls or targetoid arrangements around the nerve and blood vessel have been previously described (3,8). The authors' case was characterized by a variety of histopathological features and uniform cytological appearance, without definite perineural infiltration. Previous immunohistochemical studies have reported that PLGA stained positive for cytokeratin, variably positive for the CD117 and EMA, and negative for PSA, androgen and estrogen receptors (1,8,9). The immunohistochemical result in the present patient was compatible with PLGA, which has been immunohistochemically reported in the literature (1,8,9).

The differential diagnoses of a primary epiglottic tumor include squamous cell carcinoma (SCC), pleomorphic adenoma, adenoid cystic carcinoma or metastatic tumor. SCC originates from the surface mucosa of the larynx and can directly invade the adjacent structure. The intact mucosa on gross examination in combination with histopathology and the positive results of cytokeratin 7 immunohistochemistry may be helpful in excluding SCC in this patient. Adenoid cystic carcinoma, arising on the aryepiglottic fold, has been reported (10). Adenoid cystic carcinoma may be confused with PLGA by its architectural patterns (tubular, cribriform and solid formations), as well as uniform cytological appearance. However, the fascicular pattern of tumor cells and negative CD43 and smooth muscle actin immunohistochemical staining are not described in adenoid cystic carcinoma (11-13). Pleomorphic adenoma can arise from minor salivary gland of the epiglottis (14). However, the histological features of the epithelial and modified myoepithelial elements exhibiting mucoid, myxoid or chondroid appearances were not observed in the present case.

Surgical excision with close evaluation of surgical margin remains the cornerstone of surgical management of PLGA. Lymph node dissection is not generally performed and should usually only be considered if evidence of cervical lymph node involvement is document. PLGAs generally behave in an indolent manner and generally do not recur following complete surgical excision. The overall survival rate of the patients with conventional PLGA is excellent. However, dedifferentiation of PLGA has been reported and carries a less favorable outcome and a poor prognosis (1,15). Postoperative radiotherapy and/or chemotherapy is generally avoided, except in dedifferentiated PLGA cases due to the risk of aggressive dedifferentiation.

Perineural invasion is frequently noted with PLGA, generally characterized by indolent course and has considerable implications for prognosis and treatment. Therefore, the early and accurate detection of perineural invasion may enhance surgical planning and appropriate use of adjuvant radiotherapy.

To the best of our knowledge, this is the first reported case of the epiglottic PLGA in a 65 year-old male, presenting with intermittent sore throat and painful dysphagia, and receiving curatively treatment by a supraglottic laryngectomy. The post-operative course was uneventful with a 7 year disease free survival. In conclusion, PLGA must be considered in the differential diagnosis of laryngeal tumor. The application of immunohistochemical investigation correlating with the clinical, radiological, endoscopic and histopathological findings may assist in making the diagnosis, and lead to the appropriate treatment.

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