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Polymorphous low-grade adenocarcinoma of the tongue

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Abstract
Primary adenocarcinomas of the oral cavity in minor salivary glands are distinctive lesions which can be subclassified according to their growth patterns or histomorphology. Polymorphous low-grade adenocarcinoma (PLGA) of minor salivary tissue has been recognized as a distinct entity. We report an unusual case of PLGA of the tongue. Only a few previous cases have been reported in the English literature. The treatment is discussed and a review of the current literature concerning this tumour is included.

Key words: Tongue neoplasms; Adenocarcinoma

Introduction

In the literature on the salivary tumours, the term 'adenocarcinoma' is frequently used as a generic designation of a large group of neoplasms. However, the variation in the tissue growth patterns and histomorphology is wide. PLGA is an entity within this group with less aggressive behaviour than other adenocarcinomas of the minor salivary glands.

Case report

A 60-year-old male, a farmer, complained of a six-month history of dysphagia, 'hot-potato' voice, and progressive dyspnoea. He did not complain of dysphonia. There was no history of tobacco or alcohol use. He denied weight loss, head and neck trauma or infection. In the family history, the only significant fact was several relatives with goitre.

The physical examination revealed a 4 cm long, 5 cm wide mass in the left side of the base of tongue. The mass was covered by normal and non-ulcerated mucosa. The oral cavity and the remainder of the oropharynx were otherwise unremarkable. The larynx was normal. There was no palpable cervical lymph adenopathy.

Routine laboratory data and chest X-ray films were normal. Radioactive iodine ^{131}I uptake revealed an enlarged thyroid gland but did not show pathology in the tongue. Fine needle aspiration of the mass was negative for malignancy. Serological tests, including those for syphilis and tuberculosis were normal. An MRI scan showed a mass on the left side of the base of tongue with invasion of the surrounding tissues as well as oropharynx stenosis (Figure 1).

Under general anesthesia several biopsies of the lesion were taken. The intraoperative histopathological diagnosis was 'adenocarcinoma of salivary gland' (Figure 2). The patient subsequently underwent a partial glossectomy. The mass was resected by a mandible-splitting approach through a stepped midline osteotomy (Figure 3). The tongue defect was closed by primary closure. No neck dissection was performed and the patient was not radiated. Abnormal speech production was the only remarkable

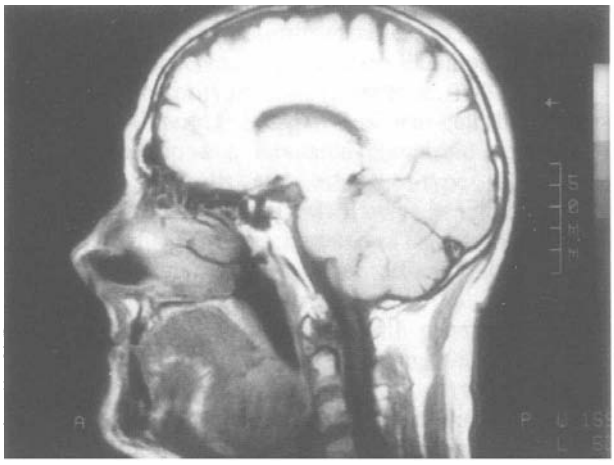

FIG. 1
MRI of tongue tumour. Notice the mass in the base of tongue covered by normal mucosa.

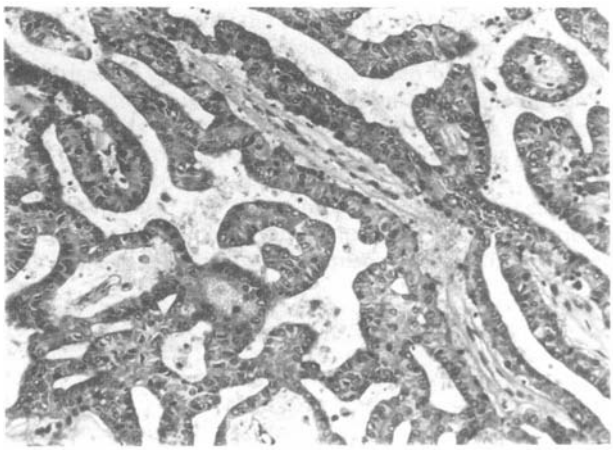

FIG. 2
Microscopical findings of the neoplasm (H & E; × 40).

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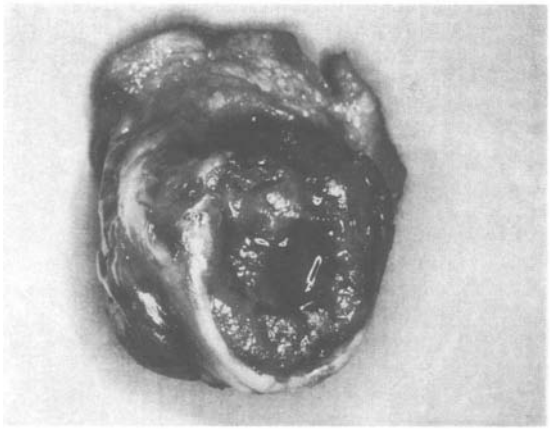

FIG. 3
Macroscopical view of the surgical specimen.

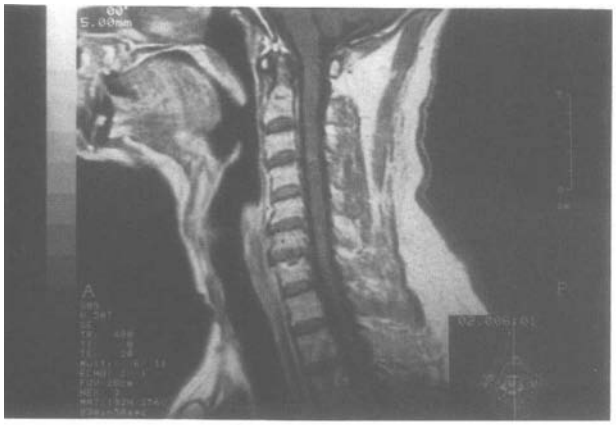

FIG. 4
MRI performed two years after surgery.

deficit after surgery. Two years after surgery the patient is alive and free of disease (Figure 4).

Histopathology

The lesion consisted of an unencapsulated, firm, grey-tan mass with haemorrhagic areas, measuring 4 × 3.7 cm, and covered by normal, non-ulcerated mucosa. Histologically, the tumour was unencapsulated, and distinctly infiltrative. The growth pattern was variable, composed mainly of papillary areas alternating with solid nests with a trabecular appearance and focal cribiform architecture (Figure 5). Despite the variations in pattern, the cells were uniform in appearance and were composed of small to medium-size, round to polygonal cells having round to oval nuclei with a vesicular chromatin pattern. The cytoplasm was eosinophilic and cell borders were indistinct (Figure 6). Cellular pleomorphism and mitoses were not evident. There was central tumour necrosis and haemorrhage. The stroma was dense, eosinophilic and hyalinized with focal mucoid-appearing areas. Vascularity was not prominent. The tumour infiltrated the normal adjacent tissues and small lymph vessels (Figure 7), and perineural invasion was also noted. Surgical margins were free of tumour. The final histopathological report was PLGA of minor salivary gland origin.

Discussion

Minor salivary glands are encountered throughout the entire upper portion of the digestive tract. The most frequent location of neoplasms derived from these stuctures is the palate (Table I), a not very surprising finding when one considers the large number of minor salivary glands normally found in this region. These tumours are malignant approximately 40 per cent of the time (Chaudhry *et al.*, 1961). Adenocarcinomas comprise 25 per cent of the malignant lesions of minor salivary gland origin (Spiro *et al.*, 1973). Twenty per cent of the malignant minor salivary gland neoplasms are found in the tongue (Batsakis *et al.*, 1983).

Histologically, PLGA of minor salivary glands is characterized by its morphologic variability, cytological blandness, and an infiltrative growth pattern. In most cases, the tumours are grossly circumscribed, although they are unencapsulated and invade adjacent tissues microscopically. Perineural involvement by carcinoma cells is often seen. Many growth patterns can be present in each tumour, including solid islands, tubules, trabeculae, cribiform nests, cysts and papillae. Lesions with papillary elements have a worse clinical behaviour (Mitchell *et al.*, 1989). Cytologically, these tumours are composed of uniform, cuboid cells with round to oval nuclei and a fine chromatin pattern. Cellular pleomorphism is not found, and mitotic figures are scarce or absent. The stroma is composed of a dense hyalinized fibroconnective tissue variably admixed with a mucoid or mucohyaline component. Peripheral infiltration into adjacent tissues, usually in a single file pattern, is the rule (Aberle *et al.*, 1985).

Differential diagnosis of this entity include mainly adenoid cystic carcinoma, monomorphic adenoma, and

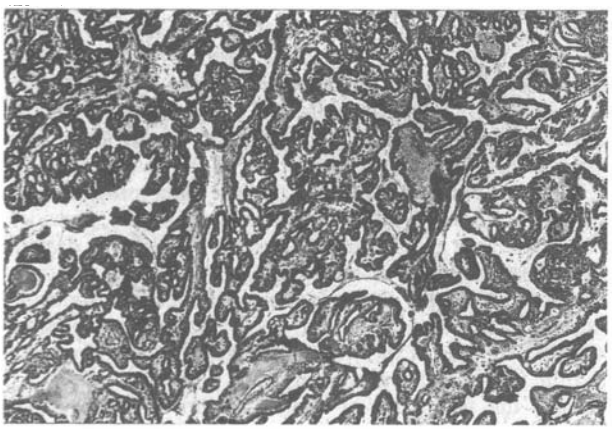

FIG. 5
Polymorphous low-grade adenocarcinoma: predominantly papillary growth pattern (H & E; × 40).

TABLE I
SITE OF ORIGIN OF THE POLYMORPHOUS LOW-GRADE ADENOCARCINOMA INCLUDING CASES REPORTED AS PAPILLARY ADENOCARCINOMA

Location	No.
Palate	65
Buccal mucosa	14
Retromolar fossa	6
Labial mucosa	6
Base of tongue	5
Mandible	1
Unknown	2
Total	99

Derived from Hjertman and Eneroth, 1970; Spiro *et al.*, 1973; Allen *et al.*, 1974; Batsakis *et al.*, 1983; Freedman and Lumerman, 1983; Evans and Batsakis, 1984; Mills *et al.*, 1984; Aberle *et al.*, 1985; Kennedy *et al.*, 1987; Slootweg and Muller, 1987; Scally *et al.*, 1988; Mitchell *et al.*, 1989; and the present case.

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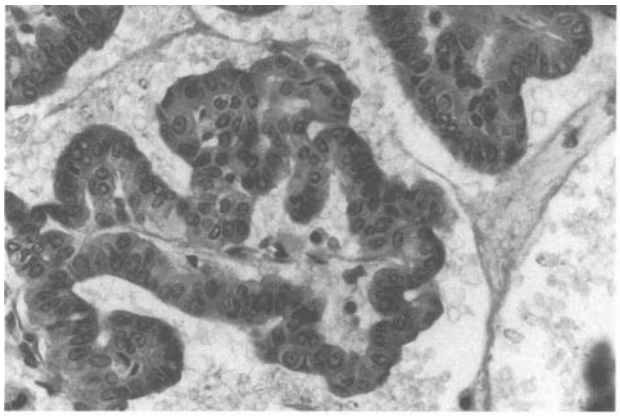

FIG. 6

Cytological detail of polymorphous low-grade adenocarcinoma: round to polygonal cells with eosinophilic cytoplasms and lack of cellular pleomorphism (H & E; × 400).

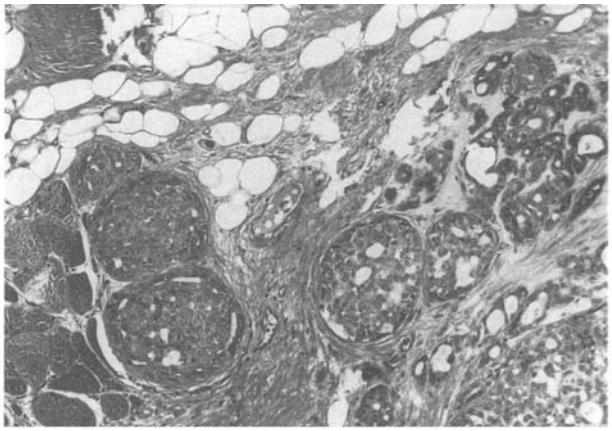

FIG. 7

Invasion of small lymph vessels at the periphery of the tumour by neoplastic cells (H & E; × 100).

pleomorphic adenoma or carcinoma (Allen *et al.*, 1974; Aberle *et al.*, 1985).

In most cases, distinction between adenoid cystic carcinoma and PLGA is based both on cytological and histological characteristics. An eosinophilic cytoplasmic staining reaction with rounded nuclear outlines characterizes the PLGA; however, this can be difficult sometimes where there are overlapping histological features. In these cases, inmunohistochemical techniques could help in the differential diagnosis, the epithelial membrane antigen (EMA) the most useful staining for differentiating these two entities. EMA is found to be diffusely positive in greater than 90 per cent of tumour cells in PLGA (Gnepp *et al.*, 1988). The practical significance in separating these two tumour entities lies in the relative malignant potential of both. Adenoid cystic carcinoma has a much more aggressive clinical behaviour and tends to feature multiple recurrences, with a worse long-term disease-free survival.

The locally infiltrating, destructive growth pattern of the PLGA, together with the prominent perineural invasion is useful to separate the monomorphic adenomas from PLGA. Occasionally, monomorphic adenomas can also have a polymorphic pattern, so this criteria by itself should not be construed as evidence of malignant behaviour.

Pleomorphic adenoma is usually well circumscribed and lacks the infiltrative margin and perineural invasion common to PLGA. However, mixed tumours of the minor salivary glands tend to be more cellular, with a minimal stromal component, and because they are usually unencapsulated, they may have a pushing, but not an infiltrating margin (Waldron *et al.*, 1988).

Malignant minor salivary gland neoplasms which arise in the base of the tongue are infrequent. When they occur they are often misdiagnosed and inadequately treated initially. Diagnosis is frequently delayed because of the submucosal location of the tumour and the lack of early symptoms other than the mass.

To our knowledge, only four cases of PLGA of base of tongue have been reported up to date (Batsakis *et al.*, 1983; Kennedy *et al.*, 1987; Mitchell *et al.*, 1989). All cases were male; the age ranged from 38 to 64 years. The clinical presentation was a painless mass in two cases; one patient complained of odynophagia and otalgia and another one of sore throat. No palpable cervical adenopathy was found in all four cases. Nevertheless, one lymph node was positive for malignancy in one of the two patients who underwent radical neck dissection (Batsakis *et al.*, 1983; Kennedy *et al.*, 1987). Histologically, the tumours in this location do not differ from PLGA at other sites.

The follow-up of PLGA indicates that this group of neoplasms may be considered as indolent, invasive and locally persistent, but slow to metastasize, tumours. These lesions have been shown to have a 10 per cent incidence of cervical metastases (Mitchell *et al.*, 1989); only one case of distant spread (to lung and vertebra), has been reported to date (Slootweg and Muller, 1987).

The mortality of these tumours varies from 1.3 per cent (low-grade polymorphous adenocarcinoma) to 13.3 per cent (low-grade papillary adenocarcinoma). Whether or not the papillary low-grade adenocarcinoma is a separate entity is not known, but it is obvious that it is a more aggressive tumour than the low-grade polymorphous adenocarcinoma.

Local extension is usually responsible for deaths. The tumour's slow growth with only local recurrence over several years, and its relative paucity of clinical symptoms tend to lull the clinician and the patient into a false sense of security. The delay before recurrence ranges from one to 20 years (Mitchell *et al.*, 1989). Therefore, five-year survival statistics are not considered adequate for these tumours because survival statistics drop significantly when observation periods approach 10 and 15 years (Kennedy *et al.*, 1987).

The treatment of choice is a wide local excision including soft tissue, and bone in palatal and retromolar lesions. Involvement of surgical margins of resection is an indication for wider excision. Perineural invasion does not appear to be of great clinical significance (Aberle *et al.*, 1985).

A mandible-splitting approach is necessary to obtain adequate exposure for lesions of the base of the tongue. This procedure allows the inner table of the mandible to be shaved as part of the resection of the primary tumour, if indicated. Likewise, this approach can be performed in combination with a neck dissection. In the case presented, we chose to perform a stepped midline osteotomy because it does not interrupt the mandibular blood supply, provides a broad surface area for bony apposition and, by its design, prevents rotation of the two fragments on one another. These factors, and the relatively symmetrical apposing muscle forces acting on the region, allow for greater stability. Healing of the wound is faster with this approach and the intermaxillary fixation is not necessary.

Since the frequency of clinical adenopathy associated with this tumour is low (10 per cent), prophylactic neck dissection does not appear to be indicated, unless the clinical examination is suggestive of metastatic lymph nodal involvement.

The benefit of post-operative radiation therapy for these lesions has not been demonstrated, though some authors believe that there is a higher rate of recurrence in those who did not undergo radiation therapy (Evans and Batsakis, 1984).

The pathologist must be aware of PLGA and must be able to make the correct diagnosis. The prognosis is much better than for other salivary adenocarcinoma. A wide local excision of the tumour with a margin of normal tissue is the treatment of choice. In order to assess the real value of adjuvant treatments to surgery further studies are required.

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