Cribriform adenocarcinoma of the tongue

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We report a case of a 73-year-old female with a tumour of the tongue, operated with two relapses. A single metastasis to the lymph node was present. Currently, the patient is alive without evidence of disease. The histological diagnosis of cribriform adenocarcinoma of the tongue was rendered. The differential diagnosis of adenocarcinomas of the tongue is discussed.

Key words: adenocarcinoma, tongue, salivary gland tumours.

Introduction

The tongue is an unusual location for adenocarcinoma. Cribriform adenocarcinoma of the tongue is a rare, recently described variant, of uncertain classification. The histological picture is fairy characteristic. We present a case of a 73-year-old woman with such diagnosis. This is the first description of this lesion in Poland.

Clinical history

A 73-year-old female with no previous history of cancer presented to her family physician with complaints of a mildly painful tumour on the left side of the dorsal aspect of the tongue, which she first noticed 3 months before. The tumour was well-defined, smooth and covered with unaltered mucosa. The regional lymph nodes were not palpable. The past history included ischemic heart disease with myocardial infarction in 2007, cardiac insufficiency, hypertension, type II diabetes mellitus, hypercholesterolemia and hepatitis B virus seropositivity. The patient did not smoke and denied the use of alcohol. The patient was admitted to the Ear, Nose and Throat Department in January 2009 and the tumour was surgically removed that month. The tumour was 3 cm in diameter, solid, of a mixed polycystic structure and easily separated from the muscles of the tongue. Histopathology of the surgical sample showed adenocarcinoma, and the tumour was partially within the margin of resection. The patient was admitted to the ENT Department for the second time in February 2009. A chest X-ray and ultrasound of the abdomen were negative for the metastases. The second operation was a partial glossectomy with neck dissection. Pathology reconfirmed the diagnosis of adenocarcinoma of the tongue, which was specified as the cribriform variant and confirmed metastasis to a single ipsilateral lymph node. The patient was admitted to the ENT Department for the third time in May 2010 with a tumour on the dorsal aspect of the tongue that had been first noticed 5 months before admission. The tumour was 3 cm in diameter, well-defined, smooth and without ulcerations. The patient underwent the third operation to excise the tumour on the base of the tongue. The patient received neither chemotherapy nor radiotherapy.

Material and methods

The material was fixed in formalin, routinely processed and paraffin embedded. From the paraffin blocks, 2 μm sections were prepared, stained by haematoxylin-eosin method and used for immunohistochemistry. Immunohistochemistry was performed using the standard method. Briefly, the slides were dewaxed, rehydrated and incubated in 3% peroxide solution for 10 minutes to block endogenous peroxidase activity. Antigen retrieval was carried out by mi-

crowaving in citrate buffer (0.2% citric acid titrated to pH 6.0 with 2N NaOH) at 750 W for 3 × 5 minutes. Primary antibodies, all manufactured by DAKO (DAKO, Denmark), are listed in Table I. The LabVision (Thermo Fisher Scientific, USA) detection system was used. 3-amino-9-ethylcarbasole served as the chromogen. The slides were counterstained with Mayer's haematoxylin (DAKO, Denmark).

Results

The specimen obtained from the first operation consisted of a fragment of the tongue measuring 2.5 cm in diameter. It was almost completely infiltrated by the tumour and covered with squamous epithelium. The histological structure of the tumour itself was similar in all specimens. On low magnification, the lesion had lobular configuration, composed of cribriform nests separated by fibrous stroma. The glands were fused back-to-back, and showed focal papillary and pseudopapillary projections. The nests were mostly roundish, and well-circumscribed, but at the periphery they were smaller and clearly infiltrative. The glands composing the lesion were lined by cuboidal to cylindrical cells. The cytoplasm was pinkish, and focally vacuolated. The nuclei were mostly oval, rather irregular, with granular chromatin, and appeared clear ("empty") in some foci. Mitotic activity was minimal. The infiltrate crossed the deep resection margins of the specimen. The generic diagnosis of adenocarcinoma was given.

The second specimen consisted of a fragment of the tongue measuring 4 cm × 1.5 cm × 1.5 cm and was completely embedded. In the central portion it contained a small infiltrate of the tumour similar to the first lesion. Immunohistochemistry was performed and the tumour cells were positive for pan-cytokeratin, cytokeratin 19, EMA, S-100, and focally for CD18, but were negative for TTF-1 and thyroglobulin. Reactivity for smooth muscle actin was present in the myofibroblasts of the stroma. On the basis of these findings, and review of the first specimen, a diagnosis of cribriform adenocarcinoma of the tongue was given. The principal specimen was accompanied by submandibular lymph nodes (two from the left, and nine from the right side) and salivary glands. One of the left-sided lymph nodes, sized 6 mm, contained a metastasis almost completely obliterating it. The salivary glands showed fatty infiltration, but no other lesions.

The third specimen consisted of a 3 cm-sized fragment of the tongue with an infiltrate measuring 2 cm in diameter. Again the histological structure was similar to the antecedent lesions. The surgical margins were free of tumour, and measured at least 4.5 mm. There were however single thin-walled vessels (CD31+, CD34+) containing collections of neoplastic glands.

Table I. Primary antibodies used in the study

Specificity	Clone/type	Dilution
S-100	polyclonal	1 : 400
TTF-1	8G7G3/1	1 : 50
thyroglobulin	Tg6	1 : 50
SMA	1A4	1 : 100
CK	MNF116	1 : 50
CK18	DC10	1 : 50
CK19	RCK108	1 : 50
EMA	E29	1 : 100
CD31	JC70A	1 : 20
CD34	QBEnd 10	1 : 50

Discussion

Cribriform adenocarcinoma of the tongue was described in 1999 by Michal *et al.* [1]. The cases published so far have been seen in adults, within quite a broad age range (25 to 70 years). The original paper reported 8 cases, and although the lesion has been consistently described in reviews of new salivary gland tumours, the number of reports remains surprisingly low [1-6].

The histological structure is quite characteristic with cribriform, tubular, glomeruloid or solid areas separated by fibrous tissue. The cells composing the lobuli are rather uniform, with vacuolated nuclei, often overlapping, and small nucleoli. The mitotic activity is minimal [5, 7]. This picture is somewhat reminiscent of thyroid carcinoma. In fact, in the original report Michal [1] pointed out a surprising similarity to the follicular variant of papillary thyroid carcinoma. Psammoma bodies, however, are not a typical feature. As a consequence, the distinction from both metastatic and ectopic thyroid carcinoma is important. It has even been suggested that the cribriform adenocarcinoma might originate from thyroid tissue remnants, which are frequent in this location. However, immunofenotyping points otherwise, and positivity for thyroid markers (such as TTF-1 and thyroglobulin) would exclude the diagnosis of cribriform adenocarcinoma. Actin, calponin and smooth muscle actin stains are also negative, but keratin and S-100 are positive at least focally [5].

Another lesion to be included in the differential diagnosis is adenoid cystic carcinoma, which, although rarely, has been reported in the tongue [8-11]. Adenoid cystic carcinoma may be even more cribriform than cribriform adenocarcinoma, but the cytologic features are altogether unalike, displaying smaller cells and dark nuclei. Due to highly aggressive nature of this lesion, an attentive differential diagnosis is required.

An unusual colonic-type adenocarcinoma with lingual localisation was described by Bell *et al*. [12]. The lesion expressed CK20, β-catenin and CDX-2, but not CK7. Thus, the phenotype may be regarded as truly colonic.

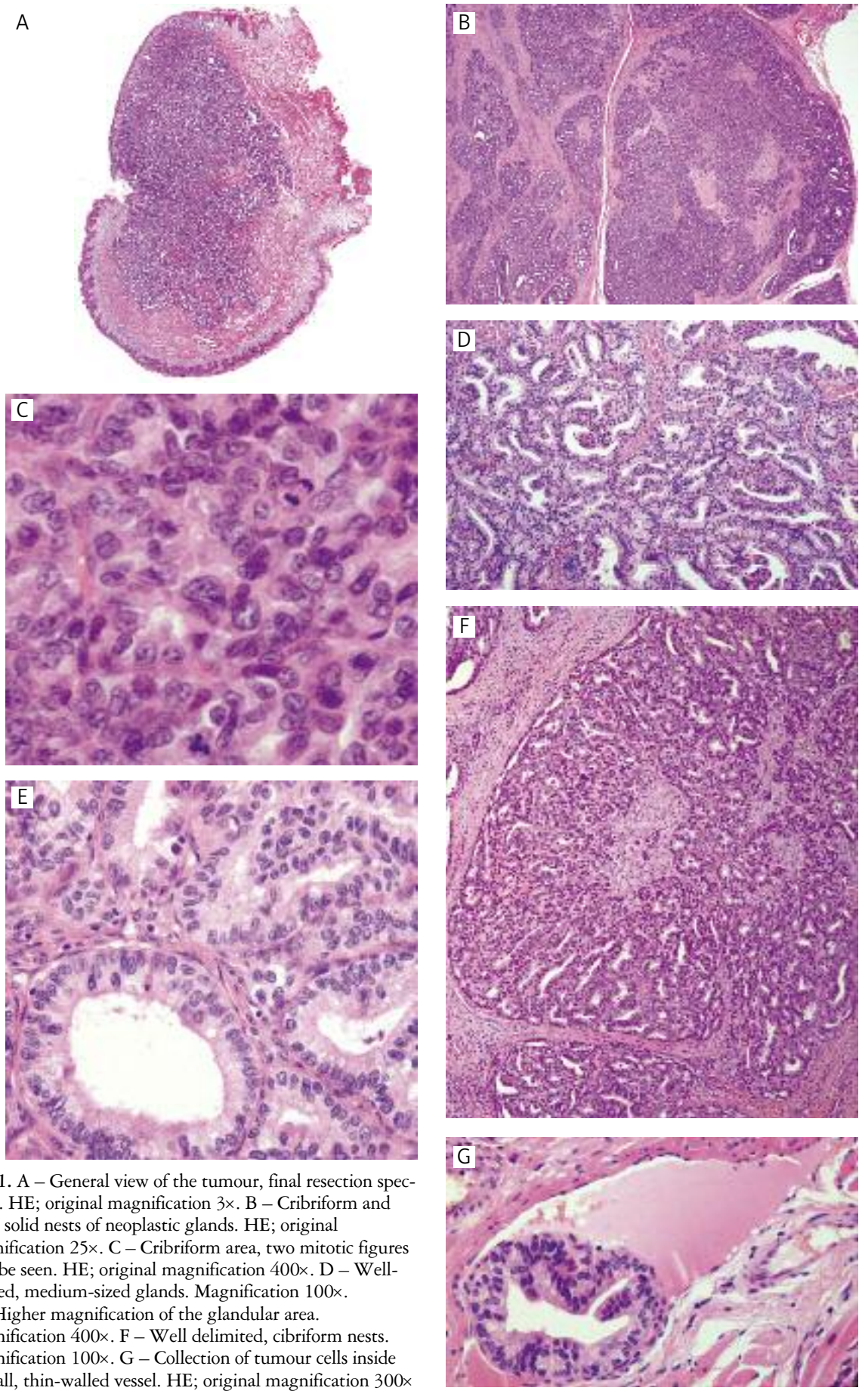

Fig. 1. A – General view of the tumour, final resection specimen. HE; original magnification 3×. B – Cribriform and more solid nests of neoplastic glands. HE; original magnification 25×. C – Cribriform area, two mitotic figures may be seen. HE; original magnification 400×. D – Well-formed, medium-sized glands. Magnification 100×. E – Higher magnification of the glandular area. Magnification 400×. F – Well delimited, cibriform nests. Magnification 100×. G – Collection of tumour cells inside a small, thin-walled vessel. HE; original magnification 300×

The lesion bears histological similarity to low-grade polymorphous adenocarcinoma of the salivary gland: combination of low-grade cytology with a minimal mitotic activity to variety of architectural patterns. Also the immunohistochemical profile with expression of epithelial markers, vimentin, S-100 protein and GFAP but not CAE or p53 is similar in both lesions. The usual low-grade polymorphous adenocarcinoma has been described in the tongue. The authors of the WHO classification felt cribriform adenocarcinoma insufficiently separated from polymorphous low-grade adenocarcinoma to merit a separate rubric [7, 13]. At the same time, frequency of lymph node metastases is higher in cribriform adenocarcinoma. In fact, it may be expected in all the cases. On the other hand, distant spread was not described, and the long-term prognosis seems to be good, in any case not worse than in polymorphous low-grade adenocarcinoma [2, 4, 5].

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