Unusual presentation of more common disease/injury

Difficulty in establishing a diagnosis in an uncommon presentation of a minor salivary gland tumour

Bernhard Attlmayr,¹ Consuelo Garrido,² David J Alderson³¹ENT Department, Royal Cornwall Hospital, RCHT, Turo, UK²Department of Histopathology, Torbay Hospital, South Devon Health Care Trust, Devon, UK³ENT Department, Torbay Hospital, South Devon Health Care Trust, Devon, UK

Correspondence to Bernhard Attlmayr, Bernhard.Attlmayr@rcht.cornwall.nhs.uk

Summary

We report the case of a man presenting with a large, airway obstructing, minor salivary gland tumour arising from the right tonsillar base. Clinically, the tumour behaved in a malignant way. A firm diagnosis of malignancy could not be made histologically. The differential diagnosis included polymorphous low-grade adenocarcinoma, basal cell adenoma and adenoid cystic carcinoma. However, on balance, based on the clinical presentation, a diagnosis of malignancy was favoured and appropriate treatment was considered. Because of the patient's comorbidities, further surgery was not an option and it was agreed that the patient should undergo radiotherapy instead. While he was waiting for radiotherapy, the tumour went into remission.

BACKGROUND

Salivary tumours are relatively rare with an estimated incidence of 0.4–13.5 cases per 100 000 annually (table 1). They account for between 3% and 10% of all head and neck tumours in the world literature.¹ The WHO histological classification is complex and currently lists 13 benign and 24 malignant salivary gland tumours.² Minor salivary gland tumours are estimated to account for up to 25% of all salivary gland tumours. Of these, 62.2% are found to be benign and 37.8% to be malignant. The most common location for minor salivary gland tumours are the palatal region (51.4%), the lip (23.5%) and the buccal mucosa (12.1%). Only in 3.3% of these cases are they found in the tongue and floor of the mouth.¹

This case report highlights the difficulty of arriving at a definitive histological diagnosis in rare salivary gland tumours especially when a resection specimen is not possible. It raises the question of why the patient went into spontaneous remission without adequate treatment.

CASE PRESENTATION

In June 2003 a 62-year-old man presented to the ear, nose and throat outpatient department with a painful right-sided swelling at the back of his tongue and dysphagia for 3 months. Medical history consisted hypertension, reduced exercise tolerance and severe chronic obstructive pulmonary disease requiring 15 h/day of home oxygen.

Clinical examination revealed an extensive tumour in his right tonsillar region, which largely occluded his pharynx and caused airway narrowing. An enlarged level 2 lymph node, estimated diameter 3 cm, was palpated. On fibreoptic nasendoscopy, the larynx and supraglottis were free of tumour.

One week later the patient was admitted for an urgent panendoscopy and biopsy under general anaesthetic. During attempted awake fibreoptic intubation, the tube

was displaced by coughing during induction of anaesthesia leading to acute airway obstruction and an emergency tracheostomy was performed in the anaesthetic room. Panendoscopy showed a large mass at the right of the tongue base. Multiple biopsies were taken.

INVESTIGATIONS

MRI (figure 1) showed a lesion centred in the right tonsil fossa measuring 4.5 × 4 cm, which reached but did not cross the midline. Right-sided level 2 and 3 nodes with a maximal diameter of 2 cm were measured. Left-sided level 2 nodes measured up to 1 cm in diameter. Subsequent CT of the chest revealed an isolated 5 mm nodular opacity in the left lung. No other abnormalities were detected in the chest or upper abdomen.

Histologically, the specimen included tissue fragments of basaloid appearance in which the architecture varied from solid to microcystic with a few ducts and possible

Table 1 Most common benign and malignant minor salivary gland tumours¹

Benign tumours	% of group
Pleomorphic salivary adenoma	65.0
Basal cell adenoma	12.4
Canalicular adenoma	12.0
Papillary cystadenoma	3.9
Myoepithelioma	1.0
Malignant tumours	% of group
Mucoepidermoid carcinoma	34.3
Adenoid cystic carcinoma	30.2
Polymorphous low-grade adenocarcinoma	16.3
Carcinoma ex-pleomorphic adenoma	6.4
Acinic cell carcinoma	3.5
Adenocarcinoma nitrous oxide systems	3.5
Basal cell adenocarcinoma	1.7

Figure 1 MR of the head showing a large mass lesion in the right tonsil fossa reaching the midline.

Figure 2 (A) Fragments of tumour showing a basaloid proliferation with solid or microcystic architecture. (B) Close-up view of the nuclear features of the tumour cells: generally ovoid, with a few angulated nuclei.

micropapillary structures (figure 2A). Peripheral palisading was seen. The nuclei were generally ovoid and a few were angulated (figure 2B). There was no nuclear pleomorphism or mitotic activity. Because of the fragmented nature of the tumour, it was not possible to fully assess invasiveness although one fragment did demonstrate invasive features.

DIFFERENTIAL DIAGNOSIS

Immunohistochemical staining (table 2) and special stains did not assist in providing a definitive diagnosis. Polymorphous low-grade adenocarcinoma (PLGA), basal cell adenoma (BCA) and adenoid cystic carcinoma (ACC) were considered in the differential diagnosis. Because

PLGA does not usually have a basaloid appearance and is rare in the tongue, this diagnostic possibility was considered unlikely. Parts of this tumour showed basaloid appearance resembling the morphology of ACC. However, the overall appearance of the tumour did not favour this diagnosis and neither did the low proliferation index (MIB1 of 4%). On balance, it was suggested that an adenoma with predominant basal cell differentiation (either BCA or canalicular adenoma) could best explain the morphology—a diagnosis which would be in keeping with the low proliferation index demonstrated by the tumour cells. However, the diagnostic possibilities of PLGA and ACC could not be fully excluded.

Table 2 Immunohistochemical staining

Marker	% of stained cells
Cytokeratin 7	100
Cytokeratin 14	100
Cytokeratin 5	80
Cytokeratin 6	80
EMA	30
S-100	50
Cytokeratin 20	neg
p63	>50
MIB1 index	4
SMMHC	NA

EMA, epithelial membrane antigen; SMMHC, smooth muscle myosin heavy chain.

TREATMENT

In spite of the histological findings it was agreed at the multidisciplinary team meeting that, clinically, the tumour was ultimately behaving like a malignancy in addition to there being strong radiological evidence of regional spread. Surgical resection was favoured but after liaison with a respiratory specialist the patient was deemed unfit for any surgical intervention or indeed for further biopsies. Therefore, palliative radiotherapy was considered and a follow-up consultation was booked to discuss further details of this treatment option.

OUTCOME AND FOLLOW-UP

Three weeks later, when the patient came for this appointment, he was managing well with his tracheostomy. Clinically, the tumour showed sloughing, appeared to be necrotic and had decreased in size. Instead of proceeding with radiotherapy at that point, the decision was made to follow the patient up at regular intervals to observe for any further changes in the tumour. Ultrasound-guided fine needle aspiration of a level 2 node performed a few days later showed no malignant cells.

At the follow-up 1 month later the mass had disappeared completely and his tracheostomy was removed. No oral mass could be found at the next consultation 2 months later.

Further follow-up in February 2004 showed a small prominence at the previous tumour site. Biopsy was considered; however, the mild swelling at the right tongue base did not change in appearance for 2 years until February 2006 when the swelling had increased in size again. Considering a potential infection, a course of antibiotics was prescribed, without effect, and a second biopsy was obtained under local anaesthetic a month later. Deep samples from the right of the tongue base showed only normal tissue. In May 2006, the swelling had significantly reduced and no further changes were detected. By March 2007, his chronic obstructive pulmonary disease had deteriorated to the extent he could no longer attend clinic and regular follow-up was discontinued.

The patient died 1 month later in April 2007. Postmortem examination was performed in Exeter. The cause of death was bronchopneumonia secondary to chronic airway disease. A tumour measuring 2.5 cm with surrounding induration in the right side of the posterior tongue was found. No further tissue samples were retained for analysis.

DISCUSSION

In this case report the histological findings of the first biopsies gave three potential differential diagnoses: ACC, PLGA and BCA. The basaloid appearance of the tissue would have been characteristic for ACC but the low proliferation index demonstrated with MIB1 immunohistochemical staining gave no support to this diagnosis. The appearance and location in the tongue base would have been unusual for PLGA. Nevertheless, immunohistochemistry and low proliferation index could have been consistent with this diagnosis. An adenoma with a predominant differentiation of basal cells was considered as a third differential diagnosis. No definite tumour invasion could be assessed microscopically. Therefore, no histological evidence of a malignancy could be confirmed as the key determining factor in establishing the malignant nature of a salivary gland tumour is the demonstration of an infiltrative margin. However, this is known to be more difficult in biopsies where it may not be possible to obtain a precise diagnosis.³

In this case, immunohistochemical stainings were unhelpful and did not differentiate between the differential diagnoses named above. The possible diagnosis of basal cell adenocarcinoma (BCAC) was not considered, although it is well documented that neither immunohistochemical methods nor ultrastructural characteristics do distinguish between BCAC and BCA.⁴

However, even though no tumour invasion could be demonstrated, the clinical presentation was that of a malignant tumour. The general consensus at the multidisciplinary team meeting was strongly in favour of malignant disease. The tumour had grown rapidly, was painful and completely occluding the pharynx requiring an emergency tracheostomy. The enlarged cervical lymph nodes and the nodular opacity in the left lung were suggestive of metastatic disease. The size of the tumour, measuring more than 4 cm in diameter, indicated a high clinical stage of tumour. Although tumour grading was not available, a poor outcome was suggested considering the relative importance of stage versus grade in minor salivary gland tumours.⁵ Treatment options were discussed and surgery would have been the preferred approach if the patient's health and fitness had allowed. Alternatively, radiotherapy was considered based on evidence from previous studies⁶ of patients receiving radiotherapy alone for minor salivary gland carcinomas. These demonstrated long-term local tumour control especially in patients unfit for surgery. In this case, as the clinical findings had much improved without starting any treatment, the decision was made to observe and follow the patient up at regular intervals.

When the first biopsies were taken, a surgical trauma occurred that might have led to a change in blood supply resulting in tumour necrosis. This represents one of many mechanisms thought to be responsible for spontaneous remission of cancer.⁷ In 1935 spontaneous regression of a carcinoma of the tongue after biopsy was reported by David Roxburgh.⁸ However, without a confirmed histological diagnosis of malignancy, our case did not fulfil the strict criteria of spontaneous regression of a cancer defined by Everson and Cole in 1956. They postulated spontaneous regression of cancer to be a partial or complete disappearance of a malignant tumour in the absence of all treatment,

or in the presence of treatment that is considered inadequate to exert a significant influence on neoplastic disease.⁹ In our case, a second attempt to biopsy the lesion was unsuccessful and no further tissues samples were taken at the postmortem examination; hence, the exact nature of the tumour, as well as the mechanism leading to its regression, remain uncertain. Histological distinction between benign and malignant basaloid neoplastic proliferations of the salivary glands is difficult and may, ultimately, rely on the demonstration of an infiltrative growth pattern or perineural invasion.

Learning points

- ▶ Difficulties in establishing a histological diagnosis from fragmented biopsies.
- ▶ Immunohistochemical stainings may not be helpful in differentiating between benign and malignant minor salivary tumours.
- ▶ The process of taking a biopsy may alter blood supply to a tumour and may contribute to tumour regression.

Competing interests None.

Patient consent Obtained.

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