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Mammary analogue secretory carcinoma of the salivary glands: a diagnostic dilemma

Abstract

Mammary analogue secretory carcinoma (MASC) is a recently identified salivary gland neoplasm that can mimic other salivary gland tumours such as acinic cell carcinoma and cystadenocarcinoma. It is distinguished from these by differences in immunohistochemical profile and the identification of an *ETV6-NTRK3* translocation (12;15)(p13;q25), which is also found in secretory carcinomas of the breast. Previous publications have suggested that MASC tumours have similar biological behaviour to acinic cell carcinoma. We report two cases of MASC that affected the upper lip, and showed an infiltrative and locally aggressive growth pattern that required several operations to ensure clearance of microscopic tumour cells.

Keywords: Mammary analogue secretory carcinoma; MASC; salivary gland malignancy; minor salivary gland; lip; *ETV6-NTRK3* translocation

Introduction

Mammary analogue secretory carcinoma (MASC) is a rare tumour of the salivary glands that was first described by Skálová et al in 2010.¹ It usually presents with microcystic architecture and low-grade cytological features, and is histomorphologically and immunohistochemically similar to secretory carcinoma of the breast. The histological features can resemble other salivary tumours such as cystadenocarcinoma and acinic cell carcinoma. Its most commonly described site is the major salivary glands, but there are only a handful of reported cases of it affecting the minor salivary glands of the lip.²

We report two cases of MASC of the upper lip, which showed locally aggressive biological behaviour and required a more aggressive treatment than that adopted for histological mimics such as acinic cell carcinoma.

Case 1

An otherwise healthy 27-year-old woman presented with a one-year history of a slow-growing 1.5 cm lump, on her right upper lip. Cytological analysis of ultrasound-guided fine needle aspirate suggested a salivary gland neoplasm that raised the possibility of acinic cell carcinoma. The lesion was excised and histopathological analysis confirmed the diagnosis of MASC after immunohistochemical studies had stained for S100 and mammaglobin. It did not stain for DOG1. Fluorescent in situ hybridisation confirmed rearrangement of the ETV6 gene. Staging scans showed no evidence of metastases. The margins of the specimen were invaded on histopathological analysis despite the impression of macroscopic clearance at operation. She subsequently had a wedge excision of the scar with a 1cm margin but then required a repeat resection after microscopic identification of residual dispersed islands of tumour that had reached the margins. The patient had no signs of local or regional recurrence nine months after her operation (Figs. 1-3).

Case 2

A 51-year-old man who used to smoke and had no other relevant medical history presented with a three-year history of an asymptomatic, firm, mobile lump in his upper right labial mucosa. Histopathological examination of an excisional biopsy specimen together with immunohistochemical profile and fluorescent in situ hybridisation again suggested a diagnosis of MASC. Staging scans showed no abnormality.

The patient had a further excision of the scar with a 1cm margin under general anaesthetic. Final histopathological analysis again showed residual tumour with a close margin at the deeper aspect of the specimen. The patient declined any further intervention so a policy of close follow-up was adopted. There were no signs of local or regional recurrence at his six-month review.

Discussion

Because MASC was not recognised as a distinct entity until 2010 it is not listed in the most recent 2005 WHO classification of salivary gland tumours.³ We know of about 90 cases of MASC that have been published - two thirds of which were in the parotid gland, followed by the intraoral minor salivary glands and the submandibular gland.⁴

MASC resembles secretory carcinoma of the breast and expresses the same ETV6-NTRK3 gene fusion protein, which leads to constitutive activation of two major effector pathways - the Ras-MAP kinase mitogenic pathway and the phosphatidyl inositol-3-kinase-AKT pathway.⁵ This translocation has not been found in conventional salivary acinic cell carcinoma. There are, however, differences in immunohistochemical profile: MASC reacts to mammaglobin and S100 while acinic cell carcinoma shows no appreciable expression of these markers.¹ The morphology of these two tumours can be similar, which can lead to errors of interpretation.^{1,6,7}

Both of these case studies involved minor salivary glands of the upper lip and we managed them the same way we would an acinic cell carcinoma. Previous publications have suggested that the management of MASC should be similar, but its histological behavior is more aggressive and it is difficult to obtain microscopically clear margins despite the impression of

adequate macroscopic clearance.⁸ We advise a more aggressive approach to the treatment of MASC tumours that affect the minor salivary glands.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

We have obtained approval from ethics and patient consent is not applicable.

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Figure legends

Fig. 1. Residual tumour after excision. (Haematoxylin and eosin, original magnification x 100).

Fig. 2. Positivity for mammaglobin. (Haematoxylin and eosin, original magnification x 40.)

Fig. 3. Positivity for S100. (Haematoxylin and eosin, original magnification x 40).

Mammary Analogue Secretory Carcinoma (MASC) of the salivary glands: a diagnostic dilemma

Abstract

Mammary analogue secretory carcinoma (MASC) is a salivary gland neoplasm that was first formally described in 2010. This newly recognised tumour can mimic other salivary gland tumours such as acinic cell carcinoma (ACC) and cystadenocarcinoma. They are distinguished from these entities through differences in immunohistochemical profile and the identification of an *ETV6-NTRK3* translocation (12;15)(p13;q25) that is also found in secretory carcinomas of the breast. Existing literature predicts that MASC tumours have similar biological behavior to ACC. We report 2 cases of MASC affecting the upper lip, which demonstrate an infiltrative and locally aggressive growth pattern requiring multiple surgical procedures to ensure microscopic tumour clearance.

Keywords: Mammary analogue secretory carcinoma; MASC; salivary gland malignancy; minor salivary gland; lip; *ETV6-NTRK3* translocation

Introduction

Mammary Analogue Secretory Carcinoma (MASC) is a rare salivary gland tumour first described by Skálová et al in 2010. These tumours usually present with microcystic architecture and low-grade cytological features and bear close histomorphological and immunohistochemical resemblance to secretory carcinoma (SC) of the breast.¹ Histological features of MASC can resemble ACC and other salivary tumours such as cystadenocarcinoma. The most commonly described

location for MASC is major salivary glands; however, there are only a handful of cases affecting the minor salivary glands of the lip reported in the existing literature.² We report two cases of MASC affecting the upper lip, which were noted to show locally aggressive biological behaviour and required a more aggressive approach to treatment to that locally adopted for histological mimics such as ACC.

Case 1

An otherwise healthy 27-year-old female presented with a one-year history of a slow growing 1.5cm lump, on her right upper lip. An ultrasound guided fine needle aspiration was carried out and cytological analysis of the aspirate suggested a salivary gland neoplasm that raised the possibility of ACC. The patient subsequently had the lesion excised for formal histopathological analysis and a diagnosis of MASC was made following immunohistochemical studies demonstrating positivity for S100 and Mammaglobin. Dog1 was negative. Fluorescent in situ hybridisation (FISH) studies confirmed an ETV6 gene rearrangement. Staging scans showed no evidence of metastatic disease. The margins of the specimen were involved by tumour on histopathological analysis despite the impression of macroscopic surgical clearance at the time of surgery. She subsequently had formal wedge excision of the scar with a 1cm margin but then required repeat surgery following microscopic identification of residual dispersed tumour islands reaching the surgical margins. The patient has displayed no signs of local or regional recurrence at her 9-month post-surgery review (figures. 1-3).

Case 2

A 51-year-old male ex-smoker with no other relevant medical history presented with a 3-year history of an asymptomatic firm, mobile lump in his upper right labial

mucosa. An excisional biopsy was carried out under local anaesthetic. The histopathological features, immunohistochemical profile and FISH again suggested a diagnosis of MASC. Staging scans were unremarkable.

The patient had a re-excision of the scar with a 1cm margin under general anaesthetic. Final histopathological analysis again demonstrated residual tumour with a close margin at the deeper aspect of the excision specimen. The patient declined to have any further surgery so a close follow-up policy was adopted. There have been no signs of local or regional recurrence at his 6-month post-surgery review.

Discussion

MASC was first recognised as a distinct entity in 2010 and so is not listed in the most recent 2005 WHO classification of salivary gland tumours.³ Approximately 90 cases of MASC have been published - two thirds of which occurred in the parotid gland, followed by the intra oral minor salivary glands and the submandibular gland.⁴ MASC resembles secretory carcinoma of the breast and expresses the same ETV6-NTRK3 gene fusion protein, which leads to constitutive activation of two major effector pathways - the Ras-MAP kinase mitogenic pathway and the phosphatidylinositol-3-kinase-AKT pathway.⁵ This translocation has not been found in conventional salivary ACC. There are, however, differences in immunohistochemical profile - MASC demonstrate reactivity to Mammaglobin and S100 whilst ACC does not show significant expression of these markers.¹ The morphology of these two tumours can be similar leading to errors of interpretation.^{1,6,7}

Both cases presented here involved the minor salivary glands of the upper lip and were managed the same way as we would manage an ACC. Existing literature suggest that surgical management of MASC probably should be similar to that of ACC; however, histologic behavior at this anatomical site appears more aggressive with difficulty in obtaining microscopically clear margins despite the surgical impression of adequate macroscopic clearance.⁸ Consequently, we advise consideration of a more aggressive surgical approach in MASC tumours affecting the minor salivary glands.

Conflict of Interest

No

Ethics statement/confirmation of patient permission

Ethics approval: No. Patient consent obtained

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Figure Captions

Figure 1. Residual tumour after excision. H+E stained section. Magnification x 100

Figure 2. Positivity for mammaglobin. Magnification x 40

Figure 3. Positivity for S100. Magnification x 40

Figure 1
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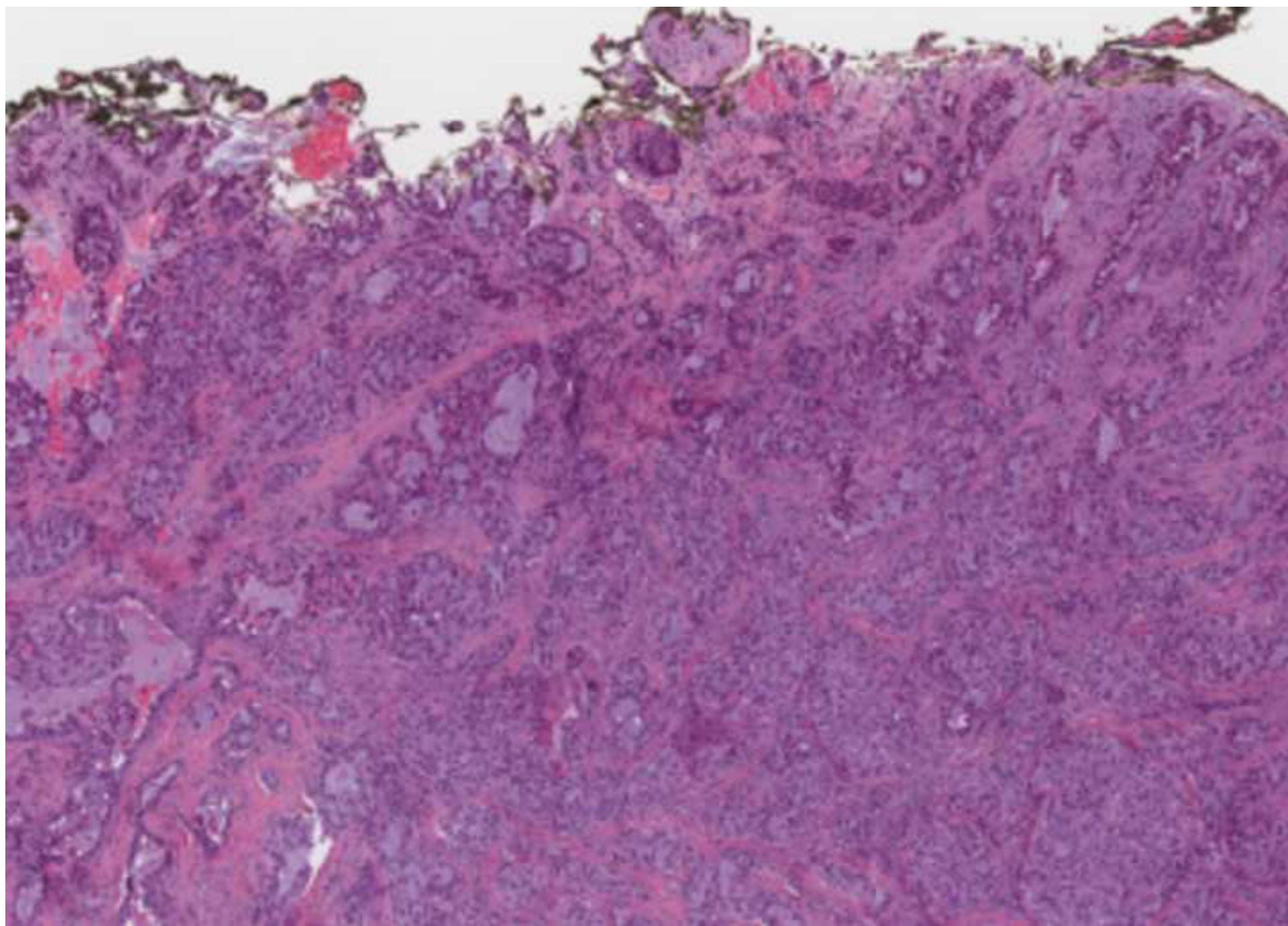


Figure 2
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