Case Report

Low-grade intraductal carcinoma in minor salivary glands: A case report and clinical insights

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Abstract

Rationale: Low-grade intraductal carcinoma (LG-IC), is a rare malignant tumour of the salivary glands which has a very good prognosis and must be differentiated from the other types of salivary gland malignant tumours, which have a totally different behaviour and a worse prognosis.

Patient Concerns: A case is presented of a 52-year-old woman who was first diagnosed and treated in another clinic in 2019 for an LG-IC in the left submandibular gland space. Two years later, she was admitted to our department with a new lesion, this time in the upper jaw lip on the left side, which also turned out to be LG-IC.

Diagnosis: Magnetic resonance imaging and positron emission tomography-computed tomography were performed in order to diagnose and adequately stage the disease prior to the therapeutic intervention.

Outcomes: A 6-month follow-up reveals no sign of recurrence.

Takeaway Lessons: Literature on this rare histopathological entity, as well as the differential diagnosis with the other malignant lesions of the salivary glands and the frequency of metastasis, were reviewed.

Keywords: Low-grade intraductal carcinoma, metastasis, minor salivary gland tumours, oral cancer, second primary cancer

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Submitted: 27-Nov-2022, **Revised:** 09-Oct-2023, **Accepted:** 10-Oct-2023, **Published:** 15-Apr-2024

INTRODUCTION

Low-grade intraductal carcinoma (LG-IC) is a rare malignant tumour of the salivary glands and mostly the parotid gland, with a good prognosis but difficult differential diagnosis, especially from the variants of adenocarcinoma, non-other specified (NOS) or cystadenocarcinoma.[1-3] The LG-IC was formerly called "Low-grade salivary duct carcinoma" or "low-grade cribriform cystadenocarcinoma", but according to the World Health Organization (WHO) classification, the tumour was renamed due to its totally different behaviour.[4] Histopathologically, they represent small, multicystic lesions (<2 cm). The intraductal carcinoma (IC) is graded as low, intermediate, or high. The LG-IC has a cribriform and papillary pattern.[1,4] Epidemiologically, the IC is a rare tumour mostly presented with its low-grade form, evenly between men and women at a mean age of 59–64 years.[5] High-grade lesions appear more frequently in older people.[5] The tumour is mostly located in the parotid gland (80–84%), with a more favourable prognosis.[1,3,5] Only 8% of LG-IC is found in the minor salivary glands.[5] Differential diagnoses are

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_500_22

How to cite this article: Louizakis A, Tatsis D, Papadopoulou S, Vahtsevanos K. Low-grade intraductal carcinoma in minor salivary glands: A case report and clinical insights. J Oral Maxillofac Pathol 2024;28:125-9.

the typical salivary duct carcinoma, other subtypes of adenocarcinoma, NOS and cystadenocarcinoma, acinic cell carcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, carcinoma ex pleomorphic adenoma, the mammary analogue secretory carcinoma of salivary glands and other benign tumours such as the cystadenoma and the intercalated duct lesion.[1–3] Treatment of choice is complete excision with a good prognosis.[1,5,6] Regional and distant metastasis has not been reported in the literature.[1,3,7]

A case of a patient is presented with two LG-IC lesions in two different sites in the oral and maxillofacial surgery (OMFS) area, specifically in the left submandibular gland and in the mucosal area of the left upper lip, during a 2-year period of which she underwent surgery. A literature review is discussed.

CASE REPORT

A 52-year-old female with an exophytic lesion, smooth surfaced and without ulceration, situated in the left mucosal area of the upper lip, was referred to our department. The tumour-sized 2.2 × 1 × 1.4 cm^3.

Tracing back her medical history, the patient underwent a submandibular space mass excision to her left side, in another department 2 years prior to the current mass. A mass, sized 2.5 × 1.7 cm^2, was excised under general anaesthesia, as imaged in the preoperative performed magnetic resonance imaging (MRI) [Figure 1], with a diagnosis of a low-grade IC (ICDO: 8500/2), with an infiltrated adjacent lymph node.

Concerning the current mass, a preoperative MRI presented a central cystic lesion 1.3 × 1.1 cm^2, with an intact submandibular gland [Figure 2]. A positron emission tomography-computed tomography (PET/CT) scan was performed postoperatively with no signs of recurrence or distant metastases. The multidisciplinary team (MDT) decided on postoperative prophylactic radiotherapy of the area (55 Gy in the submandibular area and 45 Gy in the cervical lymph nodes). Apart from that, the patient was a smoker (30 packs/year), and she also had heterozygous beta-thalassemia.

An MRI scan did not identify any pathological signs in the area of the left submandibular triangle. However, it revealed pathological signals in the left upper lip area. An excisional biopsy was performed under local anaesthesia. A mucosal incision sized 3 cm was performed on the left side of the upper lip, the submucosal plane was dissected, and the lesion was revealed and excised in clear margins, as a cystic lesion [Figure 3]. The postoperative period was uneventful.

The pathological examination corroborated a low-grade IC, identical to the previous one. The excision was performed with clear surgical margins. Intraductal epithelial proliferation with a papillary and cystic growth pattern was identified. The lesion was well demarcated without rapture. The papillae and cysts were covered with small epithelial cells (CK7+, CK8/18+) with mildly atypical nuclei and eosinophilic cytoplasm. Mitoses were rare. A lymphoid proliferation was focally recognized. There was no sign of invasion. In addition, a number of diagnostic markers were used to corroborate the malignant form of the mass, such as the keratin 8/18 and keratin 7, which were positive. Additional markers were used, estrogen receptor (ER), progesterone receptor (PR), and thyroid transcription factor-1 (TTF-1) to exclude the possibility of distant metastases. Ki-67 protein expression was low (3%). Histology and immunohistochemistry workup are summarized in Figures 4-7.

Postoperatively, a diagnostic workup was performed with a full body CT and a head and neck MRI. As these came back negative for metastases, the multidisciplinary team (MDT) decided a close follow-up.

A new PET/SCAN was performed 6 months postoperatively with no signs of disease, except for a higher standardized uptake value (SUV) in the right palatine tonsil area. Endoscopy did not reveal any clinical lesions.

DISCUSSION

LG-IC is a rare entity that grows slowly and has a favourable prognosis among other malignant salivary

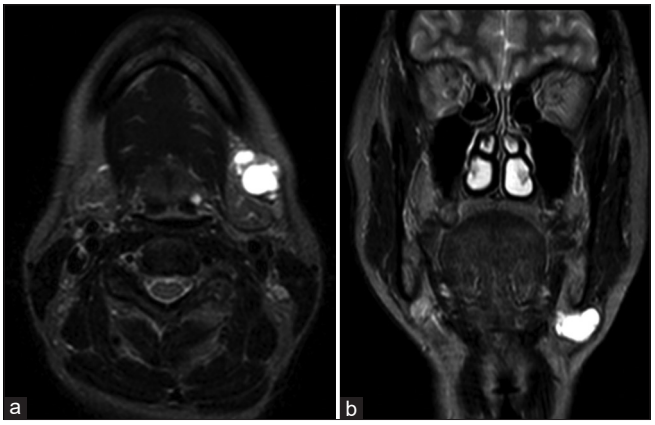

Figure 1: Magnetic resonance imaging scan. A circumcised lesion sized 2.5 × 1.7 cm^2, presenting adjacent to the left submandibular gland. (a) STIR sequence axial plane, (b) STIR sequence coronal plane

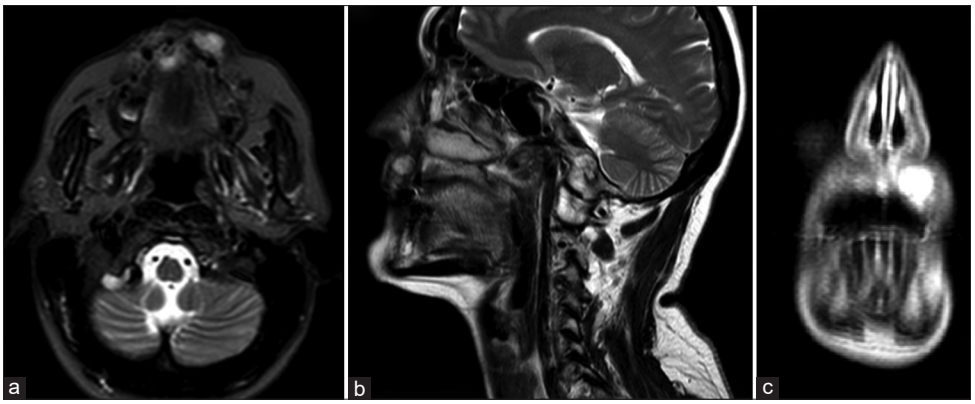

Figure 2: Magnetic resonance imaging scan. A cystic lesion sized 1.3 × 1.1 cm² is present in the left mucosal area of the upper lip. (a) STIR sequence, axial plane, (b) T2-weighted image, sagittal plane, (c): STIR sequence coronal plane. STIR: Short-TI Inversion Recovery

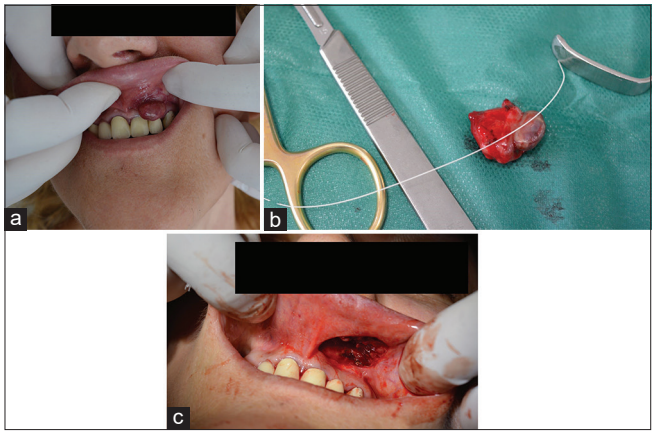

Figure 3: (a) Clinical presentation of the lesion of the upper lip shows an exophytic mass, well circumcised. (b) the excised specimen. (c) the resected area prior to surgical closure

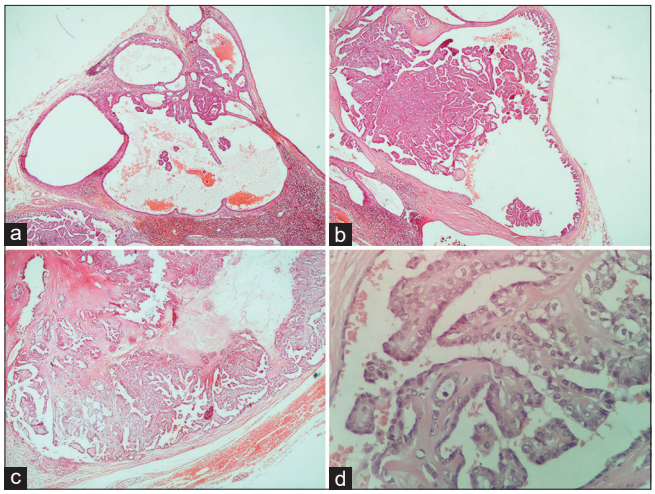

Figure 4: (a) Papillary and focally cystic pattern (haematoxylin and eosin, ×40), (b) Intraductal growth. Distended duct with tufted papillary anastomosing proliferations (haematoxylin and eosin, ×40), (c) Well circumscribed and unencapsulated at low power (haematoxylin and eosin, ×100), (d) Small cuboidal cells with eosinophilic cytoplasm and small, oval nuclei with dispersed chromatin, inconspicuous nucleoli. Low-grade nuclear features. Mild nuclear pleomorphism (haematoxylin and eosin, ×200)

gland tumours, after surgical excision and, especially when it is localized to the parotid gland (80%).[1,8] A total of 93 cases have been recorded, mainly situated in the parotid gland, whereas only 10 intraoral lesions have been reported.[8] Examining another case of high-grade IC (HG-IC) of the upper lip, we saw that in contrast to our case of LG-IC, the Ki-67 index was high, the fibrous capsule did not exist, and a higher cellular atypia and necrosis were present.[8]

Three main patterns have been described, all of which are represented by multiple cysts and intraductal growth.[1] In our case, the typical LG form is represented by multiple cystic lesions accompanied by the characteristic cribriform and papillary pattern and smaller dilated ducts. [Figure 4][1,4] Neither locoregional nor distant metastases have been described, and only two cases of recurrence have been reported in HG-IC (or invasive) lesions, one of which had verified positive surgical margins.[1,5] In order to exclude the possibility of distant metastases of another primary cancer, especially the lungs, the ovaries, the endometrium and the thyroid gland, ER, PR and TTF-1 markers are used.[9] Moreover, the fact that the Ki-67 protein expression was low (3%) and only a few scattered and with a low degree of atypicality cancerous cells were identified were facts that advocate for a low-grade carcinoma. [Figure 5][10]

Typically, the LG-IC lesions are not associated with pain or other symptomatology. Only one case of paresthesia in the greater auricular nerve was described without facial nerve participation in an LG-IC tumour, which co-existed with an invasive adenosquamous carcinoma, which also caused perineural invasion.[7]

No adjuvant radiotherapy is suggested in clear (or even close) surgical margins. It is only justified in infiltrated margins or a tumour with invasive components and

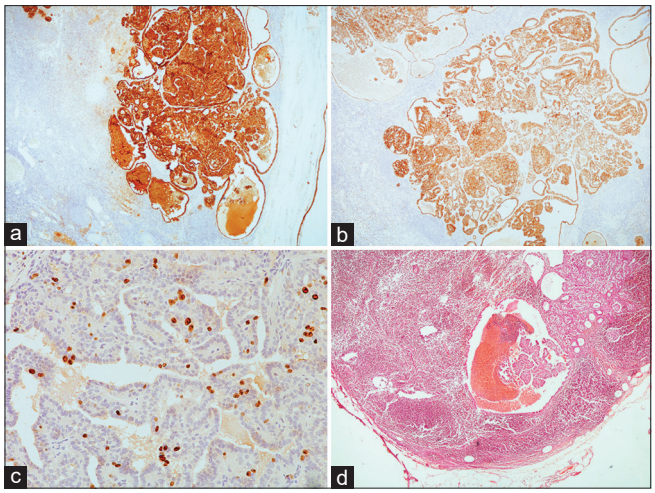

Figure 5: (a) Cytokeratin 7 (+) (×100) (b) Cytokeratin 8/18 (+) (×100) (c) Ki-67 proliferation marker 3% (×200), (d) Pathology image of the previous submandibular lesion present lymph node metastasis, similar to the upper lip lesion (haematoxylin and eosin, ×40)

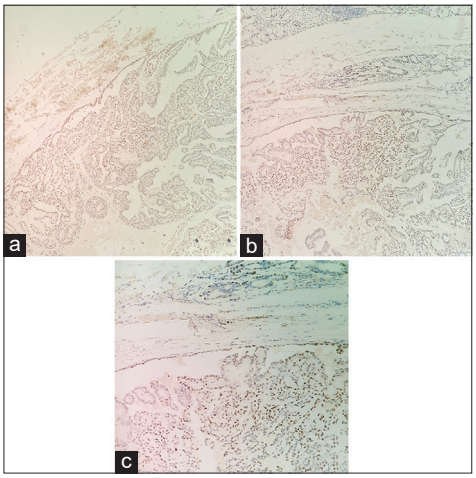

Figure 6: Demonstration by immunohistochemistry of a myoepithelial layer (p63). (a) ×10, (b) ×10, (c) ×20

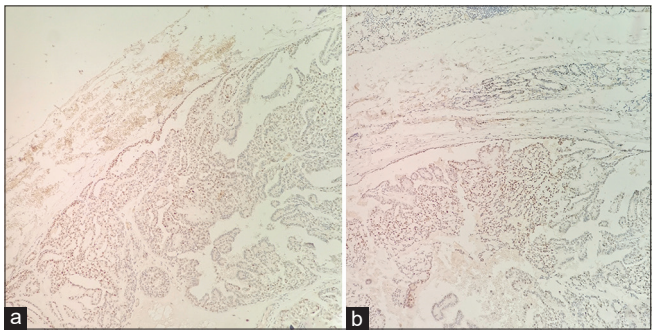

Figure 7: Demonstration by immunohistochemistry of a myoepithelial layer around cell nests (p63). (a) ×10, (b) ×10

perineural invasion.[6] Neck dissection is not indicated in N0 neck. Only one case has been reported where chemotherapy was given as a treatment, this with the co-existing LG-IC and adenosquamous carcinoma.[1,6]

As this is a case report study, the major limitation is the lack of further patients to identify and meticulously record similar findings. In addition, the reported follow-up period is short, but the patient will continue a time-lined examination period.

In conclusion, the LG-IC is a rare carcinoma of the salivary glands with a very favourable prognosis after complete excision.[1,8] Very few cases of IC have been published.[5] Differential diagnosis from the other types of salivary gland cancers is crucial because of the totally different behaviour of these tumours.[1,3,5] However, this case raises a question: whether the LG-IC that appeared in the upper lip is a second primary lesion or a locoregional metastasis from the first mass, this of the submandibular gland space 2 years before. Histopathologically, the lesions were presented with the exact same pattern. The patient is on a follow-up schedule and is currently disease-free.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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