

Case-report

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Oral Lipoma or Atypical Tumor? The Importance of Complementary Diagnostic Studies in Oral Medicine

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Abstract

Lipomas rarely affect the oral cavity, typically presenting as a slow-growing, painless submucosal mass. Histological variants featuring spindle cells, pleomorphism or myxoid change can mimic an atypical lipomatous tumor, a well-differentiated liposarcoma, or a spindle cell lipoma, creating diagnostic uncertainty. We report the case of a 61-year-old woman with a one-month history of painful swelling of the right buccal mucosa, suggestive of a lipoma. Imaging demonstrated a well-circumscribed, non-encapsulated, lobulated lesion of fat density measuring 2.4 cm. The lesion was excised by intraoral approach, preserving the parotid duct. Histopathology showed a lipomatous neoplasm with adipocytes of variable size, spindle cells without atypia, and myxoid stroma. Immunohistochemistry showed a partially discordant pattern, with cyclin-dependent kinase 4 positivity but no murine double minute 2 expression, prompting molecular testing. Fluorescence in situ hybridization excluded retinoblastoma gene loss and murine double minute 2/cyclin-dependent kinase 4 amplification, confirming a benign lipoma with myxoid change by exclusion. Recovery was favorable, with transient paresthesia and limited upper lip mobility resolving within three months, and no recurrence at follow-up. This case illustrates how integrating clinical, imaging, histopathological, immunohistochemical and molecular findings enables a safe, definitive diagnosis of atypical oral lipomatous lesions.

Highlights

- A persistent buccal mucosa nodule containing spindle cells and myxoid stroma raised suspicion of an atypical lipomatous tumor/well-differentiated liposarcoma and of spindle cell lipoma.
- Immunohistochemistry showed a partially discordant pattern (CDK4-positive, MDM2-negative), illustrating a diagnostic pitfall that fluorescence in situ hybridization helped resolve.
- Fluorescence in situ hybridization excluded both retinoblastoma gene loss and murine double minute 2/cyclin-dependent kinase 4 amplification, confirming a benign lipoma with myxoid change by exclusion.
- Clinical history and presentation, imaging, histopathology, immunohistochemistry and molecular testing must be integrated when oral lipomatous lesions show atypical histological features.

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1. Introduction

Lipomas are among the most common benign mesenchymal tumors of the body, yet they remain uncommon in the oral cavity, where they account for fewer than 5% of benign lesions.[1, 2] In a series of 125 maxillofacial lipomas, the buccal mucosa was the most common site, followed by the tongue and the floor of the mouth, typically presenting as a slow-growing submucosal mass.[2]

Most oral lipomas are of the classic subtype, composed of mature adipocytes with minimal stroma, but several variants are recognized, including fibrolipoma, angiolipoma, spindle cell/pleomorphic lipoma, intramuscular lipoma, sialolipoma and lipomas with myxoid change.[1, 3] In the fifth edition of the World Health Organization Classification of Head and Neck Tumours these variants sit within the spectrum of benign adipocytic neoplasms. However, those with spindle cell proliferation or myxoid stroma may closely mimic an atypical lipomatous tumor or a well-differentiated liposarcoma, a locally aggressive neoplasm defined by amplification of the murine double minute 2 (MDM2) and cyclin-dependent kinase 4 (CDK4) genes.[1] Because well-differentiated liposarcoma is exceptionally rare in the oral cavity but recurs locally if incompletely excised, distinguishing it from a benign lipoma or spindle cell lipoma with atypical morphology has direct implications for surgical planning, prognosis and follow-up.[1, 3]

We report an oral lipoma with myxoid change and spindle cell proliferation that raised the differential diagnosis of both an atypical lipomatous tumor/well-differentiated liposarcoma and a spindle cell lipoma, and we make explicit the molecular rationale that allowed each entity to be excluded in turn.

2. Case Report

A 61-year-old woman presented to the emergency department in early March 2025 with a one-month history of swelling of the mid-right face, stable in size since onset, that had recently become painful – an atypical feature for a lipoma, which is characteristically painless, and the reason for her presentation. Extraoral examination revealed a discreet swelling of the mid-third of the right hemiface with effacement of the nasolabial fold. Intraoral examination showed an ovoid, submucosal mass of elastic (rubbery) consistency, approximately 2 cm in size, in the right buccal mucosa. This mass was partially mobile over the deep planes, with no overlying mucosal change. The lesion lay distal to the orifice of the parotid (Stensen) duct. The initial differential diagnosis included lipoma, fibroma, minor salivary gland neoplasm and mucocele.

Contrast-enhanced computed tomography and magnetic resonance imaging of the face and neck were performed (Fig. 1). Computed tomography demonstrated a well-circumscribed, non-encapsulated, lobulated lesion of fat density measuring 2.4 cm, predominantly superficial to the zygomaticus muscle, displacing the right

parotid duct without dilating it and without post-contrast enhancement. Magnetic resonance imaging confirmed a well-defined, non-encapsulated fat-signal lesion without infiltrative margins or abnormal enhancement – consistent with a lipoma and without features suggestive of an atypical lipomatous tumor.

The lesion was excised through an intraoral approach under local anesthesia, with identification and preservation of the parotid (Stensen) duct, achieving complete removal of the non-encapsulated mass without intraoperative complications. Postoperatively, the patient developed transient paresthesia and mild limitation of upper lip mobility. This condition was attributable to neurapraxia of the buccal branch of the facial nerve and of the adjacent buccal nerve (a sensory branch of the mandibular division of the trigeminal nerve), both of which lie close to the buccal surgical field and to the anesthetic infiltration and retraction used during excision. These were anticipated, self-limited sequelae rather than surgical complications, and resolved progressively (see the section “Discussion”).

Macroscopically, the specimen was a well-circumscribed, lobulated, yellowish mass (Fig. 2).

Microscopic examination revealed a lipomatous neoplasm composed of mature adipocytes of variable size, admixed with scattered bland spindle cells without cytological atypia, set within a myxoid stroma with occasional collagen fibers (Fig. 3A). No overt morphological features of malignancy were identified. Nonetheless, because a low-grade atypical lipomatous tumor/well-differentiated liposarcoma can closely mimic reassuring lipomatous morphology on conventional staining, and morphological assessment in isolation carries a substantial risk of both over- and under-diagnosis,[4] ancillary studies were pursued.

Immunohistochemistry for CDK4 and MDM2, whose amplification defines atypical lipomatous tumor/well-differentiated liposarcoma,[1] showed moderate nuclear immunoreactivity for CDK4 (Fig. 3B) but none for MDM2 (Fig. 3C) – a partially discordant pattern that can mislead if immunohistochemistry is relied upon alone.[5] Fluorescence in situ hybridization was therefore performed for MDM2/CDK4 amplification[6] and, in parallel, for retinoblastoma gene (13q14) loss, a recurrent and relatively specific feature of spindle cell/pleomorphic lipoma.[7] Testing was carried out at an external reference center (IPO Lisboa); as a send-out test, photomicrographs were not retained, and results are presented in narrative and tabulated form (Table 1).

Fluorescence in situ hybridization was negative for retinoblastoma gene loss and for MDM2/CDK4 amplification. The absence of amplification ruled out an atypical lipomatous tumor/well-differentiated liposarcoma, while the absence of retinoblastoma gene loss argued against spindle cell/pleomorphic lipoma. The definitive diagnosis was therefore benign lipoma with myxoid change, reached by systematic exclusion of both principal

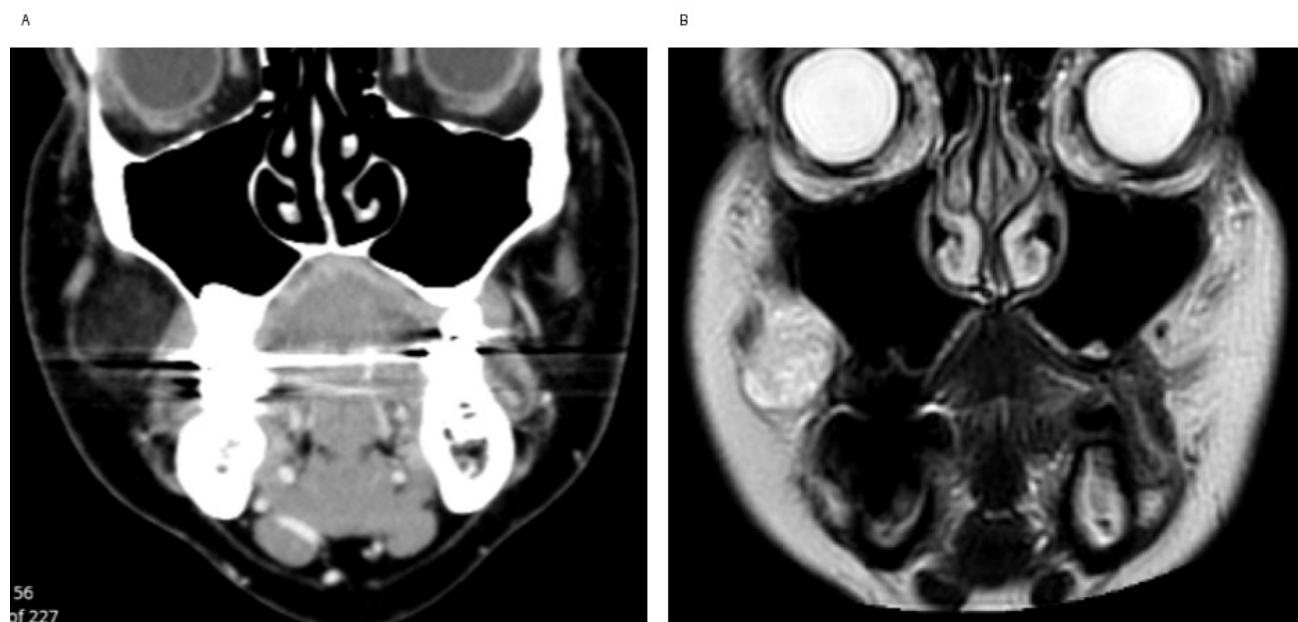


Figure 1. (A) Coronal contrast-enhanced computed tomography and (B) magnetic resonance imaging showing a well-circumscribed, non-encapsulated lesion of fat attenuation/signal in the right buccal region.

Table 1. Immunohistochemical and molecular results and their diagnostic interpretation.

Marker / test	Method	Result	Interpretation
CDK4	Immunohistochemistry	Moderate nuclear positivity	Equivocal in isolation
MDM2	Immunohistochemistry	Negative	Does not exclude ALT/WDLPS
MDM2/CDK4 amplification	FISH	Negative	Excludes ALT/WDLPS
RB1 (13q14) loss	FISH	Negative	Excludes spindle cell/pleomorphic lipoma

CDK4: cyclin-dependent kinase 4; MDM2: murine double minute 2; RB1: retinoblastoma 1; FISH: fluorescence in situ hybridization; ALT/WDLPS: atypical lipomatous tumor/well-differentiated liposarcoma.

differential diagnoses.

Postoperative recovery was favorable. The patient developed transient swelling and hematoma of the mid-right face (Fig. 4A), transient paresthesia, and mild limitation of upper lip mobility during the first two weeks after surgery, with progressive improvement and complete resolution by three months. The patient has remained under regular follow-up, with no evidence of recurrence at the most recent visit, in March 2026, twelve months after excision.

3. Discussion

Oral lipomas are rare and, unlike their cutaneous and subcutaneous counterparts, more often display histological variants that can complicate diagnosis,[2] consistent with our patient's presentation.

Imaging plays a supportive but not always conclusive role in this differential diagnosis. Simple lipomas are typically homogeneous, encapsulated, fat-signal masses, whereas thickened or nodular, enhancing internal septa

and a reduced proportion of macroscopic fat should raise suspicion for an atypical lipomatous tumor/well-differentiated liposarcoma.[8] In our patient, both modalities showed a homogeneously fat-density/fat-signal, non-encapsulated lesion without enhancement or infiltration, favoring a benign process; nevertheless, imaging cannot reliably exclude atypia at the cytogenetic level, and the histological findings alone still warranted molecular confirmation.

On histopathology, a lipomatous lesion with spindle cells and myxoid stroma must raise the suspicion for spindle cell/pleomorphic lipoma alongside atypical lipomatous tumor/well-differentiated liposarcoma. Spindle cell/pleomorphic lipoma has been reported in the oral cavity, including the floor of the mouth,[9] and is characterized by loss of the retinoblastoma gene locus at 13q14.[7] Myxoid change, as in our patient, is a recognized degenerative phenomenon that further blurs this distinction, as illustrated by a recently reported intraoral lipoma requiring immunohistochemical clarification before a benign diagnosis could be confirmed.[3] Im-



Figure 2. Macroscopic appearance of the excised lesion.

munohistochemistry is a useful first-line screen, but false-positive, false-negative and equivocal results occur.[5] In a recent case-control study, MDM2 and CDK4 immunohistochemistry achieved sensitivities of only 55.6% and 40.0% against fluorescence in situ hybridization,[4] which remains the reference standard for confirming or excluding amplification in problematic adipocytic tumors.[6]

In our patient, the isolated CDK4 positivity without MDM2 expression exhibited this exact kind of misleading pattern and made fluorescence in situ hybridization clinically necessary rather than merely confirmatory: the negative results for MDM2/CDK4 amplification and for retinoblastoma gene loss excluded both principal differential diagnoses and established a benign lipoma with myxoid change. The stakes were illustrated by well-differentiated and dedifferentiated liposarcomas of the upper aerodigestive tract initially mistaken for benign, non-adipocytic lesions on morphological grounds, and correctly identified only after molecular testing.[10] Consistent with the low recurrence risk reported once malignancy has been excluded,[2] our patient remains recurrence-free.

In adipocytic lesions, therefore, confirmatory molecular testing should be considered whenever immunohistochemistry alone yields a discordant or equivocal result, given the differing management implications of under- and over-diagnosis.

4. Conclusion

Oral lipomas with atypical histological features, such as spindle cell proliferation and myxoid change, require a comprehensive diagnostic strategy to exclude both atypical lipomatous tumors/well-differentiated liposarcomas

and spindle cell/pleomorphic lipomas. In the present case, integrating clinical, radiological, histopathological, immunohistochemical and molecular findings allowed a safe and accurate diagnosis by exclusion.

Prior Presentation

Preliminary data from this case were presented in poster format at the 8th National Congress of Stomatology (Congresso Nacional de Estomatologia), Algarve, Portugal, 2025.

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Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Claude (Anthropic) in order to assist with the writing and language of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Author Contributions

All authors participated significantly in the conception, preparation, review and approval of the manuscript, and agree to its submission in the current version.

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Patient Informed Consent

Written informed consent has been obtained from the patient to publish this paper, including the clinical photographs and imaging shown in the figures.

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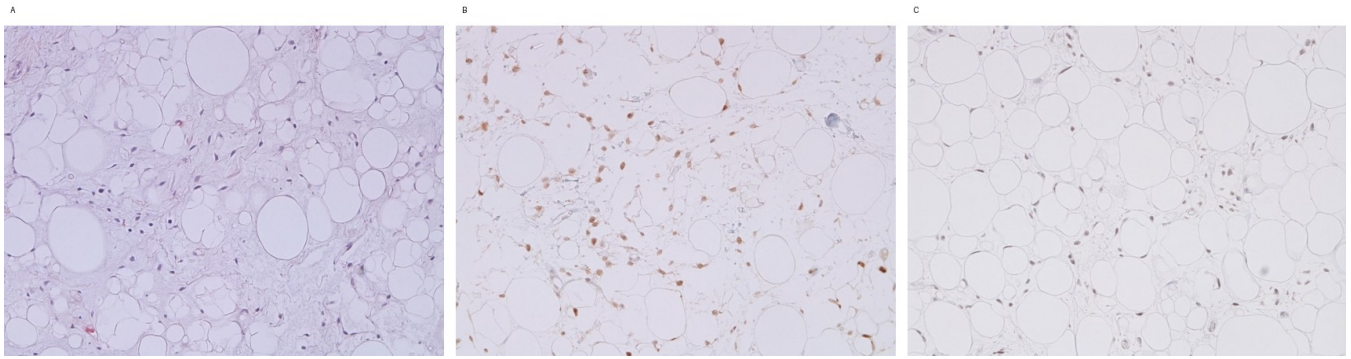


Figure 3. (A) Hematoxylin and eosin (200×): mature adipocytes of variable size, scattered spindle cells without atypia, and myxoid stroma. (B) Immunohistochemistry (200×): moderate nuclear immunoreactivity for CDK4. Immunohistochemistry (200×): absent nuclear immunoreactivity for MDM2 (C).



Figure 4. (A) Postoperative extraoral appearance, showing transient swelling and ecchymosis of the mid-right face. (B) Intraoral appearance at follow-up, showing a healed surgical site in the right buccal mucosa.

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