

# Oral liposarcoma in elderly

## Case report and literature analysis

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### Abstract

**Rationale:** Oral liposarcoma is an extremely rare lesion that is often clinically misdiagnosed as a benign lesion because of its asymptomatic and indolent clinical course. We report a case of atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) of buccal mucosa, provisionally diagnosed as lipoma.

**Patient concerns** A 97-year-old female was referred to dentistry and oral surgery department with an asymptomatic mass on the right buccal mucosa which had been present for an unknown period of time.

**Diagnosis** Magnetic resonance imaging demonstrated a well-circumscribed lesion at the right buccal mucosa, and a lipoma was suspected.

**Interventions** Surgical removal was performed, and a diagnosis of ALT/WDL was made. She and her family refused additional treatment due to her age.

**Outcomes** At the 10 months follow-up, the patient remained free of disease.

**Lessons** The indolent clinical course and small size of oral liposarcoma can lead to provisional clinical diagnosis of benign lesion.

**Abbreviations:** ALT/WDL = atypical lipomatous tumor/well-differentiated liposarcoma, CT = computed tomography, FDG-PET/CT = <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography, MRI = magnetic resonance imaging.

**Keywords:** adults aged 80 over, biopsy, buccal mucosa, elderly, liposarcoma

## 1. Introduction

Liposarcoma is the most common soft tissue sarcoma of adults, and makes up 15% to 25% of all sarcomas. It usually occurs in the deep soft tissues of the lower extremities and retroperitoneum of middle-aged adults.<sup>[1]</sup> In the head and neck region, liposarcoma is rare, and is found in up to 9% of cases.<sup>[2]</sup> Oral liposarcoma is even more rare, occurring mainly in the buccal mucosa and tongue of middle-aged adults with a male predominance.<sup>[3–7]</sup> Liposarcoma is divided into 4 subtypes:

atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL), myxoid liposarcoma, pleomorphic liposarcoma, and dedifferentiated liposarcoma. ALT/WDL is categorized as intermediate (locally aggressive) adipocytic tumors and is the most common subtype of liposarcoma, making up 30% to 40% of all liposarcomas.<sup>[1]</sup> In the oral region, ALT/WDL and myxoid liposarcoma are the predominant subtypes.<sup>[5,7–10]</sup> These tumors have a tendency of local recurrence, but distant metastasis rarely occurs unless these tumors become dedifferentiated.<sup>[2,11]</sup> Oral ALT/WDL may often be misdiagnosed as a non-malignant lesion because of its asymptomatic condition of slow-growing, painless, and circumscribed submucosal mass which may be present for several months or years before the diagnosis.<sup>[6,7]</sup> In addition, insufficient treatment may be given due to its rarity of incidence and complex histopathological features.<sup>[12–14]</sup> Herein, we report a case of ALT/WDL of buccal mucosa in a 97-year-old female, provisionally diagnosed as lipoma. We also review the English-language literature to investigate the association of preoperative diagnosis with treatment and prognosis of oral ALT/WDL.

## 2. Case report

A 97-year-old female was referred to our department with an asymptomatic mass on the right buccal mucosa which had been present for an unknown period of time. The patient's past medical history revealed dementia, type 2 diabetes mellitus, and neurogenic bladder. Intraoral examination showed a 20 mm, elastic soft, painless, smooth, and well-circumscribed yellow mass covered by normal mucosa on the right buccal mucosa (Fig. 1). Extraoral examination showed no cervical lymphadenopathy. Magnetic resonance imaging (MRI) demonstrated a well-circumscribed lesion at the right buccal mucosa. The mass revealed high-signals in

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Ethical approval not applicable. This is a case report.

Written informed consent was obtained from the patient for publication of the case and any accompanying images.

The authors have no conflicts of interest to disclose.

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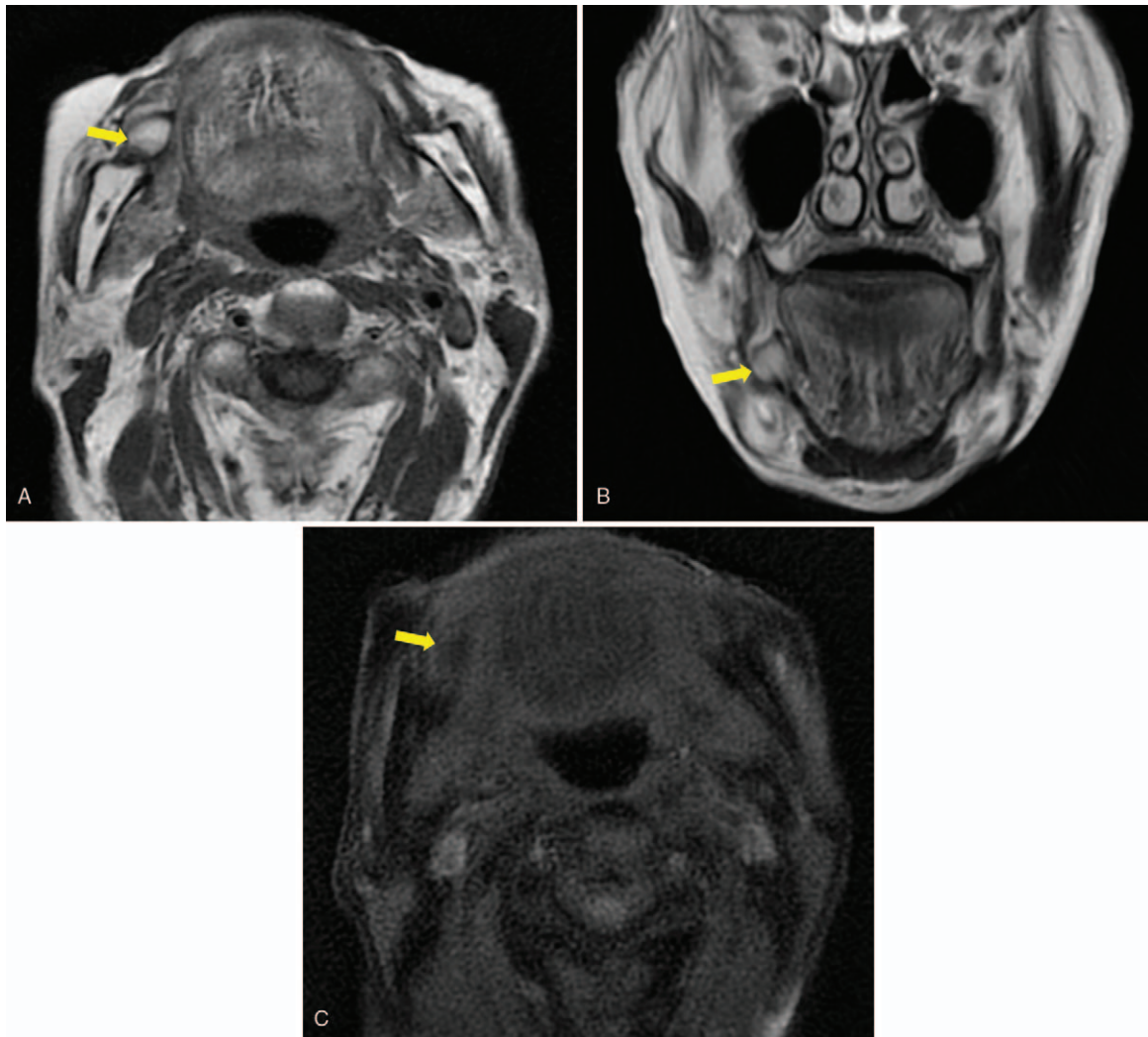


**Figure 1.** Intraoral examination showing a 20mm, elastic soft, painless, smooth, and well-circumscribed yellow mass covered by normal mucosa on the right buccal mucosa.

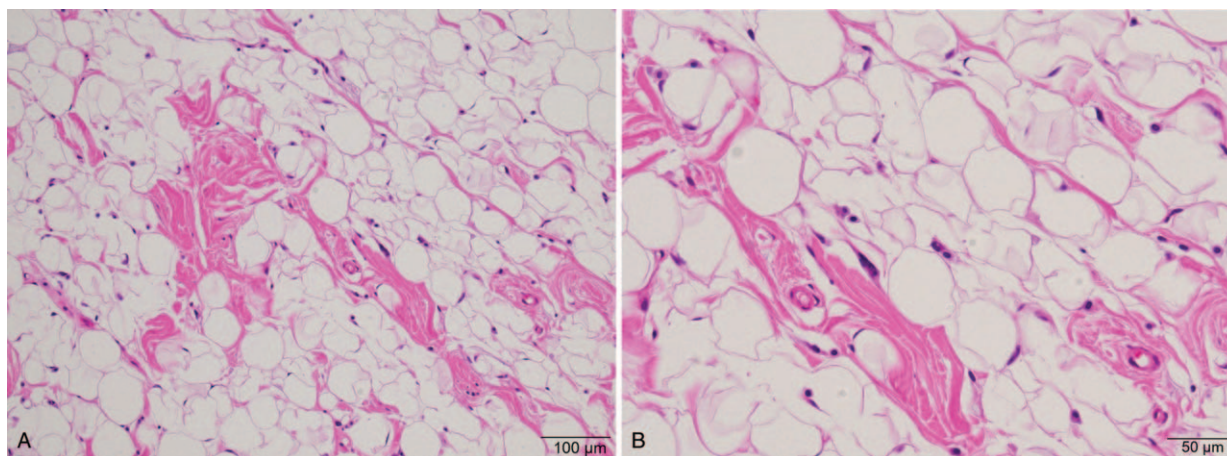


**Figure 3.** The removed specimen showing a pale yellow, non-capsulated mass.

both T1-weighted and T2-weighted images and low-signals in fat-suppression T1-weighted images (Fig. 2). With a provisional diagnosis of a lipoma, the patient underwent surgical removal of the mass under local anesthesia. The removed specimen revealed a pale yellow, non-capsulated mass (Fig. 3). Histopathological



**Figure 2.** Axial and coronal MRI images showing a well-circumscribed lesion at the right buccal mucosa. The mass revealed high-signals in both T1-weighted (A, arrow) and T2-weighted images (B, arrow) and low-signals in fat-suppression T1-weighted images (C, arrow). MRI = magnetic resonance imaging.



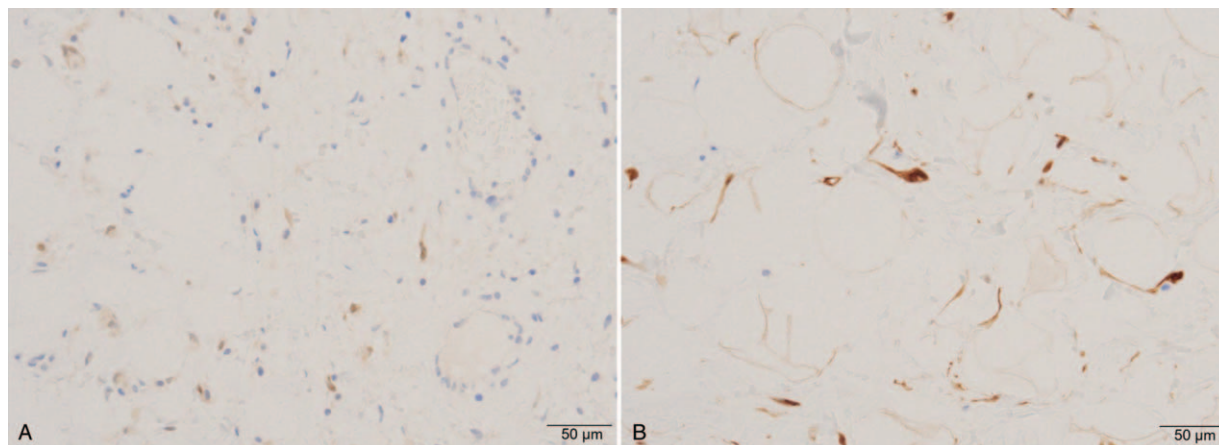
**Figure 4.** Histopathological findings showing proliferation of almost uniform sized adipocytes with hyperchromatic stromal cells in the fibrous connective tissue, hematoxylin and eosin stain; magnification, (A)  $\times 200$ , (B)  $\times 400$ .

examination revealed proliferation of almost uniform-sized adipocytes with hyperchromatic stromal cells in the fibrous connective tissue (Fig. 4). Immunohistochemical examination revealed positive results for p16 and cyclin dependent kinase (CDK4) (Fig. 5), and a few cells revealed weak positivity for murine double minutes 2 (MDM2). Based on the findings, a diagnosis of ALT/WDL (lipoma-like) was made. The patient and her family refused to take additional treatment due to her age, and we did not perform additional surgical treatment or postoperative radiotherapy.  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) scans at 1 month and 4 months after surgery revealed no evidence of local recurrence and distant metastasis. At the 10 months follow-up, the patient remained free of disease.

### 3. Discussion

We searched the English language literature published between 1979 and 2018 using PubMed and Google Scholar. We identified 120 cases of oral liposarcoma (Table 1).<sup>[3–6,8–10,12–66]</sup> The most common subtypes of liposarcoma was ALT/WDL (60.8%),

followed by myxoid liposarcoma (17.5%), dedifferentiated liposarcoma (6.7%), and pleomorphic liposarcoma (3.3%). The predominance of ALT/WDL and myxoid liposarcoma in the oral region was consistent with the previously reported studies.<sup>[5,8,9]</sup> The mean age is 50 years (from 6 months to 97 years). According to the available data in 114 cases, there was no particular sex predilection (male-to-female ratio 1:1.04). The most common location of oral liposarcoma was the tongue (40.7%), followed by cheek/buccal mucosa (31.4%), gingiva (7.6%), palate (5.9%), oral floor (5.1%), lip (4.2%), and other areas (5.1%). The most predominant site for oral liposarcoma was inconsistent among previous studies - either the tongue or cheek/buccal mucosa.<sup>[4–6,8,9]</sup> Most of cases appeared as a circumscribed, indolent, asymptomatic, firm or elastic hard or soft submucosal mass. The mean size of tumor was 29.6 mm (from 3 mm to 120 mm), and the mean duration was 25.5 months (from 0.3 to 168 months). In our review, ulcer formation was observed only in one case, and pain and bone resorption were observed in 4 and 5 cases before initial treatment, respectively. Distant metastasis or lymph node metastasis was not observed. One case of dedifferentiated liposarcoma metastatic to the



**Figure 5.** Immunohistochemical examination showing positive results for p16 (A, magnification,  $\times 400$ ) and CDK4 (B, magnification,  $\times 400$ ). CDK4 = cyclin dependent kinase 4.

**Table 1**  
Reported cases of oral liposarcoma in the English literature.

	Subtype					Total
	ALT/WDL	Myxoid	Pleomorphic	Dedifferentiated	Others*	
Case number (%)	73 (60.8%)	21 (17.5%)	4 (3.3%)	8 (6.7%)	14 (11.7%)	120 (100%)
Age, yr (mean (range))	55.1 (0.5–97)	45.1 (8–86)	37.5 (11–80)	55.9 (28–83)	47.2 (28–71)	50 (0.5–97)
Sex (male/ female/ unknown)	32/ 39/ 2	15/ 6/ 0	1/ 3/ 0	5/ 3/ 0	3/ 7/ 4	56/ 58/ 6
Duration (month) (mean (range))	30.5 (1–168)	12 (0.5–60)	8.7 (2–12)	26.5 (0.3–84)	36 (24–60)	25.5 (0.3–168)
Size** (mm) (mean (range))	25.6 (3–120)	31.9 (7–60)	56.7 (10–80)	43.3 (18–60)	39.2 (5–80)	29.6 (3–120)
Location						
Tongue	38	6	0	2	2	48 (40.7%)
Cheek/ Buccal mucosa	18	8	2	3	6	37 (31.4%)
Gingiva	3	2	1	2	1	9 (7.6%)
Palate	3	2	0	0	2	7 (5.9%)
Oral floor	4	1	0	1	0	6 (5.1%)
Lip	4	1	0	0	0	5 (4.2%)
Other areas†	1	1	1	0	3	6 (5.1%)
Clinical and imaging finding						
Pain	0	1	1	1	1	4
Ulcer formation	0	0	0	0	1	1
Bone resorption	0	1	1	1	2	5
Prognosis						
Recurrence	9	4	1	1	5	20
Died of disease	1	2	0	0	4	7

ALT/WDL = atypical lipomatous tumor/well-differentiated liposarcoma.

\*Others: liposarcoma (subtype was not described), mixed-type liposarcoma, round cell type liposarcoma, moderately differentiated liposarcoma, undifferentiated liposarcoma, fibroblastic liposarcoma.

\*\*Greatest dimension.

†Other areas: mandible (3 cases), mandibular soft tissue (2 cases), pterygomandibular space (1 case).

gingiva was reported.<sup>[56]</sup> Recurrence was reported in twenty cases, and 7 patients died of disease. The indolent clinical course, small size, and poor clinical and imaging findings of oral liposarcoma may lead to provisional clinical diagnosis of benign lesion or difficulty to suspect malignancy.

Since 1979, 6 cases of oral liposarcoma in patients aged over 80 years have been reported in the English language literature (Table 2).<sup>[4,24,26,42,47]</sup> There was no particular sex prevalence (4 males and 3 females), and the predominant site was the tongue (3 cases) and cheek/buccal mucosa (3 cases). The most reported subtype of liposarcoma was ALT/WDL. These trends resembled the 120 cases of oral liposarcoma mentioned in Table 1. The size of tumor was relatively small (the mean size of tumor was 25.7 mm) in the patients over 80 years and no cases were operated on aggressively. Although we know of only 1 case of myxoid liposarcoma of the medial thigh in a 91-year-old male,<sup>[67]</sup> to the best of our knowledge, our patient was the oldest case of liposarcoma known with disease-entity.

MRI and computed tomography (CT) can be very useful tools for the evaluation of soft tissue masses because fat can be easily identified.<sup>[68]</sup> Because of its superior soft tissue contrast resolution, MRI is the best imaging tool for evaluating the extent and internal structure of soft tissue tumors.<sup>[69]</sup> Characteristics which may assist in distinguishing ALT/WDL include age (over 60 years), size of the lesion (over 10 cm), presence of enhancing thickened septa (over 2 mm), the presence of non-adipose lesions, and lower proportion of fat (under 25% of tumor volume).<sup>[69]</sup> These image findings may help differential diagnosis. However, both ALT/WDL and lipoma consist of more than 75% fat, and the features of ALT/WDL and benign lipomatous tumors extensively overlap.<sup>[69]</sup> Therefore, the differentiation between lipoma and ALT/WDL using CT or MRI, especially in a small mass in the oral region like our case, is considered very difficult.<sup>[68,69]</sup> This is why histopathological examination is mandatory.<sup>[7]</sup> Besides, we did not use contrast medium considering the patient's burden on the kidney, which

**Table 2**  
Oral liposarcoma in elderly patients over 80 yr old in the English literature.

Case	Author	Age, yr/Sex	Duration, mo	Location	Size	Treatment (anesthesia)	Histopathological subtype	Prognosis
1	Eidinger et al <sup>[24]</sup> (1990)	80/M	2	Buccal mucosa	80 mm	Excision (ND)	Pleomorphic	6 recurrences during 5 yr
2	Azaz and Casaop <sup>[26]</sup> (1991)	86/F	2	Buccal mucosa	30 mm	Removal (Local)	Myxoid	2 recurrences at 3 and about 7 mo, died with disease at about 10 mo
3	Hattori et al <sup>[47]</sup> (2002)	81/M	2	Lip	12 mm	Excision (ND)	ALT/WDL	1 mo NED, then lost to follow-up
4	Nascimento et al <sup>[4]</sup> (2002)	80/M	12	Tongue	10 mm	ND	ALT/WDL	2 mo NED
5	Nascimento et al <sup>[4]</sup> (2002)	83/F	ND	Tongue	25 mm	ND	Dedifferentiated	ND
6	Angeles et al <sup>[42]</sup> (2005)	86/M	ND	Tongue	3 mm	Excisional biopsy (ND*)	ALT/WDL	ND
7	Present case (2019)	97/F	Unknown	Buccal mucosa	20 mm	Removal (Local)	ALT/WDL	10 mo NED

ALT/WDL = atypical lipomatous tumor/well-differentiated liposarcoma, F = female, Local = local anesthesia, M = male, ND = not described, NED = no evidence of disease.

\*Performed on an outpatient basis.

made preoperative diagnosis more challenging. We must also note the previous report of ALT/WDL of the gingiva that did not suspect liposarcoma on preoperative gadolinium-enhanced MRI.<sup>[14]</sup> Compared with ALT/WDL, other histologic subtypes of liposarcoma have a higher quota of non-adipose elements.<sup>[69]</sup> When a presumed lipoma has any complexity, liposarcoma should be taken into account.<sup>[68]</sup> Recently, intraoral ultrasonography has been utilized for preoperative diagnosis.<sup>[62,70]</sup> Sugawara et al reported that intraoral ultrasonographic findings reflected the histological findings in the cases of tongue mass lesions.<sup>[62]</sup> They showed the intraoral ultrasonographic finding of liposarcoma (subtype was not described) in the tongue; the tumor was a hypoechoic homogenous mass with an irregular border, and blood flow was observed in the center of the lesion. FDG-PET/CT also offers good sensitivity for assessment of sarcoma, including liposarcoma, and detection of their recurrence.<sup>[71]</sup> Suzuki et al demonstrated that FDG-PET is useful for differentiating between benign lipomatous tumors and ALT/WDL in the extremities.<sup>[72]</sup> Our patient was twice evaluated for local recurrence or distant metastasis by FDG-PET/CT and she remained free of disease during 10 months of follow-up.

ALT/WDL is subdivided into 3 subtypes: lipoma-like, sclerosing, and inflammatory.<sup>[1]</sup> The differentiation between lipoma-like and sclerosing type is often difficult and has limited practical importance since ALT/WDL has characteristics of both lipoma-like and sclerosing type.<sup>[1]</sup> Lipoma-like ALT/WDL typically shows a predominance of mature fat with a variety of spindled cells with hyperchromatic nuclei and multivacuolated lipoblasts. However, it is challenging to differentiate lipoblasts from their histological mimics.<sup>[73]</sup> Besides, lipoblasts are hardly identified in ALT/WDL and may exist in some benign lipogenic tumors. Recently, diagnosis is based more on the identification of atypical stromal cells rather than the identification of lipoblasts.<sup>[1]</sup> Differential diagnosis of ALT/WDL includes various neoplastic and non-neoplastic lesions, such as lipoma, intramuscular lipoma, spindle cell lipoma, pleomorphic lipoma, chondroid lipoma, myolipoma, angiolipoma, angiomyolipoma, lipoma with fat necrosis, lipoma with Lochkern (adipocyte with intranuclear vacuoles), and atrophy of fat.<sup>[1,6,73]</sup> For differentiation of ALT/WDL from various benign adipocytic lesions, additional immunohistochemical analyses are often required.<sup>[74]</sup> ALT/WDL and dedifferentiated liposarcoma are characterized by giant marker and/or ring chromosomes. The giant marker and ring chromosomes comprise an amplified sequence of the 12q13-15 region, leading to the amplification of several genes.<sup>[1]</sup> In ALT/WDL and dedifferentiated liposarcoma, both MDM2 and CDK4 are regularly amplified and expressed,<sup>[75,76]</sup> resulting in overexpressed proteins which can be detected by immunohistochemical examination.<sup>[77]</sup> MDM2 binds and inhibits tumor suppressor p53, thus decreasing apoptosis. On the other hand, CDK4 phosphorylates the RB (retinoblastoma protein), which inhibits its interaction with E2F transcription factor, allowing it to escape the G1-S checkpoint.<sup>[1]</sup> However, we must keep in mind that MDM2 expression may appear not only in tumor cells, but also in histocytes, which is observed in lipoma with degenerative changes.<sup>[74]</sup> Recent studies showed the utility of a combination of MDM2, CDK4, and p16 (cyclin-dependent kinase inhibitor 2A) as useful markers for detecting ALT/WDL and dedifferentiated liposarcoma.<sup>[77]</sup> p16 binds CDK4 and inhibits cell cycle progression and its level is supposed to be correlated with the level of MDM2 and CDK4.<sup>[78]</sup> These immunohistochemical examinations help provide a more accurate differential diagnosis,

especially when a molecular diagnosis, which uses MDM2 amplification assessed by fluorescence in situ hybridization, is not available.<sup>[77]</sup> Thway et al found that expression of MDM2 tended to be weak but that of CDK4 and p16 was mostly moderate to strong in ALT/WDL,<sup>[77]</sup> which was also observed in our case.

The treatment for head and neck liposarcoma is mainly surgery with negative margins.<sup>[7,79]</sup> Neck dissection is not necessary unless there is concrete evidence of lymph node metastasis, since lymph node metastasis is so rare.<sup>[80]</sup> McCulloch et al reported that incomplete excision was associated with 80% of local recurrence or distant metastasis in head and neck liposarcoma, and in those, 62.5% of the cases were pleomorphic or round cell (now referred as high grade myxoid type) liposarcoma.<sup>[81]</sup> In the head and neck region, a radical surgical approach can involve neurovascular and important anatomical structures and lead to functional and esthetic disorders. Some authors reported that conservative surgical excision with close follow-up should be preferred for head and neck ALT/WDL because of its clinicopathologic features and indolent biological behavior.<sup>[14,61,82]</sup> Postoperative radiotherapy should be considered in cases of large tumors, those in a deep anatomical location, high grade tumors, positive margins and local extension.<sup>[79]</sup> However, due to the absence of systemic studies comparing the outcomes of treatment with or without radiotherapy, the efficacy of radiotherapy has been obscure.<sup>[82]</sup> As for chemotherapy, myxoid liposarcoma is relatively chemosensitive compared with other subtypes of liposarcoma.<sup>[83,84]</sup>

For head and neck liposarcoma, the factors for better prognosis are associated with small size, the superficial site, and the histopathological predominance of the ALT/WDL variant. In oral liposarcoma, a maximum diameter not greater than 50 mm or 36 mm is considered a favorable prognostic factor.<sup>[5,7,38]</sup> The prognosis is poor when ALT/WDL occurs in the deep-seated area. ALT/WDL and myxoid liposarcomas have a better prognosis than the other histologic subtypes. On the other hand, pleomorphic, round cell (now referred as high grade myxoid type) and dedifferentiated liposarcomas show a higher incidence of recurrence and metastasis. Davis et al investigated 30 cases of liposarcomas in the head and neck region and reported crude disease-specific survival was 100% for ALT/WDL and myxoid liposarcoma, but 60% for round cell and 45% for pleomorphic liposarcoma.<sup>[79]</sup> This finding suggests that discrimination of the histological subtype of liposarcoma is pivotally important in predicting the prognosis.<sup>[66]</sup>

To gain a better understanding of the clinical characteristics and management of oral liposarcoma, reported cases were reviewed (Table 3). Since 1979, 45 well-documented cases have been reported in the English language literature.<sup>[3,5,6,8,9,13-17,19,20,25,29,30,32,35,38,39,41-43,47,50,52,54,57,58,60,64,65]</sup> The reported data included presence of preoperative biopsy, preoperative diagnosis, treatment and prognosis. Biopsy was undertaken in 22 cases, and 77.3% of cases were diagnosed with ALT/WDL or liposarcoma, while 18.2% of the cases were misdiagnosed with benign lesion. Among the cases diagnosed correctly, excisional biopsy was performed in 70.6%, and re-excision was performed in 58.3%, while no additional treatments were carried out in 33.3%. No recurrence was observed in the cases with excisional biopsy. In the group diagnosed as benign lesion by biopsy, incisional and not described biopsy (1 case) were performed, and 50% of the cases (2 cases) were untreated, which led to recurrence. On the other hand, 23 cases were treated

**Table 3**  
**Association of preoperative diagnosis with treatment and prognosis in oral ALT/WDL.**

Preoperative examination	Preoperative diagnosis	Biopsy technique	Treatment*	Prognosis		
Biopsy(+) 48.9% (n=22)	ALT/WDL or Liposarcoma 77.3% (n=17)	Excision 70.6% (n=12)	Re-excision 58.3% (n=7)	Recurrence 0% (n=0)		
			No treatment (only excisional biopsy) 33.3% (n=4)	Recurrence 0% (n=0)		
			Not described 8.33% (n=1)	Recurrence 0% (n=0)		
		Others 29.4% (n=5 <sup>†</sup> )	Conservative 60% (n=3)	Recurrence 20% (n=1)		
			Aggressive 40% (n=2)	Recurrence 0% (n=0)		
			Excision 0% (n=0)			
		Benign lesion 18.2% (n=4)	Not described 4.5% (n=1)	Others 100% (n=4 <sup>‡</sup> )	Conservative 50% (n=2)	Recurrence 0% (n=0)
					No treatment 50% (n=2)	Recurrence 50% (n=2)
					Aggressive 0% (n=0)	
				Excision 0% (n=0)	Conservative 0% (n=0)	
No treatment 0% (n=0)						
Aggressive 100% (n=1)	Recurrence 0% (n=0)					
Biopsy(-) 51.1% (n=23)	Unknown 100% (n=23)	Conservative 87.0% (n=20)	Conservative (with additional treatment <sup>¶</sup> ) 13.0% (n=3)	Recurrence 4.3% (n=1 <sup>§</sup> )		
			No treatment 0% (n=0)			
			Aggressive 0% (n=0)			
		Excision 100% (n=1)	Conservative 0% (n=0)			
			No treatment 0% (n=0)			
			Aggressive 0% (n=0)			

ALT/WDL = atypical lipomatous tumor/well-differentiated liposarcoma.

\* Conservative: removal, excision, debulking, cleaning surgical margins. Aggressive: resection, reconstruction, hemiglossectomy.

\*\* Others: incision, fine needle aspiration (1 case), not described (1 case).

† Include 1 case with 2 times of biopsy and 1 case with fine needle aspiration biopsy.

‡ Include 1 case of biopsy with not described technique.

§ The case eventually died of disease.

¶ wide excision, wide resection and suprahyoid neck dissection, radiotherapy.

without biopsy, and conservative surgical treatment was performed in all cases (100%), with provisional clinical diagnosis of benign tumor in most cases. In those, additional treatment was undertaken in 13% after the definitive diagnosis. Recurrence occurred in 17.4% of the cases without biopsy. These data imply that, if possible, excisional biopsy is preferable for accurate diagnosis, which may assist in avoiding inadequate treatment. In this case, the tumor was small size, located on the superficial site, and diagnosed as ALT/WDL. These conditions suggest good prognosis can be expected. However, follow-up duration of this case is short and further close follow-up is mandatory because the patient was treated conservatively and the recurrence rate is not low. A literature review by Nimura et al which investigated 50 cases of head and neck dedifferentiated liposarcoma showed that preoperative biopsy by either incision or fine needle aspiration is not reliable for the diagnosis of dedifferentiated liposarcoma.<sup>[63]</sup> In their study, dedifferentiated liposarcoma was diagnosed only in 23.1% of the cases by biopsy, and 46.2% of cases were misdiagnosed as benign lesions or failures. To overcome the

difficulty of precise preoperative diagnosis, immunohistochemical examination of biopsy specimen may be a potential diagnostic tool.<sup>[3,66]</sup>

#### 4. Conclusion

In conclusion, we reported the oldest patient with oral liposarcoma. The indolent clinical course and small size of oral liposarcoma can lead to provisional clinical diagnosis of benign lesion. Excisional biopsy is preferable for accurate diagnosis, which may assist in avoiding inadequate treatment. When conservative surgical treatment is performed before the diagnosis of ALT/WDL, and there is difficulty selecting additional treatment, close follow-up is essential.

#### Author contributions

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