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Submandibular gland cancer: Specific features and treatment considerations

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Abstract

Background: In the absence of unified treatment protocol, we evaluated the management and outcomes of submandibular gland cancers in an unselected patient series.

Methods: We included all patients with resected submandibular gland cancer treated at the Helsinki University Hospital from 2000 to 2010 with a 5-year minimum follow-up.

Results: Twenty-five patients with cancer represented 30% of submandibular gland neoplasms, and most were adenoid cystic carcinomas (ACCs; 56%). At presentation, 3 patients showed clinical signs of probable malignancy. Of 22 neck dissection specimens, 5 patients (20%) had metastases with an occult metastasis rate of 4%. Cancer recurred in 11 patients (44%), of which 7 (28%) were only at a distant site. The 5-year disease-specific survival (DSS) and overall survival (OS) rates were 76%, and disease-free survival (DFS) was 68%.

Conclusion: Most tumors were ACCs differing from the histological pattern of parotid gland cancers. Occult metastases were rare. The rarity of submandibular gland cancer, its variable histological pattern, and varying biological behavior warrant centralized management.

KEYWORDS
cancer, imaging, outcome, salivary gland, treatment

1 | INTRODUCTION

Submandibular gland tumors are rare, accounting for 7%–11% of salivary gland neoplasms,[1,2] where 30%–54% are malignant.[1–4] The 2017 World Health Organization (WHO) classification divides salivary gland carcinomas into 20 different histological types, some of which are further divided into subtypes.[1] Thus, the diagnostics and treatment of salivary gland carcinomas differ from other head and neck carcinomas, of which over 90% are squamous cell carcinomas (SCCs). Mucoepidermoid carcinoma (MEC) and adenoid cystic carcinoma (ACC) are among the most frequent malignancies encountered in the major salivary glands.[5] Treatment recommendations for salivary gland carcinomas are usually based on parotid gland tumors. Still, the biological behaviors of parotid and submandibular gland tumors can vary.[5]

The treatment of submandibular gland tumors remains challenging because the exact nature of the lesion is often unknown before or at the time of surgery. Inflammatory lesions are common and generally easy to differentiate from neoplasms using patient history, clinical examination, and ultrasound. Sometimes, inflammatory diseases, such as sclerosing sialadenitis, can resemble a malignant tumor. In the presence of neoplastic lesions, differentiating between benign and malignant lesions is often difficult. Because the histology of the tumor is seldom known preoperatively, the extent of surgical treatment to the neck is especially difficult to plan. We previously evaluated the treatment plans of all submandibular gland tumors at our institution during an 11-year period, and identified the challenges in differentiating between benign and malignant tumors.[4] In our series, 30% of submandibular gland tumors were malignant. We found fine-needle aspiration cytology (FNAC) under ultrasound guidance beneficial in treatment planning, while also considering its well-known limitations. Inadequate preoperative planning led to the need for additional surgeries when the histopathological examination revealed malignancy. Among all patients with a neoplasm, regional metastases were encountered in 6% of cases, that is, in 20% of malignancies.

Given the above, it seems obvious that applying generally accepted treatment guidelines could optimize the management of submandibular gland tumors. In the present study, we evaluate the treatment and outcome of submandibular gland cancers.

2 | PATIENTS AND METHODS

We included all patients who had undergone surgery at our institution for a malignant submandibular gland tumor between January 1, 2000, and December 31, 2010. Patient demographics, treatment, and follow-up data for 25 eligible patients were reviewed after January 1, 2017. We collected data on patient history, symptoms, clinical signs, imaging, FNAC, surgery, histopathological examination, pathologic TNM classification,[6] oncologic treatment, and follow-up. No other submandibular gland malignancies were diagnosed or treated at other hospitals within our university hospital district, which covers a population of 1.6 million people. The research ethics committee at the Helsinki University Hospital approved the study design and institutional research permission was granted.

We reevaluated and compared the histopathological specimens and MRI scans with the original pathological and imaging data. The criteria for malignancy, which is described elsewhere, were used to reevaluate the MRI scans.[7]

All patients had a minimum follow-up of 5 years or until death.

For statistical analyses, we used the IBM SPSS version 20.0 (SPSS, Chicago, IL). The 5-year overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS) figures were calculated using the Kaplan-Meier estimate. The length of follow-up was calculated starting from the last day of treatment through the end of follow-up or death from any cause (OS) and disease-specific death (DSS). The length of DFS was calculated starting from the last treatment day through the detection of cancer recurrence at any site or death.

TABLE 1 Tumor characteristics (n = 25)

Characteristics	Number	Percentage
Histology		
ACC	14	56
Salivary duct carcinoma	3	12
Acinic cell carcinoma	2	8
Carcinoma in pleomorphic adenoma	2	8
SCC	2	8
MEC	1	4
Sebaceous carcinoma	1	4
Pathological T classification		
T in situ	2	8
T1	11	44
T2	7	28
T3	3	12
T4a	2	8
Pathological N classification		
N0[a]	20	80
N2b	5	20
Stage		
0	2	8
I	9	36
II	5	20
III	4	16
IV	5	20

Abbreviations: ACC, adenoid cystic carcinoma; MEC, mucoepidermoid carcinoma; SCC, squamous cell carcinoma.
[a]Neck dissection was not performed on 3 patients with clinically N0. These patients are included in the figures.

3 | RESULTS

Our study population of 25 patients included 12 men (48%) and 13 women (52%) with a mean age of 59.6 years (range 26-88 years). The tumor characteristics are provided in Table 1. Due to the variety of tumors and their treatment, patient data are shown in Table 2.

The histological type did not change upon reevaluation in any of the cases. The most common histological type was ACC (14/25; 56%), followed by 6 other histological categories. Two tumors, both more than 2 cm in diameter, were

TABLE 2 Patient characteristics

Patient no.	Age/sex	Histology	Subtype/grade	Cytology class	pTNM	Primary surgery, including neck levels	Additional surgery	Postoperative RT (Gy)/CRT	Recurrence site and time[a] (later recurrent sites in parentheses)	Status at last follow-up	Follow-up time, years[a]
1	41/M	ACC	Cribriform	3	T1N0M0	Gland	ND I-III	. . .	Lung; 6.8 y	DWD	15.5
2	61/M	ACC	Cribriform	0	T4N0M0	Gland	ND I-III	60	Lung; 8.8 y	AWD	13.7
3	59/F	ACC	Cribriform	3	T1N0M0	Gland and ND I-III	. . .	. . .	. . .	NED	12.1
4	71/F	ACC	Solid (partly tubular)	3	T1N0M0	Gland	ND I-III	. . .	. . .	DWND	10.9
5	26/M	ACC	Solid (partly cribriform and tubular)	2	T2N0M0	Gland	ND I-III	60	. . .	NED	10.7
6	58/M	ACC	Cribriform	3	T3N0M0	Gland and ND I-III	. . .	70	. . .	NED	9.8
7	58/F	ACC	Cribriform (partly tubular)	3	T1N0M0	Gland and ND I	ND IIA-III	. . .	. . .	NED	9.0
8	52/F	ACC	Cribriform (partly tubular)	0	T1N0M0	Gland	ND I-III	56	. . .	NED	8.9
9	73/F	ACC	Cribriform (partly solid)	3	T2N0M0	Gland and ND I-III	. . .	60	Lung, liver; 2.6 y	AWD	8.7
10	59/F	ACC	Cribriform (partly tubular)	4	T3N0M0	Gland and ND I, IIA, III	. . .	60	. . .	NED	8.2
11	36/F	ACC	Cribriform	4	T2N0M0	Gland and ND I, IIA, III	. . .	60	Liver, bone; 7.3 y	DWD	7.4
12	88/F	ACC	Cribriform	1	T1N0M0	Gland	ND I	. . .	. . .	DWND	5.2
13	69/M	ACC	Solid (partly cribriform)	3	T2N0M0	Gland	ND I-III	. . .	Local; 2.2 y; (lung)	DWD	4.1
14	80/F	ACC	Cribriform and solid	3	T4N2bM0	Gland and ND I-V	. . .	56	Local; 8 mo; (base of skull)	DWD	2.1
15	53/M	SDC	. . .	2	T1N2bM0	Gland	ND I-V	66/cisplatin	Lung; 4.6 y	AWD	6.2
16	47/F	SDC	. . .	4	T1N0M0	Gland and ND IB	ND IA, II, V	66/cisplatin	. . .	NED	5.0
17	52/M	SDC	. . .	5	T1N2bM0	Gland and ND I-V	. . .	56/cisplatin	Locoregional; 1 mo; (liver, bone, lung)	DWD	2.1
18	55/F	Ca ex PA	SDC type	2	TisN0M0	Gland	. . .	. . .	. . .	NED	11.4

(Continues)

TABLE 2 (Continued)

Patient no.	Age/sex	Histology	Subtype/grade	Cytology class	pTNM	Primary surgery, including neck levels	Additional surgery	Postoperative RT (Gy)/CRT	Recurrence site and time[a] (later recurrent sites in parentheses)	Status at last follow-up	Follow-up time, years[a]
19	45/M	Ca ex PA	Adenomatous	4	TisN0M0	Gland and ND I-IIA	…	…	…	NED	11.0
20	55/M	Acinic cell ca	…	3	T2N0M0	Gland and ND I-III	…	60	…	NED	16.0
21	54/F	Acinic cell ca	…	2	T1bN0M0	Gland	…	60	…	NED	8.6
22	61/M	SCC	Grade 3	5	T2N2bM0	Gland and ND I-V	…	56	Lung, bone; 8 mo	DOD	1.0
23	69/M	SCC	Grade 3	5	T2N2bM0	Gland and ND I-V	…	50	Lung; 9 mo	DWD	1.0
24	72/M	Sebaceous ca	…	2	T1N0M0	Gland	…	…	…	NED	6.7
25	84/F	MEC	High grade	5	T3N0M0	Gland and ND I	…	…	Local	DWD	0.7

Abbreviations: ACC, adenoid cystic carcinoma; AWD, alive with disease; Ca, carcinoma; Ca ex PA, carcinoma ex pleomorphic adenoma; CRT, chemoradiotherapy; DOD, dead of disease; DWD, dead with disease; DWND, dead with no evidence of disease; Gy, Gray; MEC, mucoepidermoid carcinoma; ND, neck dissection; NED, no evidence of disease; pTNM, pathologic TNM; RT, radiotherapy; SCC, squamous cell carcinoma; SDC, salivary duct carcinoma.

[a]Time from the end of primary treatment.

reclassified as in situ carcinomas (stage 0)—both were within pleomorphic adenoma with an intact capsule. Both patients with SCC were initially identified as having unknown primaries, but the final histopathological examination of the neck dissection specimen revealed a tumor originating from the submandibular gland without any another detectable primary site.

The majority of the tumors were diagnosed at an early stage: 16 (16/25; 64%) were stage 0 to II, and altogether tumors in 20 patients (20/25; 80%) were classified as T in situ, T1, or T2 tumors. Histopathological examination revealed metastatic lymph nodes (pN+) in 5 patients (5/25; 20%). In addition, 20 patients (20/25; 80%) showed no neck metastases, 17 of which were verified from neck dissection specimens and 3 were clinically N0 (cN0) without recurrence through follow-up.

3.1 | Symptoms and clinical signs

The most common finding was a symptomless mass, in which palpation revealed only a single lump in 21 patients (21/25; 84%). Obvious malignancy was suspected in 3 cases (3/25; 12%): 1 patient had 2 palpable lumps, whereas 2 patients presented with a tumor growth (both SCCs) that raised suspicion. No patients had neurological symptoms or lingual, hypoglossal, or facial nerve functional deficits, and 21 patients (21/25; 84%) reported no pain. The average time interval between appearance of the mass and attendance at the clinic varied from an incidental finding to 10 years (<3 months, n = 7; 3-6 months, n = 5; about 1 year, n = 4; and 2-10 years, n = 9).

3.2 | Imaging

All patients underwent ultrasound and ultrasound-guided FNAC. The ultrasounds showed (1) a solid tumor with regular borders (13/25; 52%); (2) irregular borders (4/25; 16%); (3) a cystic-solid lesion (3/25; 12%); or (4) a highly vascularized lesion with low echogenicity (2/25; 8%). All 3 patients with obvious clinical findings for malignancy also showed malignant signs upon ultrasound. Abnormal or enlarged lymph nodes were reported in 6 patients, with pN + in 3 patients (3/25; 12%).

The MRI scans were performed on 15 patients (15/25; 60%) and 2 patients (2/25; 8%) underwent CT scans. The main indications included clinical signs of malignancy, FNAC classes 0, III, IV, and V, and/or suspicion of malignancy upon ultrasound. In 1 patient, the tumor was an incidental finding upon CT.

The primary MRI reports identified 2 tumors as benign, and 5 tumors as malignant, but provided no definitive statement about the tumors in the remaining 8 patients. In the neck, MRI showed suspicious lymph nodes in 5 patients, 4 of whom (4/25; 16%) had pN+.

Reevaluation of the MRI scans was possible in 12 cases showing signs of potential malignancy as follows: T2 hypointensity in 6 patients (all after FNAC), irregular margins in 8 patients, extraglandular growth in 5 patients, and perineural growth in 1 patient. Pathological lymph nodes were noted in 4 patients (these same 4 patients were also correctly diagnosed in the primary reports). At least 1 of the above-mentioned signs was present in 11 of 12 reevaluated tumors, and 10 tumors presented with at least 2 MRI signs of potential malignancy.

3.3 | Primary surgery

All 25 patients underwent surgery with a curative intent. Among the 11 patients (11/25; 44%) who only had the gland removed primarily without neck dissection, 8 did not present with any indications of possible malignancy, whereas 3 had class III upon FNAC. Furthermore, 14 patients (14/25; 56%) also had neck dissection primarily (Table 2). Frozen section analysis was used for 8 patients (8/25; 32%), and malignancy was indicated in all but 1.

3.4 | Additional surgery and neck metastases

The tumor board recommended additional surgery for 10 patients (10/25; 40%) due to inadequate margins or the type of histology or both. Eight of these patients previously underwent removal of the gland only without neck dissection. The specimens from the subsequent surgeries revealed remaining carcinoma in 5 patients (5/10; 50%) at the primary site, and pN + in only 1 patient with salivary duct carcinoma.

Including the additional surgeries in our analysis, we found that 22 patients (22/25; 88%) ultimately underwent at least levels I to III neck dissection. The exact levels of the metastatic lymph nodes remained unknown because the levels were unmarked in the dissection specimens. All 5 patients (5/25; 20%) with pN + had at least 2 ipsilateral metastases (pN2b). Only 1 patient (with SCC) had occult metastases, yielding an occult metastatic rate of 4% (1/25). Among ACCs, only 1 patient (1/14; 7%) had pN+.

3.5 | Oncologic treatment for primary tumors

Postoperative radiotherapy (RT) was given to 15 patients (15/25; 60%) with an average dose of 60 Gy (range 50-70 Gy). Among these 15 patients, 3 had salivary duct carcinomas and received cisplatin 40 mg/m^2 once weekly as concomitant chemotherapy together with RT (chemoradiotherapy [CRT]). The RT was administered using a linear accelerator with 6 MV photons. A thermoplastic head and neck mask was used for immobilization. Five patients were treated using conventional 3D RT, and 10 patients received intensity-modulated radiotherapy. The clinical target volume encompassed the surgical bed of the submandibular gland with wide margins, and 14 patients also received a total dose of up to 50 Gy at the ipsilateral neck. All patients were treated with conventional 2 Gy daily fractions administered 5 times a week.

3.6 | Recurrent tumors and follow-up

No patients were lost to follow-up, and the median follow-up time for patients alive at the end of the follow-up period was 9.0 years (range 5.0-16.0 years).

Locoregional recurrences occurred in 4 patients (4/25; 16%) within a median of 0.6 years (range 0.1-2.2 years). Three of these patients received further treatment with a curative intent and all subsequently died with disease. Distant metastasis in the lungs or liver without locoregional recurrence was encountered in 7 patients (7/25; 28%) within a median of 4.6 years (range 0.1-8.8 years).

Of the 14 patients with ACC, 6 experienced recurrence during follow-up. Two tumors recurred locoregionally and 4 patients developed distant metastasis in the lungs or liver within a median of 4.7 years (range 0.5-8.8 years).

The 5-year DSS and OS rates were both 76%, and the DFS rate was 68%.

4 | DISCUSSION

This study included all malignant submandibular gland tumors diagnosed and treated during an 11-year period within a catchment area of 1.6 million people in Southern Finland,[8] all treated at a single university hospital. We previously reported that malignant submandibular gland tumors represented 30% of all submandibular gland neoplasms in our study,[4] somewhat lower than typically reported,[2,3] yet in line with a more recent study.[9] Comparable with other reports,[9–12] most malignant tumors in our study were ACCs (56%). Reflecting our results, Han et al[10] found that salivary duct carcinoma (22%) and carcinoma ex pleomorphic adenoma (17%) were the next most common histological types encountered in submandibular gland malignancies. In addition to ACC, MEC and acinic cell carcinoma are among the most common histological types in parotid gland cancers.[13]

Although 36% of the patients in the present study sought medical attention more than a year after the onset of symptoms—which is not uncommon[14]—most tumors (64%) were still diagnosed at an early stage (stages 0-II), unlike the findings reported by others.[10,11] This may partially explain the somewhat surprising finding that only 3 patients had symptoms or clinical signs arousing suspicion of malignancy, and the most common finding of a symptomless mass only. This is in line with other studies, which showed that, in patients with ACC, a mass is the most common symptom, occurring

in 77%[14] to 98%[15] of cases. Pain was reported by 48% of patients with ACC in a study by Nascimento et al,[15] whereas another study found that only 7% of patients reported experiencing pain.[16]

An MRI or CT was used in 68% of the present patients. In our limited sample, MRI provided a somewhat higher accuracy estimating the cervical lymph node status compared to ultrasound. Particularly noteworthy, unlike ultrasound, at our institution, dedicated head and neck radiologists perform most MRI studies, possibly contributing to these results. An unblinded second review of an MRI revealed some signs of potential malignancy in all but 1 of the 12 reevaluated scans. None of the available scans included modern techniques, such as diffusion-weighted imaging, dynamic contrast-enhancement, or proton magnetic resonance spectroscopy, possibly further increasing the diagnostic accuracy of differentiating benign from malignant tumors.[17–20] In our recent publication, which also included benign submandibular gland tumors, we discussed the role of ultrasound and MRI in the diagnosis of submandibular gland lesions.[4]

Because the histology is seldom known at the time of surgery, treatment of the neck remains a challenge, especially in cases with cN0. The diagnosis of ACC generally does not call for elective neck dissection (END),[10,14] in contrast to salivary duct carcinoma.[21–23] Still, some recommend END for all patients with salivary gland carcinoma.[24] The rate of neck metastases in samples, including all submandibular gland cancers, varies. For instance, some studies report high figures of up to 45%[10] and 50%,[24] whereas we found a rate of 20%. Furthermore, our cohort included many patients at an early stage of disease. The rate of occult metastases also varies across studies. In addition to the different tumor stages and histologies reported between studies, the rate of occult metastases obviously depends on the diagnostic imaging methods. A study by Han et al[10] reported an occult metastatic rate of 20% among patients with submandibular gland cancer. Most specialists recommend END for all high-grade tumors,[5,10,25] excluding ACC,[10] which is in line with our study because ACCs carried a metastatic rate of only 7%. Hirvonen et al[16] found that 12% of patients with major salivary gland ACC presented with pN+. In their study, the occult metastatic rate was only 4%, despite that the study consisted of an older patient population treated when modern imaging methods were unavailable.[16] Similarly, Cohen et al[14] reported no occult metastases in submandibular gland ACC. By contrast, among all salivary gland carcinomas, Yoo et al[5] reported occult metastases in 19% of ACCs.

Including routine neck dissection in all cases would result in overtreatment, because most submandibular gland tumors are benign, ACC is the most common malignant tumor, and occult metastases are uncommon. Still, including additional surgeries, most of our patients with malignancy underwent level IB or more extensive neck dissection, a commonly reported tendency in retrospective studies of ACC.[14,16] We suggest that eventual neck dissection and its extent should be planned based on the cytological and radiological findings. Whenever malignancy is suspected (class III cytology or other criteria), we recommend extending surgery, at least to level IB, or to levels I to III depending on the case. Frozen section analysis can also prove useful in planning the extent of surgery, especially on the neck.[4,24,26]

Among 10 patients (40%) in our cohort, additional surgery revealed remaining malignant tissue in 5 patients, but pN + was found in only 1 patient. Some argue that the surgical field at this site may be limited due to the close proximity to vital structures, which can lead to positive surgical margins.[14] Thus, wider surgical margins may be warranted. Because positive surgical margins are often encountered in high-grade tumors,[22,23,27,28] additional surgery would probably fail to improve the margins but could compromise vital structures. Furthermore, for high-grade tumors, such as ACC, postoperative RT is usually scheduled in the presence of additional adverse factors, such as T3 to T4 tumors, incomplete resection, and bone or perineural invasion.[25,29] Postoperative RT increases local control of ACC, even in the presence of a residual tumor, although RT may also merely delay recurrence, which often occurs late during follow-up.[28] In this study, postoperative RT was administered for 60% of patients, of whom 87% were thought to have a high-grade tumor. The addition of RT was often warranted despite additional surgery.

Chemotherapy is mainly restricted to locally recurrent or distant metastatic disease,[30,31] although CRT may not improve survival.[32–34] Still, contradictory results have been reported.[35,36] Thus, postoperative CRT, usually including cisplatin, has also been used in the treatment of high-risk salivary gland carcinomas, of which the ongoing clinical trial Radiation Therapy Oncology Group 1008 should provide new insight.[37] Postoperative chemotherapy is recommended for salivary duct carcinoma, which carries a high risk for distant metastasis, even without a clear distant control or survival benefit.[22] Additionally, among older patients, adjuvant CRT carries more toxicity and mortality than RT alone.[38] Gao et al[39] reported that neither surgery nor oncologic treatment significantly impacted survival among patients with ACC with distant metastasis.

Androgen deprivation therapy[40–43] and targeted human epidermal growth factor receptor 2 therapy[40,44] for salivary duct carcinoma may prove beneficial. Anti-epidermal growth factor receptor therapy, especially in ACC, has been shown to stabilize disease progression in patients with relapse or metastases.[45] Targeted therapy was utilized in 3 recurrent tumors in our cohort.

In our cohort, 44% of patients experienced a recurrence during follow-up, and 28% incurred distant metastasis without recurrence at the locoregional site. Other researchers

reported slightly higher figures for distant metastasis; Roh et al[12] found that 31% of patients (19/62) experienced recurrence within a mean follow-up period of 64 months. A study by Han et al[10] reported a distant metastasis rate of 36% (23/64) within a mean follow-up time of 48 months—most frequently in the lungs, liver, or brain—when all submandibular gland cancers were considered, but only 12% in ACCs. By contrast, Hirvonen et al,[16] at our institution, reported that 50% of patients treated for major salivary gland ACC developed distant metastases, typically within 10 years. The solid subtype of ACC carries a higher risk for distant metastasis and a worse survival.[16,39,46] In our series, however, distant metastasis occurred in patients presenting with tumors of mainly the cribriform subtype. Due to the limited number of cases in our series, no definitive conclusions can be drawn.

Furthermore, 32% of the patients in our series died with disease during follow-up. Comparatively, Han et al[10] reported a 44% mortality rate in a series of 64 patients with submandibular gland cancer during a 5-year follow-up. The difference between these rates may result from the fact that, in the series by Han et al,[10] the rate of ACCs was lower (27%). Additionally, most patients presented with more advanced tumors because 72% were diagnosed as stage III or IV. However, in our series, 4 of the 5 patients with neck metastases died of disease and the 1 patient still living at the end of the follow-up had distant metastasis. Our 5-year DFS and OS rates are comparable to those reported by Cohen et al[14] who included only submandibular gland ACCs. However, our survival rates are higher than those reported in series that included fewer ACCs.[10,11] Because ACCs often recur years after treatment, a longer follow-up, such as > 10 years for all patients, would most likely lower the survival rates.

Some studies indicate that the prognosis of patients with submandibular gland cancer is worse than patients with parotid gland cancer.[5,47,48] Nobis et al[24] found no difference between parotid gland and submandibular gland tumors in their ability to metastasize to the neck; Terhaard et al[29] reported an opposite finding. Furthermore, a study by Armstrong et al[49] noted a higher incidence of occult metastases in submandibular gland tumors (21%) than in parotid gland tumors (9%). Additionally, the occurrence of distant metastasis in submandibular gland tumors (37%-42%) seems higher than in parotid gland tumors (17%-29%).[39,47]

5 | CONCLUSIONS

Clinical examination, preoperative imaging, and cytology may reveal no signs of malignancy or indicate benign findings in submandibular gland tumors that turn out malignant. Additionally, the lengthy time interval before the patient seeks medical attention may not raise the suspicion of malignancy. Utilizing FNAC, MRI, frozen section, and including level IB in the surgical field for inconclusive cases may assist in achieving an optimal extent of surgery. Routine extensive END does not seem advisable because occult metastases are rare and most malignant tumors are ACCs. In general, however, the higher propensity of submandibular gland tumors to metastasize to the neck compared with parotid gland tumors requires careful consideration. Due to the heterogeneity of submandibular gland malignancies, including the higher rate of distant metastasis, their evaluation and treatment must be individually tailored and centralized at experienced head and neck centers.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

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