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Primary tumors of the submandibular glands: A retrospective study based on 41 cases

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SUMMARY

We report our experience on the diagnostic approach, treatment, and follow-up of primary submandibular gland tumors. Retrospective review. Tertiary referral center. Forty-one adult patients, 22 male and 19 female, with primary submandibular gland tumors, 20 benign and 21 malignant. Age, gender, clinical findings, cyto- and histopathology, treatment and outcome were analyzed. Most tumors presented as a painless submandibular mass. Thirty three patients underwent a fine needle aspiration, the sensitivity, specificity and accuracy of which – in detecting malignant tumors – were 79%, 100% and 88%, respectively. Preoperative radiological imaging was performed in 30 cases. Patients with benign tumors were treated with surgery. Most malignant tumors were treated with a combined modality, including neck dissection and radiation therapy. Five patients developed a postoperative complication. Recurrent disease was encountered in 5 malignant tumors. The 2, 5 and 10 year disease-specific survival of patients with malignancy were 84%, 75% and 41%, respectively. The preoperative assessment of the nature of submandibular gland tumors remains challenging. Aggressive treatment of patients with malignant disease may help to avoid poor prognosis.

Introduction

Neoplasms of the salivary glands account for an estimated 3–4% of head and neck tumors and 8–22% of them involve the submandibular glands.[1,2] In the submandibular gland, 50–57% of the tumors are benign, most frequently pleomorphic adenoma, and 43–50% are malignant, with adenoid cystic carcinoma being the leading neoplasm.[1,3] Submandibular gland tumors usually present as a painless mass in the submandibular region and it is rarely possible to differentiate between benign and malignant based only on history and clinical findings. Therefore, the use of radiological imaging and fine needle aspiration cytology (FNAC) is frequently suggested in the literature.[3] The management of submandibular neoplasms remains controversial as there is no consensus with regard to the extent of primary surgery or the efficacy of neck dissection (ND) and/or postoperative radiation therapy (RT) in case of malignant disease.[3] The objective of this review is to evaluate the preoperative assessment and treatment of these tumors in a tertiary referral center over 16 years. Symptoms, clinical and radiological findings, cyto- and histopathology, surgical procedures, additional treatment and follow-up data were analyzed.

Patients and methods

In this retrospective study, 41 primary epithelial neoplasms of the submandibular gland treated between 1991 and 2007 in a tertiary referral center are reviewed. Metastatic tumors and lymphomas were excluded from the study. The mean age of patients with benign and malignant neoplasms was 57 years and 70 years, respectively. Among 20 patients with benign tumors, 11 were male and nine were female. Among 21 patients with malignant tumors, 11 were male and 10 were female. Radiological imaging was performed in 30 patients and FNAC in 33. Treatment modalities, surgical complications and recurrence rates were reviewed. For statistical analysis of survival rates the Log-rank (Mantle–Cox) test was applied using GraphPad Prism 5 software (GraphPad Software, La Jolla, CA, USA). This study was approved by the local review board of clinical investigation.

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Results

History and findings

Most neoplasms presented as a painless submandibular mass. The average time between first manifestation of disease and first medical consultation was 37 months in patients with benign tumors and 25 months in patients with malignant tumors. Among 20 benign neoplasms, one was associated with pain. Among 21 patients with malignant tumors, nine developed associate symptoms/clinical signs such as pain ($n = 3$), enlarged lymph nodes suggesting metastatic disease ($n = 2$), pruritus in the submandibular region ($n = 1$), neurological signs of lingual and hypoglossal nerve ($n = 1$), otalgia ($n = 1$) and infiltration of skin ($n = 1$).

Preoperative investigation

Computed Tomography (CT) was performed in 12 patients, Magnetic Resonance Imaging (MRI) in 12 patients and ultrasound (U/S) in six patients. Of these examinations, 8, 7 and 1, respectively identified the nature of the tumor correctly. FNAC was applied in 33 cases, 32 of which could be compared to permanent histologic outcome (Table 1). The nature of the tumor was preoperatively correctly detected in 11 out of 15 cases of malignant neoplasms evaluated with the aid of FNAC.

Histopathological findings

A pleomorphic adenoma was diagnosed in 17 out of 20 patients with benign tumor. The other three cases included a cystadenoma (oxyphilic cell), a myoepithelioma (clear cell type) and an oncocytoma. In the group of 20 operated malignant neoplasms, there were nine cases of adenoid cystic carcinomas (two of cribriform type, two tubular, two cribriform/tubular, two cribriform/solid, and one of cribriform/solid/tubular type), two mucoepidermoid carcinomas, two squamous cell carcinomas, two salivary duct carcinomas, two cases of adenocarcinoma ex pleomorphic adenoma, one epithelial-myoepithelial carcinoma, one adenocarcinoma (non otherwise specified), and one acinic cell carcinoma.

Treatment and tumor staging

All tumors suggestive of benign disease were treated with excision of the submandibular gland. The majority of malignant tumors were treated with a combined modality (surgical excision in 20 cases – 15 of which with ND – and RT in 16 cases). The only case in which no operation was performed involved a 101-year old patient with extended mucoepidermoid carcinoma, who was treated with palliative interstitial RT. Nine patients underwent ND of levels I–III (all elective), six were treated with a modified radical ND (four therapeutic, two elective) and five with exstirpation of the submandibular gland only. Altogether, 11 ND were elective and in two of them the histologic outcome revealed nodal disease. All four therapeutic ND were indicated by radiologically positive neck, two of which including clinical lymph node enlargement. The tumor resection margin was positive in nine cases. In the pT staging, four tumors were classified as pT1, nine as pT2 and seven as pT3. In the pN staging (including the 15 ND), nine patients had a pN0 neck, two were classified as pN1 (both in therapeutic ND) and four as pN2 (two in elective and two in therapeutic ND). Table 2 illustrates the pTNM classification of the 15 patients with ND. All tumors were classified as M0. The majority of patients ($n = 16$) were treated with RT, 15 of whom with external beam RT and one with interstitial RT. The radiation dose ranged from 60 to 70 Gy. Chemotherapy with carboplatine was advocated in two cases.

Complications

No complications were encountered in the group of benign tumors. There were five complications in the group of malignant tumors: Two palsies of the lingual nerve, one accessory nerve palsy (in a modified radical ND), one marginal nerve palsy and one hematoma.

Follow-up

In the group of benign neoplasms, the mean follow-up period was 5.1 years (ranging from 11 to 118 months) and no recurrence was observed. In the group of malignant neoplasms, the mean follow-up period was 4.4 years (from 15 to 120 months) and five patients developed a recurrence: one local (treated with interstitial RT), one regional/distant (treated with external beam RT and chemotherapy) and three distant (treated with chemotherapy in two cases, treatment refused in one case) recurrences. Two of the five patients with recurrent disease had no associate symptoms at the time of first diagnosis. The findings, treatment and outcome of all 21 patients with malignant disease are shown in Table 3. The 2, 5 and 10 year disease-specific survival of patients with malignant disease were 84%, 75% and 41%, respectively, whereas the 2, 5 and 10 year overall survival were 84%, 75% and 36%, respectively. It should be noted that only three patients from the malignant group had a follow-up period of 10 years. Curve comparison using Log-rank (Mantel-Cox) test showed no significant difference between disease-specific and overall survival ($p = 0.77$). The 2, 5 and 10 year recurrence-free survival were 84%, 66% and 66%, respectively (Figs. 1 and 2).

Discussion

All our patients presented with a submandibular mass. Associate symptoms/clinical findings were observed in one of 20 benign tumors and nine of 21 malignant tumors. Our series is too limited to indicate an impact of history and clinical manifestation on prognosis, which is a well-known issue in the study of rare malignancies.[3] Nevertheless, the presence of associate symptoms/findings is suggestive of malignant disease. In the group of malignancies, two out of five patients with recurrent disease had a painless submandibular mass at the time of diagnosis. Altogether, three out of

Table 1
Findings and diagnostic ability of cytological analysis in detecting malignant tumors.

Total FNAC	32
Nondiagnostic	6
True-positive	11
True-negative	12
False-positive	0
False-negative	3
Sensitivity	79%
Specificity	100%
Accuracy	88%

Table 2
pTNM classification (all tumors were classified as M0).

	N0	N1	N2	N3	Total
T1	2	–	1	–	3
T2	5	1	1	–	7
T3	2	1	2	–	5
T4	–	–	–	–	–
Total	9	2	4	–	15