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Utility of neck dissection for management of carcinoma of the parotid gland

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Abstract

To validate the use of neck dissection as part of the management of patients with parotid carcinomas, we retrospectively reviewed pathological and clinical data from the head and neck pathology archive at Guy's and St Thomas' Hospital on all patients who had primary parotid carcinomas resected between 1992 and 2014. The main outcome measure was the incidence of metastatic disease. A total of 54 of the 82 patients identified had neck dissections. Nodal metastases were detected in 10 with high-grade, invasive carcinoma ex-pleomorphic adenomas, two with salivary duct carcinomas, one with a high-grade adenocarcinoma not otherwise specified (NOS), one with an adenoid cystic carcinoma, and one with a high-grade acinic cell carcinoma. No metastases were found in those with a low-grade acinic cell carcinoma, low-grade mucoepidermoid carcinoma, epithelial-myoepithelial carcinoma, or non-invasive carcinoma ex-pleomorphic adenoma. The findings of this study support the use of routine neck dissection for the treatment of high-grade, invasive carcinoma ex-pleomorphic adenoma, salivary duct carcinoma, high-grade adenocarcinoma NOS, adenoid cystic carcinoma, and high-grade acinic cell carcinoma.

Keywords: Parotid; carcinoma; neck; dissection; lymph; node; prognosis

Introduction

Salivary gland carcinoma is a rare disease that can arise within any of the three major, or the minor glands. The parotid gland remains the most common site for newly-diagnosed cancer of the major salivary glands in England, and its incidence rose from 0.4 to 0.6/100 000 people between 1994 to 2013.[1] This rarity, combined with the varied entities, types of behaviour, and site within both the minor and major glands, has limited the construction of an evidence base to support the methods of treatment.

The United States National Cancer Database 1998-2012[2] has shown that lymph node metastases are associated with a high T stage and high grade of malignancy, and high-grade cases with metastatic disease are associated with a poor prognosis. This finding has also been supported by other US studies.[3,4] Data from UK populations, however, are limited.

The aim of this study therefore was to establish the frequency with which neck dissection was undertaken for parotid carcinoma within a London hospital, and to validate its use by establishing the incidence of metastasis to the cervical lymph nodes.

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Table 1
Pathological staging of parotid carcinomas in patients treated by neck dissection.

Type of carcinoma and grade	T1N0	T1N+	T2N0	T2N+	T3N0	T3N+	T4aN0	T4aN+	T4bN0	T4bN+	Total
Acinic cell:											
Low	3	–	6	–	–	–	–	–	–	–	9
High	–	–	–	1†	–	–	–	–	1	–	2
Adenocarcinoma not otherwise specified:											
High	–	1	–	–	1	–	1	–	–	–	3
Adenoid cystic	2	–	2	–	–	–	1†	–	–	1†	6
Basal cell adenocarcinoma	1	–	–	–	–	–	–	–	–	–	1
Carcinoma ex-pleomorphic adenoma (non-invasive)	1	–	1	–	1	–	–	–	–	–	3
Carcinoma ex-pleomorphic adenoma (invasive):											
Low	1	–	–	–	1†	–	–	–	–	–	2
High	–	–	4†	2	–	4††	–	4††	–	–	14
Carcinosarcoma ex-pleomorphic adenoma	–	–	–	–	–	–	–	–	–	1	1
Epithelial-myoepithelial	1	–	2	–	–	–	–	–	–	–	3
Secretory	–	–	–	–	1	–	–	–	–	–	1
Mucoepidermoid:											
Low	–	–	–	–	2	–	–	–	–	–	2
Intermediate	–	–	2	–	–	–	–	–	–	–	2
High	–	–	–	–	1	–	–	–	–	–	1
Salivary duct	–	–	2	–	–	–	–	1	–	1	4
Total	9	1	19	3	7	4	2	5	1	3	54

† indicates one death related to the parotid carcinoma.

Material and methods

This is a retrospective validation study for the use of neck dissection in the management of parotid carcinoma. No interventions were made on human or animal subjects.

To validate the use of neck dissection in the treatment of carcinoma of the parotid gland, we searched the oral and head and neck pathology database at Guy's and St Thomas' Hospital for patients who had primary resection of parotid carcinomas at the head and neck unit between 1992 and 2014. Pathological data were retrieved from text reports and further clinical information from the Trust's electronic patient record system. One patient was excluded as it was not possible to establish the T stage. Intraparotid and periparotid lymph nodes were included with level II. Mucoepidermoid carcinomas were graded according to the system published by Brandwein et al,[5] and staging was according to the Union for International Cancer Control (UICC) 7th edition. From 2007 patients were discussed at head and neck oncology multidisciplinary team meetings.

Statistical analysis was done with the help of GraphPad Prism 6.0g for Windows (GraphPad Software), and Welch's *t* tests were done to assess the significance of differences between groups.

Results

Histological types and patients' demographics

The group comprised 82 patients (42 women and 40 men, median (range) age 57 (10 – 84) years).

The five most common histological types of primary parotid carcinoma were high-grade invasive carcinoma ex-pleomorphic adenoma (n = 16), low-grade acinic cell carcinoma (n = 14), low-grade mucoepidermoid carcinoma (n = 8), adenoid cystic carcinoma (n = 7), and non-invasive (intracapsular) carcinoma ex-pleomorphic adenoma (n = 6). Less common types (five patients or fewer) included high-grade acinic cell, high-grade adenocarcinoma, basal cell adenocarcinoma, invasive low-grade carcinoma ex-pleomorphic adenoma, carcinosarcoma ex-pleomorphic adenoma, low-grade cystadenocarcinoma, epithelial-myoepithelial, low-grade salivary carcinoma not otherwise specified (NOS), intermediate and high-grade mucoepidermoid, low-grade myoepithelial, high-grade salivary duct carcinoma, and low-grade secretory carcinoma.

Treatments

Fifty-four patients had neck dissections and 28 did not. Of those who did not, the record of the preoperative diagnosis was not available in one, and the results of preoperative fine needle aspiration cytology were equivocal or incorrectly benign in 21. For the remainder who did not have neck dissections, the preoperative diagnoses were acinic cell carcinoma (n = 2), mucoepidermoid carcinoma (n = 3), and carcinoma ex-pleomorphic adenoma (n = 1).

Forty-three of the 54 who had neck dissections had had a preoperative diagnosis of carcinoma, and seven had had a preoperative diagnosis that was suspicious of malignancy. One who had a preoperative diagnosis of benign pleomorphic adenoma had an associated enlarged lymph node which, although benign on fine needle aspiration cytology, was excised as part of a neck dissection limited to level II. A preoperative diag-

nosis could not be found for the three remaining patients who had neck dissections.

Nineteen patients did not have radiotherapy. In six, information about its provision was unavailable for reasons such as the treatment being continued at other centres. One patient had had radiotherapy for a separate tonsillar squamous cell carcinoma (SCC) that had been diagnosed eight months previously. All patients not treated with radiotherapy had N0 and T1, 2, or 3, low-grade carcinomas. In one with a T2N0 non-invasive carcinoma ex-pleomorphic adenoma, tumour was present at the margin, but this area of the tumour was composed of a histologically benign element of pleomorphic adenoma. The disease-free margin in a T3N0 secretory carcinoma could not be established, but in all other cases it was between 0.1 and 1 mm. No perineural invasion or lymphovascular spread was recorded in the patients not treated with radiotherapy.

Outcomes of neck dissection

Histological types, T stage, and patients' demographics

Table 1 shows the final staging of patients who had neck dissection. Lymph node metastases arose in 10/14 patients with invasive, high-grade carcinoma ex-pleomorphic adenoma, the only one with carcinosarcoma ex-pleomorphic adenoma, and two of four with salivary duct carcinoma. Lymph node metastases developed in one of two patients with high-grade acinic cell carcinoma, one of six with adenoid cystic carcinoma, and in one of three with high-grade adenocarcinoma NOS (Table 1).

When all histological types were combined for patients who had neck dissections, the carcinomas with and without lymph node metastases did not differ significantly for age or T stage ($p > 0.05$).

All cases of invasive, high-grade carcinoma ex-pleomorphic adenoma without lymph node metastases were T2. Those with metastases were T2, T3, or T4a. Univariate analysis showed that a higher T stage was significantly associated with lymph node metastases ($p = 0.007$). There was no significant difference in age between patients with metastases and those without ($p > 0.05$). The numbers of patients with other types of carcinoma were too low to allow univariate or multivariate analysis.

Site and number of lymph node metastases

Neck dissections included level I in 22 patients, level II in 52, level III in 33, level IV in 20, and level V in 11 (information regarding levels was insufficient in two who had neck dissections). All those with lymph node metastases had involved nodes in level II. Metastases were present at level I in three, II in 16, III in two, IV in two, and V in one.

The involved levels were anatomically sequential in all but three cases. They were involved in levels II and IV in two and at levels II and V in the third.

In patients with lymph node metastases, the mean (range) number of involved nodes was 6 (1-34), median 3.5. Eleven or fewer nodes were involved in all but one patient who had metastases in 34 nodes. This patient was in his sixth decade and the tumour was a high-grade T4aN2b carcinoma ex-pleomorphic adenoma.

Incidence of occult lymph node metastases

Eight of the 16 patients with lymph node metastases had been preoperatively diagnosed with nodal disease. Metastases were occult in eight, all of whom had had some form of preoperative imaging. All but one patient (who had had magnetic resonance imaging and ultrasound examination) had had preoperative computed tomography (CT).

Follow up

Patients treated with radiotherapy

A total of 59 patients were treated with radiotherapy. One had radiotherapy for a separate primary carcinoma of the head and neck, and in five the data did not show whether radiotherapy had been given. Thirteen patients treated with radiotherapy died. Nine of them had had neck dissections (see under neck dissections) and had died of disease. One died from an unrelated cause, and records of the cause could not be found in two (see under neck dissections). One had had postoperative radiotherapy but had not had a neck dissection (see under no neck dissections), and the cause of death was unknown.

One who had had postoperative radiotherapy for a pT4bN0 high-grade acinic cell carcinoma developed pulmonary metastases (see under neck dissections). There were no further complications or deaths. The mean (range) follow-up time in this group was 44.1 (0.23-142.1) months, median 30.1.

Patients who did not have radiotherapy

Of the 19 patients who did not have radiotherapy, follow up data were available for all but one. One patient died from an unrelated adenocarcinoma of the lung (see under neck dissections). The mean (range) follow-up time was 32.1 (1.2 - 70.2) months, median 30.1. There were no recurrences, metastases, or disease-specific deaths.

Patients who did not have neck dissections

The mean (range) follow up in the 28 patients who did not have neck dissections was 41.7 (1.4 - 145.6) months, median 31.2. No information was available on four. No cause of death or follow-up information could be found on one patient, a man in the ninth decade who had had an epithelial-myoepithelial carcinoma (T2N0) treated with postoperative radiotherapy. One patient developed a recurrence at the primary site of a pT2N0 low-grade mucoepidermoid carcinoma. This had been incompletely excised initially and was completely excised 12.5 months after the primary operation. No metastases or disease-specific deaths were recorded.

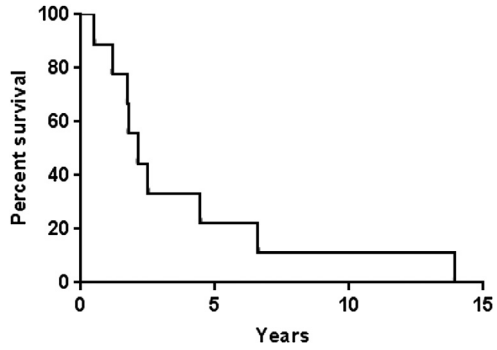

Fig. 1. Kaplan–Meier graph for overall survival in patients treated by neck dissection for high-grade parotid carcinoma.

Patients who had neck dissections

Of the 54 patients who had neck dissections, three had no follow-up information. Of those who did, the mean (range) duration of follow up was 40.7 (0.8 - 167.0) months, median 29.6.

Thirteen patients died. One, who had not had radiotherapy for the parotid carcinoma, died of an adenocarcinoma of the lung. The remaining deaths occurred in those who had had postoperative radiotherapy: one from an unrelated cause, two from unknown causes (no records could be found); and nine as a result of the parotid tumour, although biopsy confirmation of metastases and spread was not available (Table 1). These nine all related to high-grade carcinomas with the exception of a pT3N0 low-grade but invasive carcinoma ex-pleomorphic adenoma. Six of the nine patients had also had lymph node metastases. The disease-specific deaths occurred after 5.9 - 79.1 months of follow up. The other complication, pulmonary metastases from a pT4bN0 high-grade acinic cell carcinoma, was limited to one patient.

Overall survival in patients who had neck dissections for high-grade parotid carcinomas is shown in Fig. 1. Median survival was 2.11 years and five-year survival between 11% and 22%. Ten-year estimated survival was between 0 and 11%.

Discussion

Key findings and comparison with other studies

Combining histological grades, the three most common types of carcinoma in this group were carcinoma ex-pleomorphic adenoma and acinic cell carcinoma, followed by mucoepidermoid carcinoma. Other studies from the UK and US have found mucoepidermoid carcinoma to be the most common histological type of epithelial malignancy.[2,6]

The occurrence of cervical lymph node metastases in 50% or more of patients with invasive, high-grade carcinoma ex-pleomorphic adenoma and those with salivary duct carcinoma is consistent with previous series[2,7,8] and therefore supports neck dissection in such cases. The single patient with carcinosarcoma ex-pleomorphic adenoma in this series also had lymph node metastases. Although data are limited for this rare entity, it is known to be aggressive.[9] One of the two patients with high-grade acinic cell carcinoma also had lymph node metastases, which is in keeping with previously reported series that showed lymph node metastases in 40% - 49% of cases.[2,10] In our series they were found in 33% of patients with high-grade adenocarcinoma NOS. Previous series have found slightly higher incidences ranging from 45% - 65%.[2,3]

Seventeen per cent of patients with adenoid cystic carcinoma had lymph node metastases and this is also in keeping with previous reports.[2,11] It is acknowledged that distant, rather than lymph node, metastases are more typical in these cases.[11,12]

In patients who had neck dissections there was no metastatic disease in two with low-grade, and two with intermediate-grade, mucoepidermoid carcinoma, and in all three with epithelial-myoepithelial carcinoma and all three with non-invasive carcinoma ex-pleomorphic adenoma. On follow up in those who did not have neck dissections, there were no recurrences, metastases, or related deaths in three patients with non-invasive carcinoma ex-pleomorphic adenoma, three with epithelial-myoepithelial carcinoma, and two with low-grade mucoepidermoid carcinoma. Other patients in the group had low-grade carcinomas, but in numbers that were too low for useful inferences to be drawn.

The indolent behaviour described for non-invasive carcinoma ex-pleomorphic adenoma is consistent with previous studies and reviews.[7,13–15] The behaviour of mucoepidermoid carcinoma and epithelial-myoepithelial carcinoma is also consistent with previous studies. In an American group that included more than 20 000 patients, the incidence of lymph node metastases among those with epithelial-myoepithelial carcinoma was 6.4%.[2] In our group the overall incidence in patients with mucoepidermoid carcinoma was 20.2%. A high histological grade and high T stage were found to be predictive of lymph node metastases. Régis De Brito Santos et al[16] reported a risk of 11.1% for low-grade, and 16.7% for intermediate-grade, mucoepidermoid carcinoma. In a clinically N0 group, Lau et al[17] reported rates of metastases of 0% and 10% for low and intermediate-grade mucoepidermoid carcinoma, respectively. Our data, although limited, therefore support previous series and show a low incidence of metastases from non-invasive carcinoma ex-pleomorphic adenoma, epithelial-myoepithelial carcinoma, and low-grade mucoepidermoid carcinoma.

Limitations of study

It is acknowledged that the refinement of surgical treatment based on histological type and grade requires accurate preoperative diagnosis by cytological or histological investigation, which may not always be possible. The primary limitation of this study was the size of the group, together with varying numbers of patients with each histological type. It was further limited by the variation in the levels included in the neck dis-

sections, the number of lymph nodes yielded, and the varied and, in some cases, limited follow-up time. This was particularly pertinent in the case of salivary carcinomas, which have a propensity for delayed local recurrence and metastasis (sometimes more than 30 years after initial presentation).[7]

The variable behaviour of these carcinomas, and the complex interactions of stage, grade, and patient factors, emphasise the importance of preoperative imaging, biopsy, and discussion by the multidisciplinary team.

Clinical applicability of the study

This paper summarises the 22-year experience of the treatment of patients with primary parotid carcinomas in a tertiary centre, and provides data from the one of the largest UK groups. Our findings are in keeping with those of previous authors and, in this context, support the use of neck dissection when treating patients with high-grade, invasive carcinoma ex-pleomorphic adenoma, salivary duct carcinoma, high-grade adenocarcinoma NOS, and those with adenoid cystic carcinoma, and high-grade acinic cell carcinoma. Our data concerning low-grade carcinomas are more limited and require further evaluation in a multicentre setting.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

This retrospective study used anonymised patient data approved by the audit department of the hospital. Patients' permission not applicable- no identifying information included.

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