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Primary Parotid Neoplasms: Tumour Diversity and Characteristics Predictive of Malignancy

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Abstract

Purpose: To analyze tumor diversity and identify patient and tumor characteristics predictive of primary parotid malignancy.

Materials and Methods: Records were reviewed for patients who underwent a parotidectomy at The Palmerston North Hospital in New Zealand. Patients with primary parotid neoplasms were separated into benign or malignant subgroups. A multivariate logistic regression model was employed to compare categorical (gender, lesion side, nature of presentation, ethnic group, background of immunosuppression) and numerical variable (age) between the benign and malignant groups.

Results: 105 patients underwent parotidectomy between 2012 and 2022. Eighty-six that is 82% (86/105) of the patient cohort had benign pathology. Malignant pathology was present in 19 patients, that is 18% (19/105) of our cohort. Pleomorphic adenoma was the most common primary parotid tumor, making 51.4% (54/105) of cases followed by Warthin's tumor with 21.9% (23/105) of cases.

The most common malignant tumor was Acinic cell carcinoma. This tumor represented 21% (4/19) of the cases in the malignant group. Ninety-four percent (99/105) of patients had a palpable lump on presentation. No statistically significant relationship existed between malignancy and age, nature of presentation, lesion side and ethnic group. There was a predominance of males in the malignant group with them representing 73.7% (14/19) of cases in this cohort. This was statistically significant (p=0.01). Forty seven percent (9/19) patients in the malignant group had a background history of immunosuppression as compared to 15 out of 86 patients in the benign group (17%). There was a statistically significant difference between the two groups (p=0.007).

Conclusion: Our results show that most of these patients present with an asymptomatic slow growing parotid lump. Benign lesions are more common than malignant ones. The most common diagnosis for a patient presenting with a parotid lump is pleomorphic adenoma followed by Warthin's tumor.

A malignant tumor is more likely to be present in a male patient presenting with a parotid lump. Immunosuppression is another significant patient characteristic that is predictive of malignancy.

In summary , this study shows that in a cohort of patients who present with a parotid lump, with no signs of facial nerve palsy or skin changes, a higher degree of clinical vigilance is warranted in males and in patients with a background history of immunosuppression.

In the context of increasing pressures on Health systems which was made even worse by the recent COVID pandemic, this information can assist clinicians in their decision-making process when triaging and decision to expedite investigations when assessing a referral of a patient with a parotid lump.

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Introduction

Primary parotid tumors are rare entities. They represent between 2% to 5% of all reported head and neck malignancies [1]. The parotid gland is the most common site for salivary gland tumors. Between 70% to 85% of salivary gland tumors develop within the parotid gland [2]. Most parotid gland tumors are benign in nature, with around 20% being malignant.

The most common clinical presentation of a parotid tumor is that of a slow growing painless mass, usually in the tail of the parotid. History and physical examination can provide clinicians with important clues as to whether the mass is likely to be benign or malignant. The next line of investigation would include an ultrasonography and this is often complimented by an MRI to look at the deeper parotid tissue and for surgical planning. An US guided biopsy provides information on the histology. However, the definite diagnosis is only achieved through partial or total removal

of the gland. So, most patients presenting with a parotid lump will require open surgery to get a definite diagnosis.

Most of the literature on primary parotid neoplasms focuses on prognostic factors that influence disease free survival, overall survival, local and distant metastasis [3-5]. Other prognostic factors that have been investigated include tumor grading, facial nerve involvement, cervical lymphadenopathy, histological subtype and perineural involvement [6].

Given the relative paucity of information on patient characteristics that can clinically predict primary parotid malignancy, we sought to share our experience and add to the literature by providing insight into the clinical and demographic features of patients who underwent parotid surgery for a primary parotid tumor in our institution.

Our study has two aims

1. Analyze primary parotid tumor diversity with the aim of familiarizing clinicians about the different pathologies that can present as a parotid lump.

2. Identify any patient and tumor characteristics that can be predictive of primary parotid malignancy. This will allow for a more accurate clinical prediction of the risk of primary parotid gland malignancy.

Study design and ethics

This is a retrospective chart review study. The study was assessed by the Mid Central District Health Board Ethics Committee and deemed low risk. Ethics clearance was granted by the board.

Materials and Methods

The patient database at Palmerston North Hospital in New Zealand was interrogated to identify patients who underwent parotidectomy between 2012 and 2022. This search revealed 105 patients underwent parotid surgery for primary parotid tumors. Patients who underwent a parotidectomy for metastatic disease were excluded. The medical records of these patients were reviewed and the following variables were extracted: Age, sex, ethnicity, side of lesion, nature of presentation, histopathology and a background history of immunosuppression. The following ethnic groups were identified: New Zealand European, Other Europeans, Maori, and Asians, Chinese, Samoan and Indian origin. The side of lesion was left, right or bilateral. The medical history of all the patients was reviewed. Patients were divided into two groups, namely: Patients with a history of immunosuppression and those who did not have a history of immunosuppression. Conditions predisposing to immunosuppression were: A malignancy with or without a history of radio or chemotherapy, diabetes mellitus, advanced stage chronic kidney disease and being on immunosuppressive therapy such as prednisone and methotrexate.

Patients were divided in three categories to define the reason for presentation: Palpable mass, palpable symptomatic mass, Incidental finding on imaging.

Tumor diversity was analyzed and divided into benign and malignant groups.

A multivariate logistic regression model was used to compare variables between the benign and malignant groups. A p value of <0.05 was considered significant.

Results

There was a total of 105 patients who underwent a parotidectomy for primary parotid neoplasms between 2012 and 2022. Eighty-six, that is 82% (86/105) of the patient cohort had benign pathology. Malignant pathology was present in 19 patients, that is 18% (19/105) of our cohort.

Tumor diversity

Pleomorphic adenoma was the most common primary parotid tumor, making 51.4% (54/105) of cases followed by Warthin's tumor with 21.9% (23/105) of cases.

Pleomorphic adenoma was the most common primary parotid tumor in the benign category, making 62.8% (54/86) of benign cases. Warthin's tumor was the second most prevalent benign primary tumor, with 27% of cases (23/86).

Both these tumors made up nearly 89% (77/86) of benign primary parotid tumors. The remaining benign diagnosis included basal cell adenoma, apocrine cyst, papillary oncocytic cystadenoma, benign oncocytoma, chronic sialadenitis, chronic sialadenitis (lymphoepithelial).

The most common malignant tumor was Acinic cell carcinoma. This tumor represented 21% (4/19) of the cases in the malignant group. The other malignant tumor presentations were Ductal carcinoma of the parotid, large cell Neuroendocrine carcinoma, Hodgkin Lymphoma, Salivary duct carcinoma of the parotid, Epithelial myoepithelial carcinoma, Pleomorphic adenocarcinoma, Mammary analogue secretory carcinoma of the parotid, Peripheral nerve sheath tumor of the parotid, Spindle cell Squamous Cell Carcinoma of the parotid gland, and Secretory carcinoma. Patient characteristics (age, sex, Ethnicity, History of Immunosuppression) and tumor characteristics (nature of presentation and side of lesion) were evaluated to identify if there was a relationship between these variables and the diagnosis of malignant primary parotid tumor.

Age

Patients with malignant pathology were slightly older. The mean age of patient with benign pathology was 56.3 and malignant pathology was 63.3. The difference in age groups was not statistically significant ($p=0.099$).

Sex

Fifty seven out of the 105 patients were females (54%) and 48 out of the 105 patients were males (46%). Females represented the majority 60.4% (52/86) of cases in the benign group, with males making 39.6% (34/86) of that cohort.

On the other hand, there was a predominance of males in the malignant group with the 73.7% (14/9) of cases in this cohort. Females made up 26.3% (5/19) of malignant cases.

The difference between the two groups was statistically significant (p value =0.010).

Females have higher odds of having benign pathology compared to males, with an odds ratio of 4.282.

Ethnic groups

The majority of patients in both the benign (58/85) and malignant groups (14/19) were of New Zealand European origin. Given the low numbers in some of the ethnic groups, we grouped them together to look for any statistical significance. Ethnicity did not predict whether

a patient is more likely to have benign or a malignant tumor.

Side of lesion

Sixty percent of patients had left sided parotid masses (62/105) with 39% (41/105) presenting with right sided lesions. Two patients were found to have bilateral lesions.

In the benign category, 48 patients had left sided lesions with 36 patients presenting with right sided lesions. In the malignant category, 14 patients had left side lesions with 5 patients presenting with right side lesions. The two patients with bilateral lesions both had benign pathologies. There was no statistical difference between lesion side (p=0.190).

Immunosuppression

Given the low numbers in each category, we decided to test the variable of immunosuppression as either present or absent. Nine out of 19 (47%) patients in the malignant group had a background history of immunosuppression as compared to 15 out of 86 patients in the benign group (17%). There was a statistically significant difference between the two groups (p=0.007). The odds ratio of 0.235 indicates that patients with immunosuppression have higher odds of having malignant pathology.

Nature of presenting complaint

Ninety-four percent (99/105) of patients had a palpable lump on presentation. The remaining 6 patients were incidental findings from imaging. A comparison was only made between two groups – palpable mass, palpable symptomatic mass compared to benign and malignant groups. There was no statistically significant difference between the two groups of patients. There were no patients in our cohort who presented with a facial palsy.

Discussion

We performed a retrospective chart review of patients who underwent a parotidectomy over the last 10 years in our institution (n=105). Patients who had a parotidectomy for metastatic disease were excluded.

Our study had two objectives

1. Firstly, we aimed to analyze tumor diversity in our cohort of patients who underwent a parotidectomy. The objective is to familiarize clinicians about the different pathologies that can present as a parotid lump.

2. Secondly, we aimed to identify any patient and tumor characteristics that could be evaluated to allow a more accurate clinical prediction of the risk of primary parotid gland malignancy.

Our findings are consistent with the literature, with 82% of our cases being benign in nature. A 25-year review of tumors of major and minor salivary glands by Nagler and Laufer revealed that 80% of parotid tumors are benign in nature [8], with pleomorphic adenoma being the most common parotid tumor (60%) followed by Warthin's tumor (10%). Fifty-one percent of our patients had pleomorphic adenoma and around 22% of our cohort were diagnosed with Warthin's tumor.

Given the similarities between our cohort and the publications in the literature, the results we present should be applicable to other institutions.

In our patient cohort, the most common malignant tumor was Acinic cell carcinoma. This is in contradiction with the literature which reports mucoepidermoid carcinoma as the most common primary malignant parotid tumor [9]. We have low number (n=19) in the malignant cohort, this could potentially explain this finding.

It is important to keep in mind the other pathologies that can present within the parotid gland. Our benign cohort of patients also presented with basal cell adenoma, apocrine cyst, papillary oncocytic cystadenoma, benign oncocytoma, chronic sialadenitis, chronic sialadenitis (lymphoepithelial).

In our malignant tumor group, our patients were diagnosed with Ductal carcinoma of the parotid, large cell neuroendocrine carcinoma, Hodgkin Lymphoma, Salivary duct carcinoma of the parotid, epithelial myoepithelial carcinoma, pleomorphic adenocarcinoma, mammary analogue secretory carcinoma of the parotid, Peripheral nerve sheath tumor of the parotid, Spindle cell Squamous Cell Carcinoma of the parotid gland and Secretory carcinoma.

After examining tumor diversity, we looked at tumor and patient characteristics that can be predictive of malignancy.

The main complaint of patients with parotid tumors was a lump in the parotid area. This is consistent with the literature. Our patients presented with either a slow growing lump with no symptoms or a lump associated with some tenderness in the parotid area. All the symptomatic patients had mild discomfort, not requiring analgesia. We had no patients presenting with skin changes or facial nerve palsy. Again, this could be due to the fact that we had only 19 patients who presented with malignant primary parotid tumor. Junior et al. reviewed 600 cases of parotid neoplasms and in their cohort, 50% of malignant parotid tumors had clinical findings similar to those of benign tumors, such as slow growth, mobility over underlying tissue and absence of symptoms [10].

Our study showed a statistically significant difference between sex in the benign and malignant groups (p=0.01). Males were more likely to have malignant pathology as compared to females. Females were found to have higher odds of having benign pathology compared to males, with an odds ratio of 4.282. This is consistent with the literature [11]. This information means that greater vigilance is required if an elderly male presents with a new parotid lump.

Although our patient cohort in the malignant were on average older (63 years) as opposed to the benign group (56 years), this difference was not statistically significant.

Stein et al. reviewed 771 patients with a primary parotid malignancy. They showed a statistically significant difference between the mean age of patients in the benign and malignant groups. They demonstrated a 2.4% increase in the risk of malignancy with each additional year of age. In their cohort, patients with malignant disease had a peak tumor occurrence between the age of 70 and 80 where as those in the benign category peaked between the age of 50 to 60 years old [12].

There was no statistically significant difference in our patient cohort when ethnicity and side of lesion was compared in both the benign and malignant group.

Forty-seven percent of patients in the malignant group had a background history of immunosuppression as compared to 17%

in the benign group. There was a statistically significant difference between the two groups (p=0.007). The odds ratio of 0.235 indicates that patients with immunosuppression have higher odds of having malignant pathology. Forty to fifty percent of immunosuppressed patients have head and neck lesions [13]. This represents a cohort of patient who has HIV infection, diabetes mellitus, transplant patients, patients treated with immunosuppressive drugs or post radiotherapy. The most common head and neck organs affected are the salivary glands, the lymph nodes, the sinonasal tract, the orbits, the temporal bones and the pharyngo-laryngeal mucosa [13]. Oddone et al. [14], looked at 250 patients who had metastatic cutaneous squamous cell carcinoma of the head and neck. They identified 4 significant variables that were important predictors of prognosis: Immunosuppression, treatment, extra capsular spread and margin status. One study reported that no immunosuppressed patient was alive at 2 years post treatment compared with 87% of patients who remained in the immunocompetent group [15].

We acknowledge that there are many important limitations to our study. This is a retrospective study, hence only patients who underwent a parotidectomy were included. There is a cohort who presented with a parotid lump who did not end up having surgery. We recognize that a group of 105 patients is not that large when studying tumor diversity as well as patient and tumor characteristics that can be predictive of malignancy. On the other hand, despite our low numbers, our results were similar to the literature which suggests that our findings can be applicable to other institutions.

In summary, we performed a retrospective analysis of patients with a primary parotid neoplasm who underwent a parotidectomy. Our results show that most of these patients present with an asymptomatic slow growing parotid lump. Benign lesions are more common than malignant ones. The most common diagnosis for a patient presenting with a parotid lump is pleomorphic adenoma followed by Warthin's tumor. A malignant tumor is more likely to be present in a male patient presenting with a parotid lump. Immunosuppression is another significant patient characteristic that is predictive of malignancy.

Our study shows that in a cohort of patients who present with a parotid lump, with no signs of facial nerve palsy or skin changes, a higher degree of clinical vigilance is warranted in males and in patients with a background history of immunosuppression. In the context of increasing pressures on Health systems which was made even worse by the recent COVID pandemic, this information can assist clinicians in their decision-making process when triaging and decision to expedite investigations when assessing a referral of a patient with a parotid lump.

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