Clinicopathological pattern of malignant parotid gland tumors in Saudi Arabia

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ABSTRACT

الأهداف: لنقل خبرتنا عن التظاهرات السريرية المختلفة والأشكال التشريحية المرضية النسيجية المتنوعة للأورام الخبيثة في الغدة النكفية وطرق علاجها في مشفى تعليمي ثالث الرعاية.

الطريقة: تحليل رجعي لنتائج المرضى المشمولين بالدراسة تشمل الأنماط النسيجية للأورام النكفية الخبيثة في مستشفى الملك خالد الجامعي في الرياض في المملكة العربية السعودية خلال فترة 20 سنة من 1984م–2004م. تم تحليل السجلات الطبية الخاصة بهؤلاء المرضى حيث تم استعراض صفاتهم الذاتية والمظاهر السريرية والعمليات الجراحية التي أجريت لهم والأشكال المرضية المتنوعة.

النتائج: شملت الدراسة 32 مريضا ولوحظ أن معظم المرضى كانوا ذكورا بنسبة تزيد عن الإناث بـ 2،2 إلى 1 (22 رجلا و 10 نساء) وكان متوسط عمر المرضى 51،8 سنة (بمجال من 81–28 سنة). لقد كانت ملاحظة كتلة غير مؤلمة هي التظاهر السريري الأكثر تكرارا بين الحالات حيث شوهد في 23 مريض (71،8%) تلاه الخلل الوظيفي في العصب الوجهي في 14 حالة (43،7%). لقد تم استئصال الغدة النكفية عند 22 مريضا (68.7%) منهم 16 مريضا اجري لهم استئصال الفص السطحي للغدة النكفية أما الـ 6 الباقين فأجري لهم استئصال لكامل الغدة. تمت التضحية بشكل جزئي بالعصب الوجهي في 14 عملية (43،7%) أما التضحية الكاملة فكانت في 9 حالات (28،1%). أربع مرضى (12،5%) اكتشف لديهم نقائل خبيثة في العقد اللمفاوية مما تطلب تسليخ عنق جذري. 9 مرضى (28،1%) كان لديهم من نمط السرطان المخاطي البشروي 8 مرضى (25%) سرطان كيسي غدائي و 6 مرضى (18،7%) سرطان غدي غير محدد وفي حالتين (6،2%) فقط كان هناك سرطان في ورم غدي متعدد الأشكال. عينة (62.5%) أظهرت افات شديدة الخباثة منها 19 حالة (59،3%) أتوا بالمرحلة الثالثة أو الرابعة من المرض.

خاتمة: أورام الغدة النكفية الخبيثة تعتبر من الأورام النادرة جدا وتظهر عادة بشكل متباين في مراحل سريرية متأخرة. الأورام النكفية الخبيثة يمكن أن تظهر في فئات عمرية باكرة نسبيا مع نسبة حدوث مسيطرة عند الرجال في بلدنا مقارنة مع الغرب. كما أن الأشكال النسيجية للأورام الموضعية متقاربة مع الأورام ذات السلوك الهجومي.

Objectives: To report our experience of varied presentations and diverse histopathological spectrum of parotid gland malignancies.

Methods: This retrospective analysis incorporated patients with histological evidence of malignant parotid tumors at King Khalid University Hospital, Riyadh, Saudi Arabia over a 20-year period from 1984 through 2004. The medical records of these patients were analyzed for their demographic characteristics, clinical features, operations performed, and pathological diversity.

Results: Thirty-two patients comprised this study group. There is a male preponderance over females with a ratio of 2.2:1 (22 men and 10 women) and mean age of 51.8 (range 28-81 years). A painless lump was the most frequent clinical manifestation observed in 23 (71.8%) patients followed by facial nerve dysfunction in 14 (43.7%) patients. Parotidectomy was performed in 22 (68.7%) patients: 16 superficial and 6 total. A partial facial nerve sacrifice was undertaken in 14 (43.7%), and total nerve sacrifice in 9 (28.1%) patients. Four (12.5%) patients presented with cervical lymph node metastases necessitating radical neck dissection. Nine (28.1%) patients had mucoepidermoid carcinoma, 8 (25%) adenoid cystic carcinoma, 6 (18.7%) adenocarcinoma, not otherwise specified, and 2 (6.2%) were reported to have carcinoma in pleomorphic adenoma. Twenty (62.5%) specimens revealed high-grade aggressive lesions, and out of these, 19 (59.3%) patients presented with stage III/IV disease.

Conclusion: Malignant parotid tumors are exceedingly rare, occurring at a relatively earlier age group with male preponderance, and invariably declare at a late clinical stage in our community. Histopathological features hallmark a locally advanced disease with an aggressive behavior.

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Primary parotid cancers are rare and represent 1-3% of all tumors in the head and neck region.[1] At the same time, 75-85% of the salivary gland tumors occur in the parotid gland, of which 20-25% are malignant.[2,3] There are conflicting epidemiological reports and inadequate data regarding the origin, biological nature, and pathological characteristics of malignant parotid lesions. The purpose of this study is to highlight the spectrum of clinical features and cytoarchitectural variation of malignant parotid tumors in our community, which often tend to frustrate the accurate diagnosis of parotid malignancies.

Methods. The medical records of all consecutive patients who underwent surgical procedures for parotid cancers at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia over a 20-year period from 1984 through 2004 were analyzed for age, gender, presenting features, operative procedure, and histological details. The study was approved by our local ethics committee. After the year 2004 parotid tumors were referred to another university hospital with a specialized team consisting of head and neck surgeons, ear, nose, and throat (ENT) surgeons, maxillofacial surgeons, and other ancillary services. The clinical classifications, as well as stage grouping were reviewed and reclassified by the author pathologist using the 1992 Union International Contra Ia Cancrum (UICC) Tumor Nodes Metastasis (TNM) classification.[4] All tumors were classified to 3 grades based on different levels of biological behavior. Mucoepidermoid carcinoma and adenocarcinoma were sub classified into low- and high-grade in accordance with the histological characteristics.[5] The resection margin was considered positive for malignancy when tumor cells extend within 5 mm from the resected margins, or when the tumor directly involves the margins.[6]

The record was incorporated on software package (SPSS Inc., Chicago, IL) for maintenance and basic statistical analysis of data.

Results. Thirty-two patients comprised this study group: 22 men (median age 57, range 28-76) and 10 women (median age 50, range 36-81). Twenty-three (71.8%) patients presented with a painless lump and 14 (43.7%) with facial nerve dysfunction: paralysis in 9 (28.1%) and paresis in 5 (15.6%) as shown in **Table 1.** In this study, all patients with facial nerve paralysis were reported to have adenocarcinoma not otherwise specified (NOS), reaffirming the observation that facial nerve paralysis is more common in adenocarcinoma than in other malignant tumors of the parotid gland.[7] Parotidectomy was performed in 22 (68.7%) patients: 16 superficial, and 6 total. A partial facial nerve sacrifice was undertaken in 14 (43.7%) and total nerve sacrifice in 9 (28.1%) patients. Four (12.5%) patients presented with cervical lymph node metastases necessitating radical neck dissection. Mucoepidermoid carcinoma (MEC) was the most common tumor encountered in this series followed by adenoid cystic carcinoma (ACC) as outlined in **Table 2.** Eight (25%) specimens revealed histological evidence of perineural invasion: 5 adenoid cystic carcinoma (3 intermediate-grade, 2 high-grade), 2 mucoepidermoid carcinoma (both high-grade), and one high-grade adenocarcinoma. Histologically, positive margins were reported in 7 (21.8%) cases and out of these, 5 had perineural invasion. At the same time, 6 of these patients presented with stage III/IV disease with high-grade tumors. Overall, 20 (62.5%) patients showed high-grade parotid cancers, and out of these, 19 (59.3%) presented with stage III/IV lesions.

Table 1 - Clinical features of parotid carcinomas (n = 32).

Feature	Number	(%)
Asymptomatic lump	23	(71.8)
Facial nerve dysfunction	14	(43.7)
Nerve paralysis	9	(28.1)
Nerve paresis	5	(15.6)
Trismus	5	(15.6)
Salivary fistula	2	(6.2)
Painful lump	1	(3.1)
Fluctuant, tender lump*	1	(3.1)
Fixation to skin/muscle	1	(3.1)

*Patient with mucoepidermoid carcinoma presented as paratoid abscess

Table 2 - Histopathological features of malignant parotid tumors (n = 32).

Histopathology	Stage			Grade			Total
	I	II	III/IV	Low	Inter-mediate	High	No. (%)
Mucoepidermoid Ca	1	3	5	2	-	7	**9 (28.1)**
Adenoid cystic Ca	1	3	4	-	3	5	**8 (25.1)**
Adenocarcinoma NOS	-	4	2	2	-	4	**6 (18.7)**
Acinic cell Ca	1	-	3	3	-	1	**4 (12.5)**
Ca in pleomorphic adenoma	-	-	2	-	-	2	**2 (6.2)**
Clear cell adenocarcinoma	-	-	1	-	-	1	**1 (3.1)**
Squamous cell Ca	-	-	1	-	1	-	**1 (3.1)**
Undifferentiated Ca	-	-	1	-	1	-	**1 (3.1)**

NOS - not otherwise specified, Ca - cancer

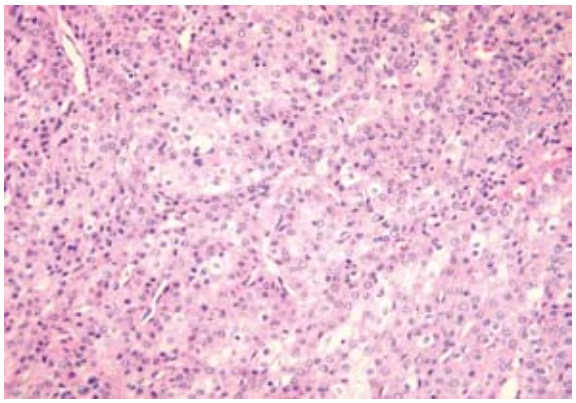

Figure 1 - Mucoepidermoid carcinoma showing tumor cells arranged in solid pattern with squamous differentiation and clear cell component. Hematoxylin and Eosin stain X 200.

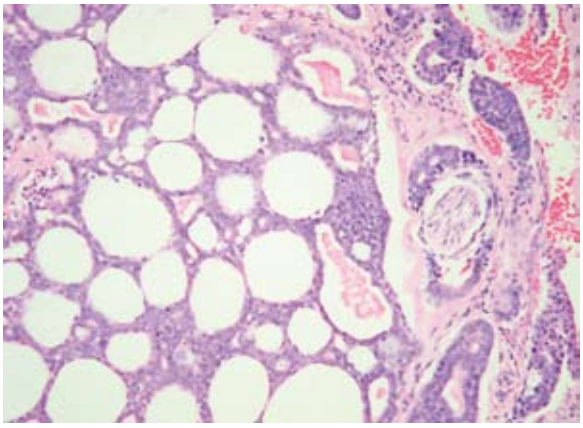

Figure 2 - Adenoid cystic carcinoma demonstrating small cells arranged in cribriform pattern with perineural invasion. Hematoxylin and Eosin stain X 200.

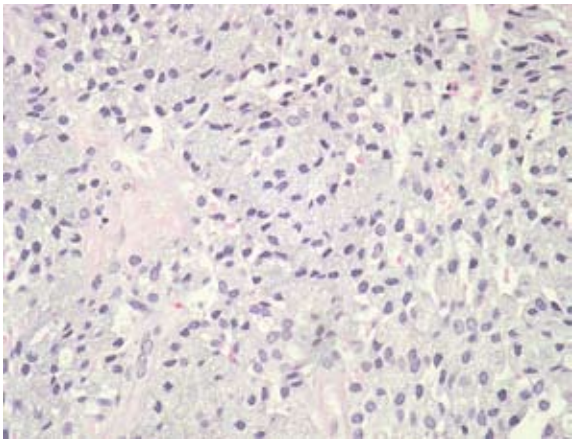

Figure 3 - Solid sheets of rounded cells having round nuclei with fine chromatin and abundant granular basophilic cytoplasm. Hematoxylin and Eosin stain X 200.

Discussion. Malignant parotid gland tumors are most frequently encountered in the sixth and seventh decades with a female preponderance ranging from 1.2:1 to 1.8:1 for different histological variants.[8,9] Our series demonstrated a male preponderance over females with a ratio of 2.2:1 and tumors occurring at an earlier age peaking at the beginning of the fifth decade (median age of 51.8 years). Approximately 50% of parotid cancers present with asymptomatic, slowly growing, firm elastic swelling, the remainder reveals signs of malignant disease such as painful lump,[10] facial nerve dysfunction, metastatic cervical lymph nodes, trismus, and/or tumor fixation to the adjacent structures.[1] The incidence of facial nerve dysfunction in the present study matched the reported figures.[11] Malignant infiltration of the facial nerve is more common in high-grade tumors and carries a high risk for distant metastases,[12] predicting high recurrence,[5] and influencing prognosis.[13] Parotid lesions were managed by a diversity of general surgeons during the 20-year period of the present study, resulting in diverse surgical outcomes, especially inadequate resections for malignant lesions (more partial versus total parotidectomy) and a relatively high positive resection margins rate, which definitely influence the surgical outcome and prognosis. The MEC and ACC are the most frequent malignant tumors of the salivary glands, some authors have reported a higher incidence of MEC,[14] while others mentioned ACC.[15] Approximately 50% of MEC of salivary glands occur in the parotid[16] with peak age incidence in the fifth through seventh decade of life, but no age is exempt.[17] Parotid MEC usually presents as a slowly growing, firm, and painless mass. The microscopic hallmark is epidermoid and mucous cells, however, intermediate, clear, and columnar cell types are also common (**Figure 1**). Low-grade MEC show a predominance of mucous-producing cells with cystic spaces and intermediate-grade tumors demonstrating a tendency to form solid nests of squamous cells with nuclear atypia. High-grade lesions are characteristically solid, and their biological behavior is usually more aggressive with higher tumor size (T) and lymph nodes involvement (N) status at presentation, which reduces survival.[18,19] We documented 4 patients with preoperative cervical lymph node metastases and all of them were found to have high-grade MEC, which reaffirms the correlation between lymph metastases and tumor grade as reported by Hosokawa et al.[20] Prognosis is worse when high-grade MEC are associated with stage III and IV disease.[21] The ACC is essentially a highly malignant tumor of adulthood with a definite peak incidence in the fourth to sixth decades of life,[17] showing an equal gender distribution.[22,23] Invasion of and tracking along the nerves is characteristic of ACC. Perineural invasion has been identified as an unfavorable prognostic factor.[24] Rapidis et al[7] confirmed that the perineural invasion

by ACC facilitated distant metastases, thus adversely affecting the final outcome. Histologically, myoepithelial differentiated cells with clear cytoplasm, poorly defined cell borders, and angular nuclei are the striking features. The most commonly reported cribriform pattern of ACC has a typical "Swiss Cheese" appearance (**Figure 2**). The factors that influence the prognosis of ACC are stage, presence of tumor at the margins, size of primary lesion, degree of atypia, and lymph node metastases.[25] This series showed 5 high-grade ACC with gross cellular atypia but surprisingly, with no cervical lymph node metastasis. Adenocarcinomas represent 8.8-44.7 percent of malignant salivary gland tumors, a range that reflects inconsistent classification.[26] The majority of lesions are asymptomatic, however, 20% cause pain or facial weakness. Histologically, adenocarcinomas demonstrate a wide range of architectural patterns, glandular differentiation and infiltrative growths that determine their grading. The 15-year survival for low-, intermediate-, and high-grade adenocarcinomas are reported to be 54%, 31%, and 3%.[7] Two (6.2%) patients in our study showed malignant transformation in pleomorphic adenoma. A history of sudden increase in lump size and intractable pain was noted in both. Invasion of the soft tissue beyond the capsule of the original neoplasm is an important landmark to confirm a malignant change, and the prognosis depends on the microscopic grade and proliferative index.[27] The majority of acinic cell carcinoma of the salivary glands are found in the parotid gland, which affects patients of all ages with slight female preponderance.[17] Two cases with acinic cell carcinoma (**Figure 3**) in our series presented with salivary fistula and trismus, which was also observed by Adekeye and Ord.[28] On a broader basis, tumor stage, and size, margin status, lymphatic spread, DNA aneuploidy, and survival are significantly related to the tumor grade in salivary gland lesions.[29] All patients with positive resection margins, high grade tumors, and stage III/IV were referred to other local hospitals with more facilities for possible adjuvant chemotherapy and/or radiotherapy. Limitations of this study include no follow-up for long-term and final outcomes, which were not feasible due to some logistic barriers over that long period. Although this is very important, however, this was not our objective in this study.

To conclude, malignant parotid tumors are exceedingly rare, occurring at a relatively earlier age group with male preponderance, and invariably declare at a late clinical stage in our community. Histopathological features hallmark a locally advanced disease with an aggressive behavior. Surgical and possibly prognostic outcomes are better if these cases are referred early to centers having specialized head and neck surgeons with good ancillary services.

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