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ORIGINAL ARTICLE

PRESENTATION AND CLINICAL OUTCOME OF PATIENTS WITH MALIGNANT SALIVARY GLAND TUMORS

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Aim: *Salivary gland cancer is a rare disease and comprises approximately 5 to 6 % of cancers of the head and neck and 0.3% of all cancers. These tumors display a diverse biological behaviors and clinical presentation. Currently, many series has described site, size stage, histology and grade of the tumors as important prognostic factors affecting the outcome. Aim of the work was to evaluate the presentation and management outcome of patients presented with salivary gland cancer in search of prognostic factors for locoregionl control, disease free survival, and overall survival.*

Methods: *The records of all patients with malignant salivary gland tumors presenting for treatment at our institution between October 1997 and October 2002 were reviewed. Variables were collected and outcome measures were defined in terms of locoregional, and distant control, and overall survival and disease-free survival (DFS), in 5 years follow up. Survival was described using the Kaplan-Meier method.*

Results: *This study included 46 patients (24 males and 22 females) ranging in age from 22 to 86 years with mean age of 53±18 years. The disease-free survival and overall survival rate were 65.5% and 69.5%, at 5 years, respectively. We found that survival was significantly better in younger patients (P = 0.05), male patients (P = 0.001) early stage (P = 0.001), patients with parotid cancer (P = 0.004), low/intermediate grade (P = 0.0006) and patients who received postoperative adjuvant radiation (P = 0.003).*

Conclusions: *The majority of our patients presented in advanced stage, which necessitated aggressive surgical treatment. Postoperative adjunctive radiotherapy seems to play an important role in those patients. However, the benefits of combined modality therapy await prospective clinical trials. This study confirmed the contributions of age, sex, site, stage, and grade for locoregional control and survival.*

Keywords: *salivary gland cancer, clinical presentation, management outcome, prognostic factors.*

INTRODUCTION

Salivary gland cancer is rare and comprises approximately 5 to 6% of cancers of the head and neck and 0.3% of all cancers.[1,2] Yet, it provides a challenge both for the surgeon and the radiation oncologist. These tumors display a diverse biological behaviors and clinical presentation depending on the stage and grade of the tumor.[1,3] In the evaluation of salivary gland tumors, the importance of a thorough history and comprehensive examination of the head and neck is critical. Factors suspicious for aggressive malignancy include ipsilateral facial nerve paralysis, sudden tumor growth, associated pain, tumor fixation to the overlying skin or surrounding soft tissues, and cervical lymphadenopathy.[4]

Surgery remains the mainstay of treatment for malignant neoplasm of the major and minor salivary glands.[5-8] Currently, many series had described the site, size, stage, and grade of the tumors as important prognostic factors affecting the outcome.[9-11] There has been lack of surveys of these studies in our locality. This study describes the clinical and pathological pattern of histologically proven carcinoma of salivary glands. It also, evaluates locoregional and distant recurrence, survival characters, and various prognostic factors of this disease in our patients.

PATIENTS AND METHODS

This study included all patients with histopathologically confirmed salivary gland cancer treated in our Institutions in the period from October 1997 to October 2002. Patients with pathologic diagnosis of sarcoma, lymphoma, or metastatic lesions to the salivary glands were excluded. Patients who did not receive any form of treatment or who were lost to follow up were also, excluded from the study. A total of 46 patients were identified and found to be eligible for this study. The age ranged from 22 to 86 years with mean age of 53±18. They were 24 males and 22 were females. Data concerning patient demographics, clinical, histopathological characteristics, treatment modalities and their outcome were obtained from a retrospective review of the medical records in our departments. The data collected included the age, sex, clinical presentation, primary anatomic site, metastatic site if present, preoperative diagnostic modalities, histopathology, stage of the tumour and treatment received.

Preoperative diagnosis: All patients were subjected to examination by ultrasound and CT. MRI was done in 12 patients (26%). FNAB and tru-cut needle biopsy were done in 10 (21.7%) and 7 patients (15%), respectively. Incisional biopsy was done in all patients of minor salivary gland tumors. Patients were classified into two groups according to the age. Group I included cases with age < 50 years, while group II included those who were ≥ 50. According to the site of the malignancy, the patients were classified to 4 groups (parotid, submandibular, sublingual and minor salivary gland). Stage classification was done according to the American Joint Committee on Cancer (AJCC) which has designated staging by TNM classification.[12]

Treatment: Complete excision with safety margin was adopted in the malignancy of submandibular, sublingual and all minor salivary glands. Superficial, total conservative and radical parotidectomy was the surgical options in malignancy of parotid gland. Modified/radical cervical neck dissections were done when appropriate. Various reconstructive procedures were done in 19 cases, while post operative radiotherapy was offered to 29.

Follow up studies and data analysis: The patients were evaluated by physical examination and proper investigation when needed, for loco-regional or distant relapse. This was done monthly in the first year, every two months in the second year, and every three months in the next three years, following the surgery. October 2007 or death of the patient was considered the closing date of follow up with recording survival rate. All these variables were correlated to the age, sex, site, stage and grade of the tumor, and postoperative adjuvant radiotherapy. The overall free survival rate was calculated by Kaplan-Meier method, at 5 years (Fig. 1). Comparison between groups was made by Chi-Square test. P value was considered significant when it was < 0.05.

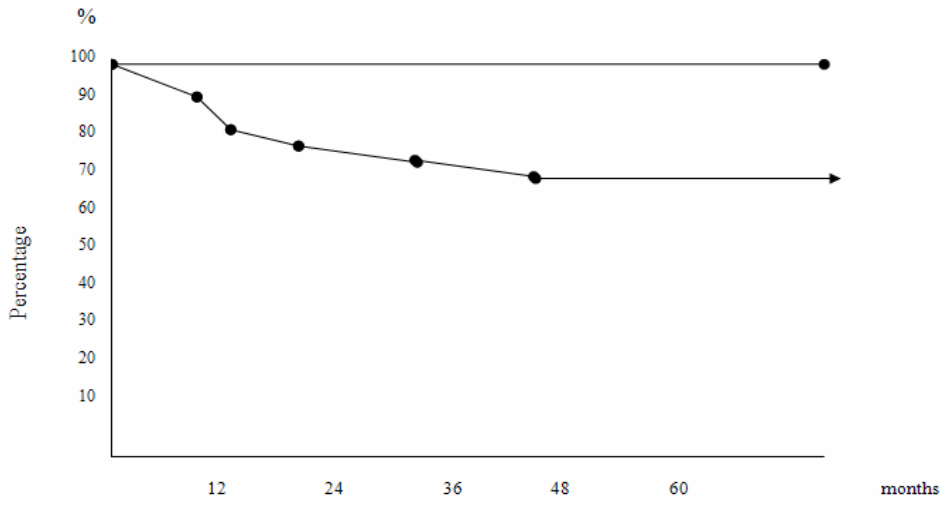

Fig 1. 5 years overall survival rate: 69.5%

Table 1. Clinical and pathological characteristics of study cases.

	Number of cases (%)
Presentation:	
Painful mass	33 (71.7)
Sudden increase in size	25 (54.3)
Metastatic lymph nodes	18 (39)
painless mass	13 (28.3)
Site:	
Parotid	28 (60.8)
Submandibular	8 (17.3)
Sublingual	1 (2.2)
Minor salivary	9 (19.5)
Histopathology:	
Mucoepidermoid carcinoma	20 (43.4)
Adenocarcinoma	12 (26)
Adenoid cystic carcinoma	5 (10.9)
Salivary duct carcinoma	2 (4.3)
Acinic cell carcinoma	2 (4.3)
Mucous secreting adenocarcinoma	2 (4.3)
Squamous cell carcinoma	2 (4.3)
Basal cell carcinoma	1 (2.2)

RESULTS

This study included 46 patients with salivary gland malignant tumors at different sites. Male to female ratio was 1.1:1 with no statistically significant difference. The most common symptom prompting the patient to seek medical advice was painful swelling, which was seen in 33 (71.7%) of our patients followed by sudden increase of a previously painless mass 25 (54.3%) Table 1.

In our study, the salivary cancer was observed mainly in the parotid gland 28 (60.8%), with significant minority in the minor salivary glands 9 (19.5%) Table 2.

More than half of the cases (63%) were treated with adjuvant external beam radiation therapy to a dose of 50 to 70 Gy. Nineteen patients (41.3%) were immediately reconstructed at the time of surgery using local/ regional or free vascularized flaps.

More than two thirds were Stage 111 and Stage 1V 31(67.5%). Histopathologically, mucoepidermoid carcinoma and adenocarcinoma were the commonest 20 (43.4%), 12 (26%), respectively. High grade tumor were seen in 14 patients (30.4%) and Low/intermediate grade in 32 (69.6%).

During the follow up period, there were 7 (15.2%) local recurrences, 3 (6.5%) with regional, and 6 (13%) with distant metastasis. Five years DFS was 65.2% while, overall survival was 69.5%.

We found that survival was significantly better in younger patients (P=0.05), male (P=0.001), early stages (P = 0.001), parotid (P = 0.004), low/intermediate grade (P=0.0006) and patients who received post-operative adjuvant radiation (P = 0.003) Table 3.

Table 2. Treatment options according to our department policy were surgery ± post operative radiotherapy.

Site	Number (%)	Treatment	Neck dissection	Reconstr-uctive surgery	Radiotherapy
Parotid	28(60.8)	Superficial parotidectomy			2
(Fig. 2: a,b,c)		5			
		Total Conservative parotidectomy	5		4
		7			
		Radical parotidectomy	13	5	13
		16			
Submandibular (Fig. 3: a,b,)	8(17.3)	excision	8	4	6
Sublingual	1(2.2)	excision	1	1	_
Minor salivary (Fig. 4: a,b)	9(19.5)	excision	5	9	4
Total (%)	46 (100)		32(69.5)	19(41.3)	29(63)

Table 3. Recurrence and DFS in correlation to the prognostic factors.

		No (%)	Local	Regional	Distant	Total recurrence	No (%) of 5 ys. DFS	P value
Age	Group I	15 (33)	2	1	1	4	11 (73)	0.05
	Group II	31 (67)	5	2	5	12	19 (61)	
Sex	Males	24 (52)	3	1	2	6	18 (75)	0.001
	Female	22 (48)	4	2	4	10	12 (54.5)	
Stage	Early	15 (32.5)	2			2	13 (86.6)	0.001
	Late	31 (67.5)	5	5	4	14	17 (54.8)	
Site	Parotid	28 (60.8)	3	1	2	6	22 (78.5)	
	Subman	8 (17.4)	1	1	1	3	5 (62.5)	0.004
	Minor	9 (19.7)	3	1	3	7	2 (22.5)	
Grade	High	14 (30.4)	4	2	4	10	4 (28.5)	0.0006
	Low/intermediate	32 (69.6)	3	1	2	6	26 (81.5)	
Radiotherapy	Yes	29 (63)	3	1	3	7	22 (75.8)	0.003
	No	17 (37)	4	2	3	9	8 (47)	
Total (%)		46 (100)	7 (15.2)	3 (6.5)	6 (13)	16 (14.7)	30 (65.3)	

DISCUSSION

Salivary gland cancer is rare and comprises approximately 5% to 6% of malignancy of the head and neck and 0.3% of all cancers. The US incidence of salivary gland cancer is 0.9 per 100,000 and mortality is approximately 0.2 per 100,000.[13]

Most of these tumors arise in major salivary glands, however malignant tumors of minor salivary glands are considerable.[14,15] These reports agreed with our results.

There was no significant difference between patients groups according to their gender in our cases. This is consistent with other authors who concluded no sex predilection or slightly higher incidence in males in malignant salivary tumors.[16-17]

The mean age at time of presentation was 53±18 years. This agreed with other series.[14,17]

The majority of our cases presented in advanced stages of the disease. More than two thirds were stage 111 and stage 1V 31 (67.5%). This had reflected on mode of presentation of our patients. Painful mass was seen in 33 (71.7%), and sudden increase of a previously painless mass in 25(54.3%) This agreed with Lee et al.,[17] where the most common symptom was sudden increase in size of a painless swelling which was seen in 46 out of 58 (79.3%). However, these data disagreed with the findings of Bell et al.,[15] where the most common symptom was painless swelling (63%). This can be explained by that about two thirds of their patients presented in early-stage disease (stage I = 36, stage II = 17, stage III = 8, stage IV = 25).

Mucoepidermoid carcinoma and Adenocarcinoma were the commonest malignant tumors in our series 20 (43.4%), 12 (26%) respectively. This agreed with Bell et al., (15), who reported 47% of cases were mucoepidermoid carcinoma followed by adenoid cystic carcinoma in 18%.and agreed with Bhattacharyya et al.,[16] who reported 40.6% of cases were mucoepidermoid carcinoma.

Neck dissection was performed in 69.5% of patients, and more than half (63%) were treated with adjuvant external beam radiation therapy to a dose of 50 to 70 Gy. This differs with Bell et al.,[15] who said that neck dissection was done in 29% of patients where about two thirds of their patients presented in early-stage disease.

In our study, high grade tumour was seen in 14 patients (30.4%) and low/intermediate grade tumor in 32 (69.6%). This agreed with current series, (14, 16, 17) where high grade tumour constituted 31%, 32.8%, 28% of the cases respectively.

The outcome of our patients after treatment came at the lower values of most of the reported studies. In our study, five years DFS was 65.2% and loco regional control rate was 78.3%. Bell et al.,[15] found that DFS and locoregional control rate at 5 years were 77% and 86%, respectively.

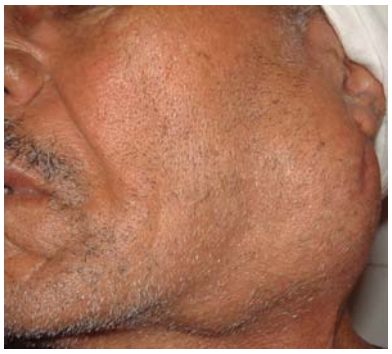

Fig 2a. An elderly patient with advanced hard fixed parotid lump and upper cervical lymphadenopathy.

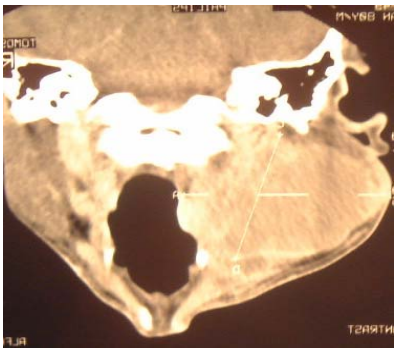

Fig 2b. CT, the tumour was involving both the superficial and deep lobe of the parotid.

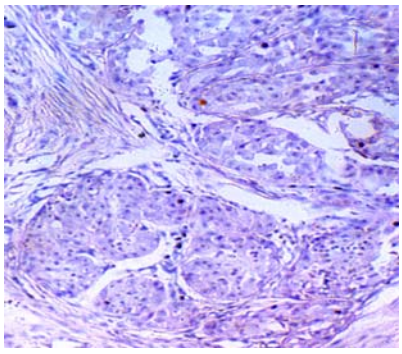

Fig 2c. Histopathology revealed Mucoepidermoid carcinoma X200.

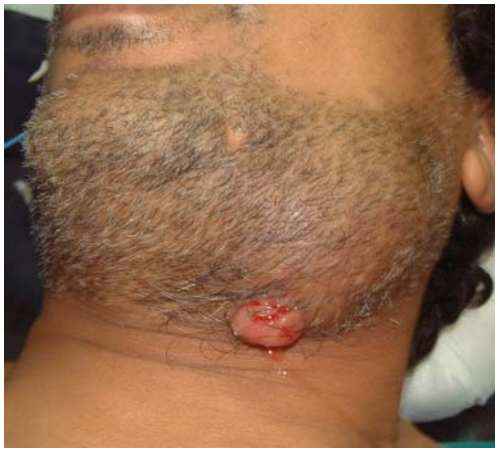

Fig 3a. Locally advanced Left submandibular salivary gland cancer.

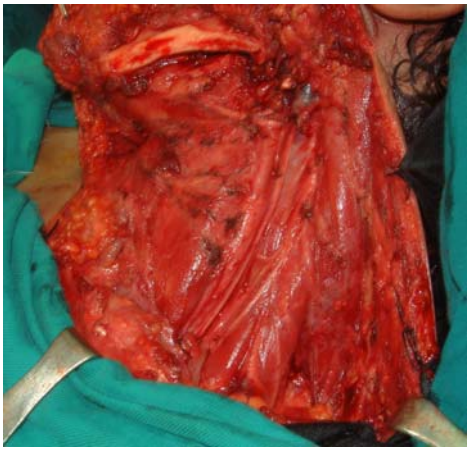

Fig 3b. After excision and radical neck dissection with lower marginal mandibulectomy.

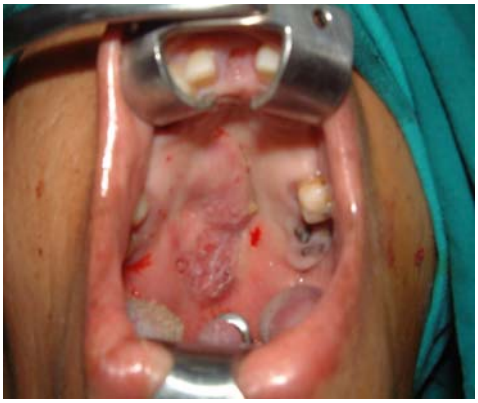

Fig 4a. Adenoid cystic carcinoma of the hard and soft palate.

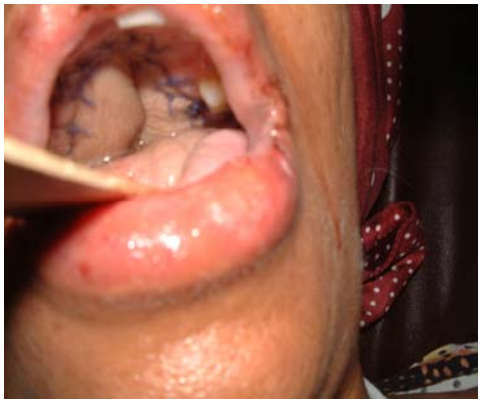

Fig 4b. After excision and reconstruction with free radial forearm flap.

Pandy et al.,[14] reported that the DFS at five years for a 42 patients with minor salivary gland cancer was 72%, while it was 22% in our cases.

More than that, Plambeck et al.,[18] have reported a much better DFS of their 55 cases (92%). The obvious low outcome in our results could be explained by that the majority of our cases were presented in a late disease stage. This is in addition to that the probability of the rarity of the disease and so the limited experience in its management.

Age and sex of the patient, stage, site, and grade of the tumor influenced the outcome significantly, in our study. This is paralleled to many series.[11,15]

It has been reported that survival was significantly improved in patients who underwent surgery and followed with radiotherapy.[19-21] This agreed with our study where DFS was better in patients who received postoperative radiotherapy than in patients who did not receive 75.8% versus 47%.(P=0.003). However, this needs further confirmation with prospective controlled studies.

In conclusions the majority of our patients presented in late stages which necessitated extensive surgical treatment and post-operative radiotherapy. Several prognostic factors were identified that influence loco-regional control, distant metastases, and disease specific survival. These factors were age and gender of the patient; site, stage, and grade of the tumor; and post-operative adjuvant radiotherapy. To improve the outcome we should find solution to bring the patients in early stages, and offer them effective treatment modalities.

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