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Original Research Article

Skin adnexal tumors: a 5 years single institutional experience

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ABSTRACT

Background: Skin tumors comprise of innumerable benign and malignant lesions. They vary in behaviour and malignant potential. Apart from more common melanomatous and squamous cell carcinomas, there exist unexplored arena of adnexal tumors that are rare and most often pose a dilemma for treating doctor. Their demography and presentation are yet to be standardized globally.
Methods: This is a cross-sectional descriptive study undertaken in department of surgical oncology, government Royapettah hospital, Chennai from January 2013 to 2019, primarily focused to analyze the various cutaneous adnexal tumors with regard to age, sex, site, size, behavior, origin of these tumors and to correlate with the clinical presentation. Descriptive characteristics like frequencies were computed for categorical variables like gender, histologic diagnosis, primary site of disease, and type of surgical treatment, while numeric variables were summarized using mean with standard deviation, median and range.
Results: Thirteen cutaneous adnexal lesions were reported in the past 5 years at our institute. Out of the 13 cases two were benign and eleven were of malignant skin adnexal tumors. Sweat gland tumors were the most common tumors encountered and were found to be more common in males below age of 60, trunk being common site of occurrence.
Conclusions: One should have high index of suspicion, aided by proper histopathology followed by aggressive treatment is necessary for proper control. Most of them need adjuvant treatment. No standardized treatment poses some problem, that needs to be addressed with proper documentation.

Keywords: Skin adnexal tumors, Porocarcinoma, Eccrine, Apocrine, Chemotherapy

INTRODUCTION

Skin adnexal tumors are a heterogeneous group of rare tumors without consensus on management guidelines. They include different histologic entities varying from eccrine, apocrine, sebaceous, sweat duct, or ceruminous glands within the skin or follicular cells.[1] They vary in behavior and malignant potential. Paucity of scientific information on these tumors is reflected by the fact that categorization under the WHO classification of skin carcinomas was performed only in 2005.[2] The AJCC staging for non-melanoma and non-Merkel cell skin tumors may be applied to this group of tumors.

The age-adjusted incidence rate is 5.1 per one million person-years around the world. The incidence rate among men is statistically significantly higher than women (6.3 vs 4.2, respectively; male to female incidence rate ratio is 1.51; $p<0.001$). In the last three decades, the incidence rates for these tumors have increased by as much as 150% making it imperative that we expand our understanding of these tumors to make informed decisions regarding prognosis and treatment.

Incidence of these tumors in India is low with a cumulative incidence of 0.5 to 2 per 10,0000 population according to various tumor registries.[3] With this in mind, we sought to define our experience in past 5 years.

METHODS

A retrospective review of all skin adnexal tumors treated at government Royapettah hospital, Chennai between January 1, 2013, and January 31, 2019, was carried out as our institute gets a relatively heterogenous population representative of Indian population. An institutional review board approval was obtained for the study. These patients were identified through the Institute's tumor registry.

All patients with a diagnosis of skin adnexal tumors were included into study. Those with melanomatous, squamous cell carcinoma, Merkle cell carcinoma and other non-adnexal tumor patients were excluded from study. Relevant demographic, clinical staging, treatment, pathologic and outcome data were obtained for each patient.

Descriptive characteristics like frequencies were computed for categorical variables like gender, histologic diagnosis, primary site of disease and type of surgical treatment, while numeric variables were summarized using mean with standard deviation, median, and range.

Variables used in the regression analyses include age, gender, primary site of disease, histologic subtype, nodal involvement, lympho-vascular and perineural involvement, type of surgical treatment, chemotherapy, radiation treatment.

RESULTS

Patient characteristics

Thirteen patients were identified in this analysis. Sixty one percent (8 out of 13) of patients in our series were males, while fifty three percent (7 out of 13) were less than or 60 years old (Table 1). The median and mean ages for the series were 56 and 55.84 years, respectively.

Tumor characteristics

Over half of the series (53.84%) involved the trunk region (Table 1). The histology subtypes are outlined in Table 1, with sweat gland carcinoma as the most frequently diagnosed tumor. Malignant lesions were more frequently encountered than benign lesions. Clinically lymph-nodes were diagnosed in 8 patients (61.53%) whereas pathologically positive lymph-nodes were found in only 7 cases (53.84%). One patient who did not have preoperatively any clinical lymph nodes, turned out to have metastatic lymph node deposit and one patient who had clinically nodal involvement proved to have no lymph-nodal deposit post operatively. Perineural invasion and lympho-vascular invasion were uncommonly observed (7.6% each).

Table 1: Patient characteristics frequency.

Patient characteristics	Number (%)
Sex	
Male	8 (61.53)
Female	5 (38.46)
Age (in years)	
<60	7 (53.84)
>60	6 (46.15)
Site	
Head and neck	4 (30.76)
Trunk	7 (53.84)
Upper extremity	1 (7.6)
Lower extremity	1 (7.6)
Nodes clinically	
Yes	8 (61.53)
No	5 (38.46)

Table 2: Tumor characteristics frequency.

Tumor characters	Number (%)
Type	
Benign	2 (15.38)
Malignant	11 (84.61)
Histology	
Sweat gland adenocarcinoma	4 (30.76)
Sweat gland duct carcinoma	2 (15.38)
Porocarcinoma	2 (15.38)
Microcystic adnex carcinoma	1 (7.6)
Mebomian gland carcinoma	1 (7.6)
Myofibroblast carcinoma	1 (7.6)
Choroid syringoma	1 (7.6)
Poroma	1 (7.6)
Size	
<2 cm	9 (69.23)
>2 cm	4 (30.76)
LVI	
Present	1 (7.6)
Absent	12 (92.30)
PNI	
Present	1 (7.6)
Absent	12 (92.30)
Pathological nodes	
Positive	7 (53.84)
Negative	6 (46.15)
Adjuvant treatment	
Yes	7 (53.84)
No	6 (46.15)

Treatment

All 13 patients underwent wide local excision with or without lymph-nodal dissection, with either primary closure or split thickness grafting or with flap reconstruction. Seven patients (53.84%) received adjuvant chemoradiotherapy. Adjuvant chemotherapy

included combination of cisplatin and paclitaxel; radiotherapy consisted of 50Gy EBRT in 25#. The indications for adjuvant treatment were nodal metastasis (7 patients), positive margin and perineural invasion (1 patient).

As per the records and follow-up data, none of the patients presented with recurrence.

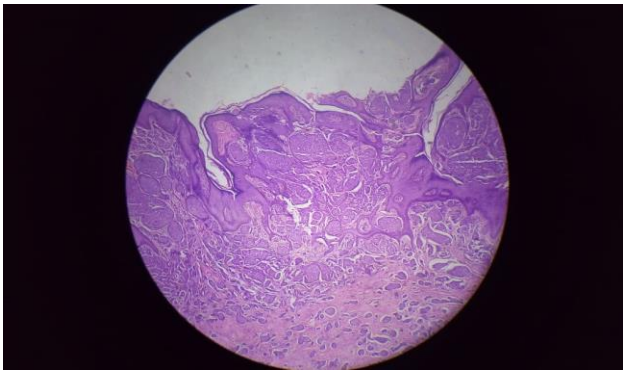

Figure 1: Porocarcinoma surface cuts.

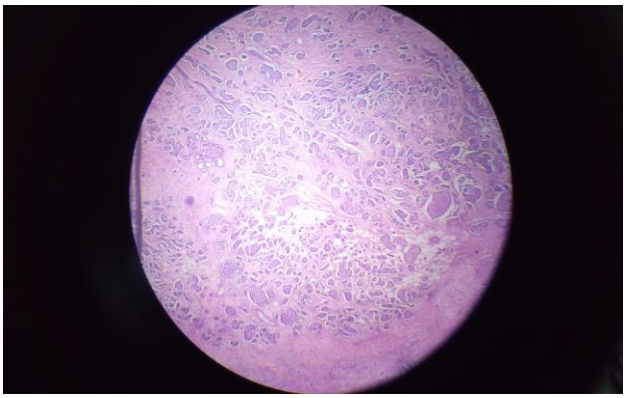

Figure 2: Porocarcinoma.

DISCUSSION

Previous studies have reported median ages ranging from 68 to 70 years.[1,4,5] The mean and median ages reported in our series were closer to those reported in a 48 patients series of micro-cystic adnexal carcinoma/sclerosing sweat duct carcinoma, however they constituted only 7.69% of histologic subtypes in our series (Table 2).[6]

There is a male predominance (56%) pattern in our study, a finding concordant with the Blake's series, but in contrast with other similar studies.[4,3,7]

More than half (53.84%) of these skin adnexal tumors in our series were located in the trunk region which is not consistent with most series where head and neck was the most common site.[1,4,5] Head and neck constituted second commonest (30.76%) in our series, upper and lower extremity constituted equal incidences. The size of most tumors was less or equal to 2 cm (69.23% of pts.). More tumor size was a negative predictor of recurrence-free survival on univariate analysis (p=0.04), but this trend failed to persist on multivariate analysis. As per literature, unlike squamous cell carcinoma of the skin and melanoma, there was no association between tumor size and nodal metastasis.[8,9] None of the patients in our series had distant metastasis on presentation. Distant metastases were recorded in the literature for nodular hidradenocarcinoma, eccrine porocarcinoma, apocrine carcinoma, and microcystic adnexal carcinoma.[10,11]

The pathology reporting system for this group of tumors has evolved over the years, with grade reported for the more recent cases. This trend was similarly observed in other series, with undocumented histologic grades in the range of 76 to 81% of patients.[1,5] Our series documented 84.61% cases to be malignant adnexal tumors and rest to be benign (Table 2). Some studies reported survival advantage for well-differentiated tumors on univariate analysis, but this variable was not predictive on multivariate analysis.[5] Some other studies also demonstrated survival advantage with better histologic grades, albeit after excluding patients with distant metastasis.[1] We did not identify any histologic grading in our analysis. The existing literature, however, showed a mixed picture, with some reporting an advantage for microcystic adnexal carcinoma, while other studies favored sebaceous adenocarcinoma, or apocrine adenocarcinoma.[5,1,4,12]

Surgical nodal staging was done for 69.23% of the patients in our series. Histopathologic nodal evaluation varied from 11 to 29% in the literature. There were no standardized criteria for selecting patients who required nodal sampling. Patients who had nodal basin evaluation in our series underwent the procedure because of clinically positive lymph nodes (61.43%). Seven out of nine patients demonstrated nodal metastasis. Ogata et al, in a series of nine patients with apocrine carcinoma who had wide local excision and routine regional lymph node dissection, showed nodal disease in all but one patient.[13] This group called for routine nodal staging, at least for apocrine carcinoma.

Experience from breast cancer and melanoma has shown that nodal metastasis can be present in the absence of clinically positive lymph nodes. Since nodal basin is grossly under evaluated, we do not have accurate information yet on incidence of nodal metastasis and its effect on recurrence and survival. It is worthwhile to evaluate adnexal tumor population with nodal metastasis with a view to determine predictors of nodal metastasis and then prospectively validate identified predictors. Prospective validation requires a larger cohort of patients which is always a challenge when addressing key issues on these rare tumors. Same could be said to apply to histologic criteria like grade, perineural invasion, and angio-lymphatic invasion. These have been shown to be important in prognostication for melanoma and many gastrointestinal cancers. If validated, they should be

incorporated into the staging system which means pathologists would report these features. Only 7.6% of patients in our series were positive for perineural invasion and lympho-vascular invasion. We observed most studies on adnexal tumors did not address these two important criteria.

The role of adjuvant radiation and chemotherapy is not well defined for malignant adnexal tumors. To address this, we need a combination of large study population and details on regimen of treatment. Previous studies had reported on adjuvant chemoradiation. The large population-based series from SEER database were limited, as there was no information on chemotherapy while radiation treatment was documented as a categorical variable without detailed information on selection criteria and dose. Unfortunately, for these rare and heterogeneous tumors, it will always be challenging.

Current proposals on the role of adjuvant radiation support the use of postoperative radiotherapy for cases in which sufficient resection margins cannot be achieved because of the anatomic site of the lesion or with positive resection margins.[13,14] There are no defined guidelines/protocols for adjuvant chemotherapy in the management of these tumors, but there are reported cases of recurrent or metastatic diseases treated with chemotherapeutic and targeted agents.[15] Various chemotherapeutic agents like doxorubicin, mitomycin, vincristine, 5-fluorouracil, cyclophosphamide, anthracycline, bleomycin, paclitaxel, cisplatin, and carboplatin were used in different combinations for metastatic disease.[16,17] Results varied from no response to stable disease and partial response. This trend was noticed in seven patients (53.84%) who received chemoradiotherapy in our series. According to literature, the role of chemotherapy in these patients needs further study. Treatment with radiation, while not associated with poor survival outcome, did not translate to survival advantage either.

None of the patients had recurrences, this is in contrast to other studies.[18] where 12% of pts in the series had recurrences. In that study, recurrence-free survival analysis was done and showed median RFS of 56 months. Five years and 10 years RFS were 47.4% (95% CI 28.2-64.4) and 41.5% (95% CI 22.21-59.8), respectively. Univariate analysis showed age greater than 60 years, positive nodal status, and advanced T stage as predictors of RFS, but only age and positive nodal status persisted as independent predictors of RFS on multivariate analysis. Data on recurrence pattern is crucial to patient's education about the prognosis of these tumors. There is paucity of similar data in the literature.

CONCLUSION

So far, there are few large population-based studies available on adnexal tumors of the skin. Most of these were derived from the SEER database. These studies had the benefits of large study population and broader representation of the population at large. They were, however, not without their shortcomings which included lack of uniform pathology reporting, absence of detailed information about margin status, recurrences, and selection criteria for nodal sampling, adjuvant chemotherapy, and radiation treatment. We reviewed our 13 patients, single-institution series and were able to address some of these limitations, albeit with limited numbers.

This series shows the disease to be more frequent in males, age less than 60. Trunk appears to be a more common site of occurrence and, most tumors were of small size, with nodal involvement in more than half of the patients. Lympho-vascular and perineural involvement appears to be less frequent, and wide local excision with or without nodal basin dissection usually suffices the treatment. Chemoradiotherapy is a choice as adjuvant in some selected patients with high risk features. Lymph node basin staging is worth considering in the workup and treatment. More importantly, strategies that promote early detection and prompt treatment should be emphasized in addressing this disease.

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