Histopathological Study of Epithelial, Melanocytic And Adnexal Tumors Of Skin- A Retrospective Study In A Tertiary Care Centre

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ABSTRACT

Background and Objectives: To classify and identify various skin tumors and study their variations according to age and sex. The most common predisposing factors being fair skin, sun exposure, chemical exposure, HPV infection in the setting of immunosuppression.

Methods: This was an observational study carried out in the Department of Pathology at private Medical College of coastal Andhra from July 2018 to June 2020.

Result: The present study included histopathological study of 71 cases of tumors of skin and its adnexae over a period of two years. Out of the 71 tumors, 43 were diagnosed as benign and 28 as malignant tumors of skin constituting 61% and 39% respectively. The ratio of benign to malignant tumors was 1:0.63. Among the 43 benign tumors 20 (46.5%) were tumors of skin appendages, 15 (34.9%) were tumors of epidermis, 8 (18.6%) were of melanocytic origin. Among the 28 malignant tumors 25 (89.3%) were tumors of epidermis, 2 (7.1%) were melanocytic tumors and 1 (3.6%) was tumor of skin appendages. Among the malignant epidermal tumors squamous cell carcinoma was the most common constituting 42.9% (12 cases).

Conclusion: The present study concludes that benign tumors are most common when compared to malignant tumors of skin. Among the malignant tumors, Squamous cell carcinoma falls as the most common variety of skin followed by Basal cell carcinoma and verrucous carcinoma. Among the benign tumors, tumors of epidermal origin are most frequent followed by tumors of sweat gland and adnexal-hair follicle origin.

Keywords: Keratinocytic tumors, Melanocytic tumors, Hidradenoma, Spiradenoma, Basal cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC)

Introduction

The skin or integument is a complex organ with many functions and with three main anatomic components: epidermis and skin adnexae, melanocytic system, and dermis and subcutis. The skin is a heterogenous organ with varied elements having ectodermal and mesodermal origins. Most of the individual elements are capable of producing skin tumors. Based on their primary site of origin, they can be divided in to the following: i) Keratinocytic tumors ii) Melanocytic tumors iii) Appendageal tumors iv) Soft tissue tumors.

Of all the diagnosed cancers in India, less than 1% of tumors are of skin cancers. Worldwide BCC is the commonest cutaneous malignancy, but in India SCC is reported to be the most prevalent skin cancer. There has been an alarming increase of skin cancer among fair skinned populations. Differences in trends and rates of skin cancer may be due to variation in skin types, geographical latitudes, occupational exposure, behavior in terms of sun exposure and skin protection and differences in disease awareness and surveillance. Keratinocytic tumours account for approximately 90% or more of all skin malignancies, of which approximately 70% are basal cell carcinomas.

Appendageal tumours are neoplasms whose differentiation is towards one or more of the adnexal structures of the skin. Depending on their presumed origin, adnexal tumours are categorized into those with apocrine and eccrine, follicular and sebaceous differentiation. Neoplasms with ductular differentiation often have debatable histogenesis.

The study of adnexal neoplasms present unique difficulties in part related to the wide variety of tumors, the substantial frequency of one lesion exhibiting histological features of two or more adnexal lines and the complicated nomenclature. The study of skin tumors is interesting, more intriguing, fascinating and challenging because of its wide variations and there has been no systemic study being done earlier. Keeping in view these facts, an attempt is made to study the different varieties of tumors of skin which will bear impact on patient management and prognosis. The aid of histopathology is crucial in clinching the right diagnosis and in further management. The aims of the present study are to

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1. To find out the incidence of different epithelial, melanocytic and adnexal tumors of skin.
2. To classify and identify various skin tumors and study their variations according to age and sex.
3. To study the histopathology of different skin tumors.

**Materials and Methods**

All the biopsies, specimens and reference materials submitted to the Department of Pathology at private medical hospital of coastal Andhra for histopathological study during the period from July 2018 to June 2020. Tissue specimens received to the department of pathology was noted and fixed in 10% formalin for 12-36 hours. Extent of sampling depended on the size of tumor as follows. This study got approved by institutional ethics committee.

Specimens measuring 3 mm or less were submitted in toto. Specimens measuring 4-6 mm were cut through the centre and both halves submitted for processing. Specimens measuring 7 mm or more, a 2-3 mm slice was cut through the centre and submitted for processing. Further tissue was processed and embedded in paraffin blocks. Sections of 3 to 5 microns thickness were taken and stained with hematoxylin and eosin and studied.

**Inclusion criteria:** Tumors of epidermis along with melanocytic tumors and tumors of skin appendages without restricting the study to a particular age limit.

**Exclusion criteria:** Mesenchymal tumors, hematological tumors, skin secondaries and non-neoplastic lesions are excluded from the study

**Statistical methods applied:** Data was analyzed using number and percentage of statistical methods in the present study.

**Result**

During the 3 years study from July 2018 to June 2020, there were 71 cases of tumors of skin. Out of the 71 cases, 28 cases are malignant and 43 cases are benign tumors of skin constituting 39% and 61% respectively. The ratio of malignant to benign tumors was 0.63:1 (Table 1).

In the present study the peak incidence of benign tumors of skin and its adnexae was between 4th and 5th decade with female preponderance. The peak incidence of malignant tumors of skin and its adnexae was in 6th decade with male preponderance. Out of 71 skin tumors, malignant epidermal tumors were most common (35.2%), followed by benign tumors of appendages (28.2%), benign tumors of epidermis (21.1%), benign melanocytic tumors (11.3%), malignant melanoma (2.8%) and malignant adnexal tumor (1.4%). Seborrheic keratosis comprises majority of cases among the benign tumors of skin and its adnexae constituting about 11 cases with a percentage of about 25.6% and with male preponderance followed by benign melanocytic nevi, and others. In this study, 6 cases of intradermal nevus were seen. Peak incidence was seen in 5th decade. Histologically the dermis showed nests, cords and sheets of nevus cells showing maturation. Two cases of compound naevi were encountered in the present study and the age of the patients were 23 and 55 years respectively. Histologically epidermis was thinned out and showed junctional activity with dermal component of nevus cells showing maturation. (Table 2)

In the present study among the malignant tumors of skin and its adnexae, Squamous cell carcinoma constitutes about 42.9% followed by basal cell carcinoma of 39.3%, Malignant melanoma and verrucous carcinoma of 7.1% each and malignant adnexal tumor of 3.6%.

All squamous cell carcinoma were graded conventionally as well, moderate and poorly differentiated. Majority of squamous cell carcinomas were well differentiated (58.4%) and the other two grades of squamous cell carcinomas constitute about 41.6%. In the present study 11 cases of basal cell carcinoma were encountered and accounted for 39.3% of the malignant tumors of the skin. Basal cell carcinomas showing no differentiation were categorized as solid basal cell carcinoma. In the infiltrating variant of basal cell carcinoma, the basaloid cells were arranged in the form of cords and showed deep infiltration in the dermis. One case of Basosquamous carcinoma was found in which the basal cell carcinoma coexisted with squamous cell carcinoma and it was seen as an ulcer in a 45 years old male patient. Among the histological types of basal cell carcinoma, pigmented type was the most common constituting 45.4%. Peak incidence was in 4th and 5th decade. Male to female ratio was 1.75:1. (Table 4)

In the present study 21 cases of skin adnexal tumors were encountered, out of which 20 were benign and 1 was malignant. In the present study benign tumors formed the majority (95.2%). Among the benign tumors the occurrence of sweat gland tumors (61.9%) was the highest followed by hair follicle tumors (33.3%). Among the malignant tumors a single case of sweat gland carcinoma (4.8%) was encountered. Malignant tumors of hair follicle differentiation and benign and malignant tumors of sebaceous differentiation were not encountered in the present study.

**Discussion**

Skin malignancies are rare in India compared to western countries. In India skin malignancies constitute about 1-2% of all diagnosed cancers. Keratinocytic tumours are
Table 1: Distribution and incidence of benign and malignant tumors of skin.

|                     | Number of Epidermal Tumors | Number of Adnexal Tumors | Number of Melanocytic Tumors |
|---------------------|-----------------------------|---------------------------|------------------------------|
| Benign              | 15 (21.1%)                  | 20 (28.2%)                | 8 (11.3%)                   |
| Malignant           | 25 (35.2%)                  | 1 (1.4%)                  | 2 (2.8%)                    |
| Total               | 40                          | 21                        | 10                           |

Table 2: Incidence of various benign tumors of skin and its adnexae.

| Tumors                      | Number of Cases | Percentage (%) |
|-----------------------------|-----------------|----------------|
| Epidermal tumors            |                 |                |
| Seborrheic keratosis        | 11              | 25.6           |
| Verruca vulgaris            | 03              | 7.0            |
| Keratoacanthoma             | 01              | 2.3            |
| Adnexal – Hair follicle tumors |               |                |
| Pilomatricoma               | 06              | 14             |
| Trichoepithelioma           | 01              | 2.3            |
| Sweat gland tumors          |                 |                |
| Hidradenoma                 | 07              | 16.3           |
| Cylindroma                  | 04              | 9.3            |
| Spiradenoma                 | 02              | 4.6            |
| Melanocytic tumors          |                 |                |
| Melanocytic naevi           | 08              | 18.6           |

Table 3: Incidence of malignant tumors of skin and its adnexae.

| Type of Malignant tumor     | Number of Cases | Percentage |
|-----------------------------|-----------------|------------|
| Squamous cell carcinoma     | 12              | 42.9       |
| Verrucous carcinoma         | 2               | 7.1        |
| Basal cell carcinoma        | 11              | 39.3       |
| Malignant melanoma          | 2               | 7.1        |
| Malignant adnexal tumor     | 1               | 3.6        |

Table 4: Histological types of basal cell carcinoma.

| Histological Type          | Number of cases | Percentage |
|----------------------------|-----------------|------------|
| Pigmented                  | 05              | 45.4       |
| Solid                      | 02              | 18.2       |
| Adenoid                    | 01              | 9.1        |
| Infiltrating               | 02              | 18.2       |
| Baso-squamous              | 01              | 9.1        |

Table 5: Incidence of skin adnexal tumors.

| Type of the Tumor          | Number of Benign tumors | Number of Malignant tumors | Total |
|---------------------------|-------------------------|---------------------------|-------|
| Hair follicle differentiation | 7 (33.3%)               | –                         | 7 (33.3%) |
| Sweat gland differentiation | 13 (61.9%)              | 1 (4.8%)                  | 14 (66.7%) |
| Sebaceous differentiation  | –                       | –                         | –     |
| Total                     | 20 (95.2%)              | 1 (4.8%)                  | 21    |
Fig. 1: Keratoacanthoma Photomicrograph showing central crater surrounded by keratinocytes. (H&E x 100).

Fig. 2: Pilomatricoma Photomicrograph showing basaloid cells and eosinophilic keratin material (H&E x100).

Fig. 3: Verruca vulgaris Photomicrograph showing acanthosis, hyperkeratosis and papillomatosis (H&Ex 100).

Fig. 4: Clear cell hidradenoma Photomicrograph showing Hidradenoma with tumor cells containing clear cytoplasm. (H&E x400)

Fig. 5: Cylindroma Photomicrograph showing jigsaw puzzle like arrangement of tumor cells. (H&E x100).

Fig. 6: Spiradenoma Photomicrograph showing nodules of basaloid cells in the dermis. (H&E x100).
derived from epidermal and adnexal keratinocytes and comprise a large spectrum of lesions ranging from benign proliferations (acanthomas) to malignant squamous cell carcinomas which occasionally show aggressive growth and even metastatic potential. Keratinocytic tumours are very frequent and, despite their low mortality rate, pose a significant public health problem. The main etiologic factor is solar radiation\cite{9}.

All the tumors arising from mucocutaneous junctions (including tumors around eyelids, anterior nares, mouth, corona gland is penis, vulval orifice and the anal orifice, dermal tumors and secondaries were excluded from the study. Among the 71 skin tumors 43 were benign tumors and 28 were malignant tumors of skin and its adnexae. The ratio of benign (43) to malignant tumors (28) was 1:0.63. The ratio of benign epidermal tumors (15) to malignant counterparts (25) was 0.6:1. The ratio of benign adnexal tumors (20) to malignant adnexal tumors (1) was 20:1. The ratio of benign melanocytic tumors (8) to malignant counterpart (2) was 4:1. Out of 71 skin tumors, malignant epidermal tumors were most common (35.2%), followed by benign adnexal tumors (28.2%), benign tumors of epidermis (21.1%), benign melanocytic tumours (11.3%), malignant melanoma (2.8%) and malignant adnexal tumor (1.4%).

In the present study squamous cell carcinoma accounted for maximum number of cases (42.9%) which is similar to the observations made by Deo SV et al\cite{10}, Chakravorthy RC and Choudhuri DR\cite{11} and Bhudaraja SN et al\cite{12} (Table 6).

![Fig. 7: Malignant melanoma Photomicrograph showing sheets of pleomorphic tumor cells (H&E x100).](image)

Table 6: Comparative incidence of different malignant tumors of skin in India.

| Type of the Tumor          | Deo SV et al\cite{10} | Chakravorthy and Choudhuri\cite{11} | Bhudaraja et al\cite{12} | Present Study |
|----------------------------|-----------------------|-------------------------------------|--------------------------|---------------|
| Squamous cell carcinoma    | 55.8%                 | 72.21%                              | 50.34%                   | 42.9%         |
| Verrucous carcinoma        | –                     | –                                   | –                        | 7.1%          |
| Basal cell carcinoma       | 18.1%                 | 16.5%                               | 17.65%                   | 39.3%         |
| Malignant melanoma         | 26.1%                 | 8.69%                               | 29.41%                   | 7.1%          |
| Adnexal carcinoma          | 2.6%                  |                                     | 2.6%                     | 3.6%          |

Table 7: Comparison of incidence of benign adnexal tumors.

| Type of the tumor   | Solanki et al\cite{13} | Nair\cite{14} | Reddy et al\cite{15} | Present Study |
|---------------------|-------------------------|---------------|----------------------|---------------|
| Hair follicle tumors| 22 (23.4%)              | 12 (36.36%)   | 13 (22%)             | 7 (35%)       |
| Sweat gland tumors  | 50 (53.2%)              | 19 (57.58%)   | 43 (73%)             | 13 (65%)      |
| Sebaceous gland tumors | 22 (23.4%)         | 2 (6.06%)     | 3( 5%)               | –             |
| Total number of cases | 94                     | 33            | 59                   | 20            |

Table 8: Comparison of histological types of basal cell carcinoma.

| Histological Type       | Solanki RL et al\cite{12} | Present Study |
|-------------------------|----------------------------|---------------|
| Pigmented               | 6.4%                       | 45.4%         |
| Solid                   | 60.5%                      | 18.2%         |
| Adenoid                 | 15.7%                      | 9.1%          |
| Keratotic               | 9.3%                       | –             |
| Infiltrating            | 4.6%                       | 18.2%         |
| Basosquamous            | 3.5%                       | 9.1           |
Malignant tumors of epidermis
In the present study among the tumors of adnexal origin, benign tumors formed the majority (95.2%). In the study by Reddy et al\textsuperscript{14} et al also benign tumors formed the majority (Table 7). The occurrence of sweat gland tumors (65%) was higher in the present study which correlates with the studies done by Solanki et al\textsuperscript{13} (53.2%), Nair SP\textsuperscript{14} (57.56%) and Reddy et al\textsuperscript{15} (73%).

6 cases of Pilomatricoma were noted in the present study accounting for 85.7% of the hair follicle tumors, with male to female ratio of 1:1 which correlates with the study by Solanki RL et al\textsuperscript{13}. The mean age at presentation was 45 years in the present study where as it was 28 years in the study by Solanki RL et al\textsuperscript{13}. Histologically the tumors were well circumscribed small to large-sized, cystic lesions lined focally by aggregations of basaloid cells and few squamoid cells and filled centrally with large masses of eosinophilic cornified material containing shadow (ghost) cells as well as a few keratin filaments.

One case of trichoepithelioma was encountered in the study accounting for 14.3% of the hair follicle tumors. The patient is female of age 47 years. Histologically, they showed islands of basaloid cells in the dermis with peripheral palisading of cells. Horn cysts and presence of fibrous stroma was noted. These observations were similar to those of Solanki RL et al\textsuperscript{13}. 7 cases of Hidradenoma were encountered in the present study accounting for 53.8% of sweat gland tumors, with a male to female ratio of 0.75:1. In the study by Solanki RL et al\textsuperscript{13} hidradenoma accounted for 27.6% (13 cases) of sweat gland tumors with a male to female ratio of 1.16:1. 4 cases of cylindroma were noted in the present study accounting for 30.8% of sweat gland tumors of which 2 were males and 2 were females with male to female ratio of 1:1. Solanki RL et al\textsuperscript{13} observed all the 3 cases in males. 2 cases of Spiradenoma were noted in the present study accounting for 15.4% of sweat gland tumors of which one was male and the other one was female patient with male to female ratio of 1:1.

In the present study pigmented type of BCC was the most common type. In the study by Solanki RL et al\textsuperscript{13} solid BCC was the most common type(Table 8). Histologically the tumor showed lobules, columns, bands and cords of basaloid cells associated with scant cytoplasm and a characteristic outer palisade of cells associated with a surrounding loose fibromucinous stroma. Artefactual retraction spaces between the tumour and stroma were often present study.

Conclusion:
Skin tumors include tumors of epidermis, epidermal appendages and melanocytes. The diagnosis of skin tumors presents unique difficulties, in part, related to the wide variety of tumors and the complicated nomenclature. The present study concludes that benign tumors are most common when compared to malignant tumors of skin. Among the malignant tumors, Squamous cell carcinoma falls as the most common variety of skin followed by Basal cell carcinoma and verrucous carcinoma. Among the benign tumors, tumors of epidermal origin are most frequent followed by tumors of sweat gland and adnexal-hair follicle origin. A diagnosis is a clinical tool that assists in the process of codifying patients into disease groups that tends to share a common outcome and a common set of responses to therapy. Thus, there is a close relationship between diagnosis and prognostication. Finally, the quintessence of the subject of study of skin tumors is its vastness, its enormity and its interesting histomorphology.

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