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Malignant Tumors of Skin and Its Adnexae in Karnataka

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ABSTRACT

Skin is being complex and the largest organ of the body, is vulnerable to wide range of diseases, like malignancy. It is most exposed part to harsh environment and its pollutants. Like increase in amount of Ultraviolet radiations involved in tumor induction and also co-carcinogen, ionizing radiation, nitrogen mustard, electron beam irradiation, chemical carcinogens, Viral infections acting as direct carcinogens or as promoting agents are predisposed to cutaneous malignancies. Diagnosis of skin tumors depends on correlating clinical clues and histological features. This study "occurrence of malignant tumors of skin in Karnataka" was carried out for 18 months, from 2005 to 2007. 54 skin tumors were studied. Out of these 40 were malignant tumors 74.07%.Skin tumors constitute a small but significant proportion of cancer patients. Unlike in the Western countries, SCC is the commonest histological variety. In India, the carcinogenic potential of both chemicals and radiation cannot be ignored.

Keywords: skin & adnexal malignancies, cancer of skin, cutaneous malignancy.

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INTRODUCTION

The skin is a complex and the largest organ of the body. Its complexity makes it vulnerable to wide range of diseases, like tumors from surface epidermis, epidermal appendages and dermal tissue. The vast diversity of these lesions often overlapping (clinical, histological) produces confusion for nomenclature and diagnosis.[1] Histopathological study is most valuable means in dermatology for diagnosis. But it has its own limitations; sometimes no definitive diagnosis can be made. In case of tumors, difficulties in diagnosis may also arise. For instance, distinction of squamous cell carcinoma from pseudoepitheliomatous hyperplasia or from keratoacanthoma is not always possible.[2] The distinction between benign and malignant neoplasm are rather more difficult to define when they appear in skin than when found elsewhere[3] and histopathological examination is frequently required to establish a definitive diagnosis. Diagnosis of skin tumors usually done by, correlating clinical and histological features. which can be supported by histochemistry, electron microscopy and immuno-histochemistry.

Historical Aspects

First clear cut study of carcinogenesis was made by Sir Percival Pott in 1775. He discovered that soot is a carcinogen in chimney sweepers.[4] Sir Jonathan Hutchinson in 1887 recognized association between arsenic administration and subsequent development of both cutaneous and systemic malignancy. Hyde recognized ultraviolet light as a carcinogen. Thus by the beginning of this century, the carcinogenic potential of both chemicals and radiation was recognized. Yamagiwa and Ilchikawa in 1918 described experimental induction of skin cancer by chemical carcinogens. Khanolkar described the Dhoti cancerin 1945.

Some history of adnexal tumours

Eccrine Spiradenoma was first characterized as an entity by Kersing and Helwig in 1956.[5] Trichilemmoma was designated as neoplasm of outer root sheath in 1962 by Headington and French. Papillary eccrine adenoma was described by Rulon and Helwing in 1977.[6]Micro cystic adnexal carcinoma was described by Goldstein et al.[7] in 1982.

Etiology of skin tumors

Skin tumors have multifactorial causes related to combination of several factors like genetic, chemical, hormonal, nutritional, viral and environmental acting in concert within a susceptible individual.

A. Host factors

Genetic factors

Individual with xeroderma pigmentosum and albinism develop varieties of skin cancers at an early age. Some of the benign tumors like trichoepithelioma, glomangioma and neurofibroma show an autosomal dominant pattern of inheritance.

Immunologic factors

Immunosuppression following immunosuppressive therapy, HIV infection, occult malignancies

B. Environmental factors

Ultraviolet radiation

Ionizing radiation

Chemical carcinogens

Chemicals cause skin cancers by acting as direct carcinogens or as promoting agents. These agents include coal tar, petroleum oil, tar oil, anthracine oil, wax and carbon black.[14]

Viral infections

They are human papilloma virus (HPV) and retro viruses.[14]Epstein-Barr virus and retroviruses have been implicated in etiology of lymphomas and leukaemias. Kaposi's sarcoma, squamous cell carcinoma and keratoacanthoma.

Others

Skin tumors especially squamous cell carcinoma is known to arise in sites of burn scars (Marjolin's ulcer), chronic leg ulcers, vaccination scars and even sites of trauma.

METHODOLOGY

This study of "Tumors of the skin" was carried out from 2005 to 2007 over a period of 18 months.

Inclusion Criteria: All malignant tumors of skin and adnexae were included.

Exclusion Criteria: All non-neoplastic lesions and mesenchymal tumors were excluded.

Brief clinical history and findings were noted in each case. Nature of biopsy either incisional or excisional biopsy was noted. Specimens were fixed in 10% formalin for 10-36 hours and the gross features were examined. Sampling depended on the size of tumor. Further, tissue was processed and embedded in paraffin blocks. Sections of6 micron thickness were taken and stained with H&E and studied. Special stains were used wherever needed. According to WHO classification of skin tumors (1974)[8] cases were classified into:

1. Epidermal tumors and tumors-like lesions
2. Precancerous lesions

Statistical Methods Applied

1. Cross tabs Procedure

2. Chi-square test

3. Descriptive statistics

RESULTS AND DISCUSSION

During November 2005 to April 2007, total 790surgical specimens received, in Department of Pathology for histopathological study. Out of these 54 were skin and adnexal tumors.

Table 1: Incidence of skin and adnexal tumors

Total number of tumors	Number of skin and adnexal tumors	Percentage
790	54	6

Of the 54 cases, 14 were diagnosed as benign tumors and 40 as malignant tumors. The benign tumors constituted 25.92% and malignant tumors constituted 74.07%.

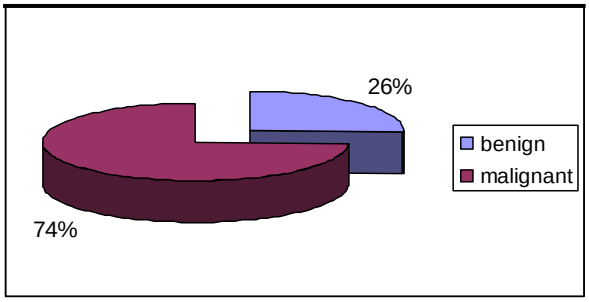

Figure 1: Incidence of benign and malignant tumors of skin and adnexae

Table 2: Distribution and incidence of malignant tumors of skin and Adnexae

Type of malignant tumors	Malignant	
	No.	%
Epidermis	33	82.5
Epidermal appendages	2	5
Melanogenic system	5	12.5
Total	40	74.07

$\chi^2 = 18.548$; $p < 0.000$ (Highly Significant)

The study also showed there was male predominance and the male to female ratio was 2.7:1.

Table 3: Age incidence of malignant tumors of skin and adnexae

Age in years	Number of cases	Percentage
0-19	2	4
20-29	2	4
30-39	1	2
40-49	13	23.5
50-59	11	20
60-69	13	23.5
70-79	10	19
80-89	2	4
Total	54	100

$\chi^2 = 30.741$; $p < 0.000$ (Highly Significant)

In the present study the peak age group was between 5th and 7th decade. Malepredominance with the male to female ratio of 2.7:1.

Malignant tumors of skin and adnexae

In the present study malignant tumors were 40 in number, of which squamous cell carcinoma was commonest (67.5%).

Table 4: Incidence of malignant tumors of skin and adnexae

Tumor	Number of cases	Percentage
Squamous cell carcinoma	27	67.5
Basal cell carcinoma	5	12.5
Neuroendocrine carcinoma with areas of squamous differentiation	1	2.5
Mucoepidermoid carcinoma	1	2.5
Hidradenocarcinoma	1	2.5
Malignant melanoma	5	12.5
Total	40	100

$\chi^2 = 64.5$; $p < 0.000$ (Highly Significant)

Malignant tumors of epidermis

Squamous cell carcinoma

In the present study, twenty-seven cases were encountered, peak incidence was in fifth decade (33%) with male preponderance (85%) and maximum number of cases occurred in the anogenital region (55%).The peak incidence was seen in the 5th decade. Most of the tumors were between 0.5 to 6 cms. Fifteen cases were of Broder's grade-1, showing atypicality of cells, infiltration of dermis with more number of malignant epithelial pearls with occasional mitotic figures. Six cases were of Broder's grade-2, showing more than 50% of differentiated squamous cells, with few epithelial pearls and occasional mitotic figures. Five cases were of Broder's grade-3 showing more than 25% of differentiated squamous cells, with atypicality of cells, individual cell keratinization, an occasional epithelial pearl and a few mitotic figures.

Verrucous carcinoma

One case was encountered. It was a growth over penis in a 65 year old male. Histologically, it showed hyperkeratosis, acanthosis, papillomatosis and elongated rete ridges extending into deep dermis with pushing margins. Also seen were individual cell keratinization, few epithelial pearls and occasional mitosis.

Basal cell carcinoma

The present study included five cases (12.5%) of basal cell carcinoma. Peak incidence was in

seventh decade with male preponderance and all cases occurred on the face.

Table 5: Age distribution of basal cell carcinoma

Age in years	Number of cases	Percentage
40-49	1	20
50-59	1	20
60-69	1	20
70-79	2	40
Total	5	100

Table 6: Sex incidence of basal cell carcinoma

Sex	Number of cases	Percentage
Male	4	80
Female	1	20

Table 7: Histologic types of basal cell carcinoma

Type	Number of cases	Percentage
Pigmented BCC	2	40
Keratotic BCC	1	20
Basosquamous carcinoma	1	20
BCC with mucin and squamous differentiation	1	20
Total	5	100

Most of the tumors were between <0.5 cm to 4 cms. Histologically, two cases of basal cell carcinoma showed melanin pigment within solid islands of basaloid cells with peripheral cell layer of the tumor masses showing a palisade and arrangement of the nuclei. One case showed solid nodule of tumor cells with horn cysts, which were composed of fully keratinized cells, but one case showed areas of mucin and squamous differentiation and another case showed basal cell carcinoma with squamoid features such as individual cell keratinization and epithelial pearl formation.

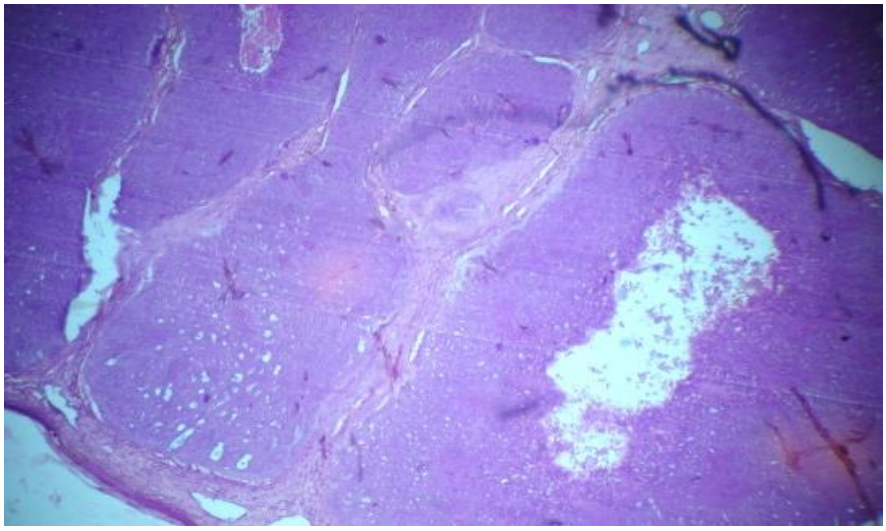

Figure 2: Basal cell carcinoma with mucinous and squamous differentiation. (40X)

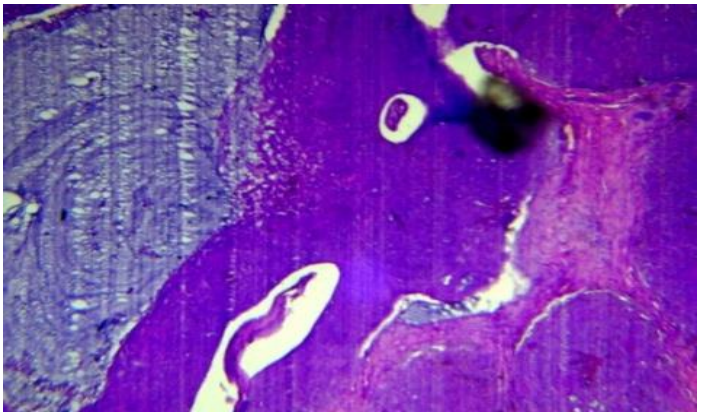

Figure 3: Basal cell carcinoma with mucinous and squamous differentiation(100X) Neuroendocrine carcinoma with squamoid differentiation

One rare case was encountered in this study. The patient was a 55 year old male who presented with an ulcerated growth over the penic. The specimen showed amputated penis with a grey white growth over the prepucial skin showing infiltration into glans and shaft of the penis. Histologically, it showed round to oval tumor cells in solid sheets and nests with vesicular nuclei, small nucleoli and scant cytoplasm. However some areas showed foci of squamous differentiation.

Figure 4: Neuroendocrine carcinoma with squamoid differentiation

Gross: Partial penectomy specimen with growth in the prepucial skin

Figure 5: Neuroendocrine carcinoma with squamoid differentiation

Gross: Cut section shows grey white growth over the prepucial skin with infiltration into glans and shaft of the penis.

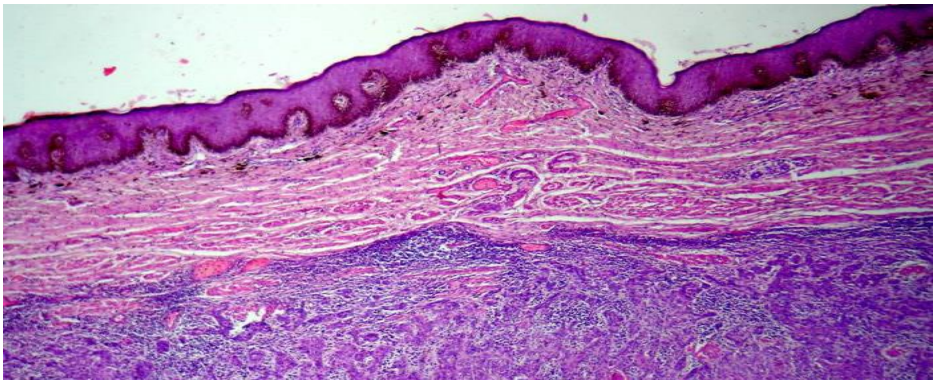

Figure 6B: Neuroendocrine carcinoma with squamoid differentiation

HP: Dermal tumor with small round cells and squamous cell nests. (100X)

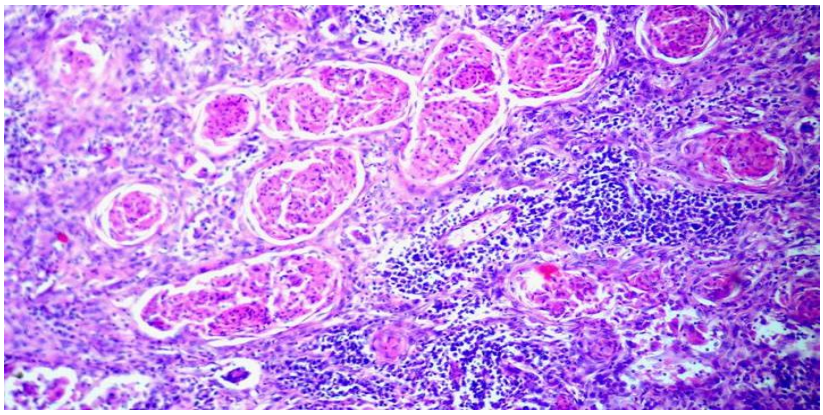

Figure 6A: Neuroendocrine carcinoma with squamoid differentiation

HP: Dermal tumor with small round cells and squamous cell nests. (40X)

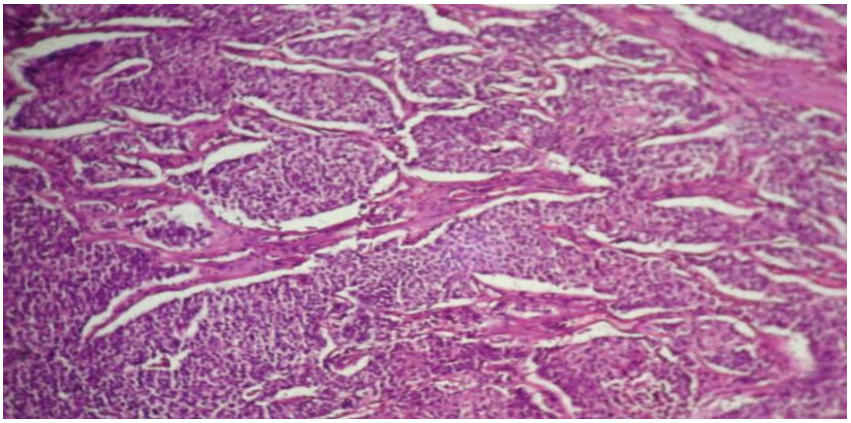

Figure 7: Neuroendocrine carcinoma with squamoid differentiation

HP: tumor cells in classical organoid pattern. (100X)

Malignant Adnexal Tumor

Malignant Hidradenoma

One case of hidradenocarcinoma was encountered in this study. The patient was a 22 year old male who presented with swelling in the axilla. Gross specimen showed a grey white irregular tumor mass measuring 3x3 cms infiltrating into surrounding tissue. Histologically, it showed lobulated tumor located in the dermis and extending into the subcutaneous fat. Tumor was composed of lobulated masses of squamoid cells with prominent vesicular nuclei, prominent nucleoli and pale cytoplasm. Also seen were duct like structures containing secreted material, cystic spaces, few mitosis, necrosis and chronic inflammatory cell infiltrate in deep dermis.

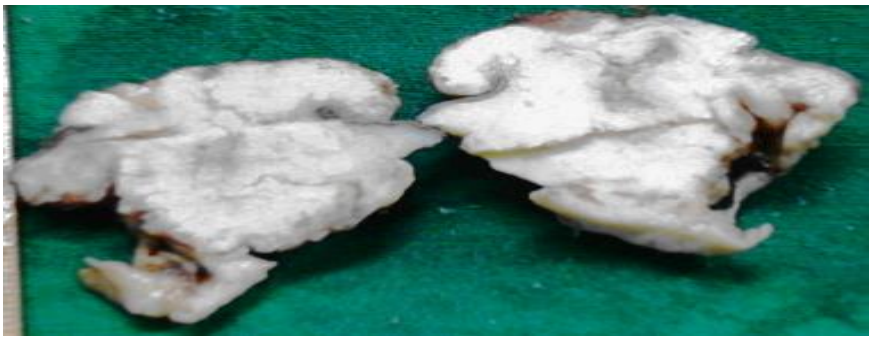

Figure 8: Hidradenocarcinoma

Gross: Grey white irregular tumor mass infiltrating into surrounding tissue

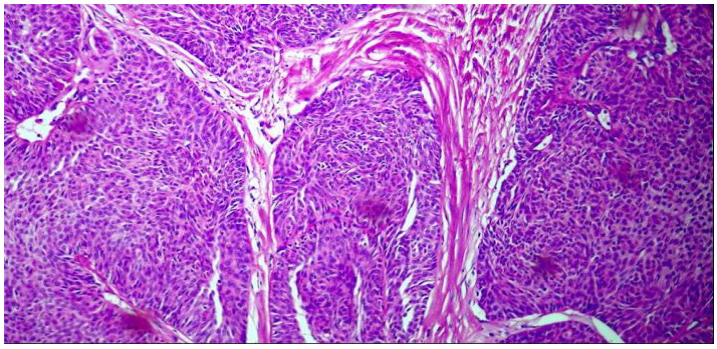

Figure 9: Hidradenocarcinoma

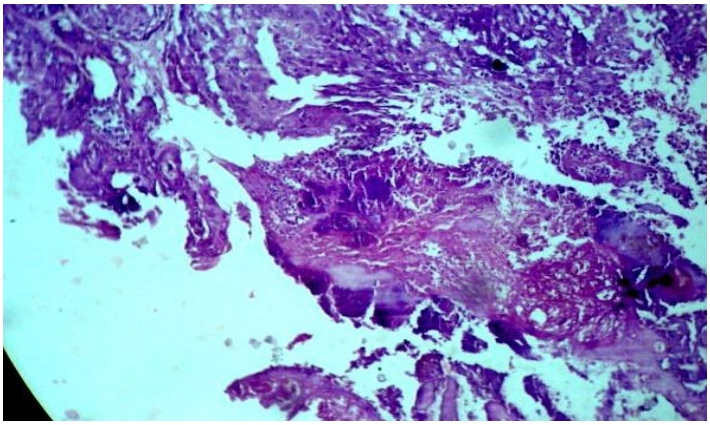

Figure 10: Hidradenocarcinoma HP: Areas of necrosis. (100X)

HP: Lobular arrangement of tumor cells. (400X)

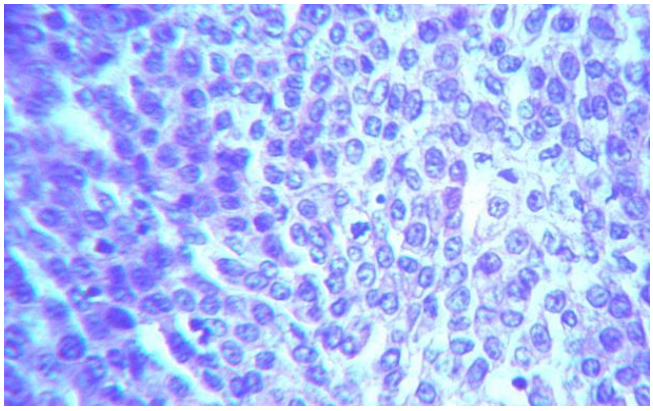

Figure 11: Hidradenocarcinoma

HP: Clear cell foci with abnormal mitosis. (400X)

Muco-epidermoid carcinoma

One case of muco epidermoid carcinoma was encountered in this study. The patient was a 55 year old female with a swelling over scalp. Gross specimen showed nodular tumor measuring 2x1 cms fungating through the surface. Cut section showed solid well circumscribed tumor involving epidermis and dermis. Histologically, it showed tumor composed of combination of squamous and mucus-secreting cells arranged in sheets and cystic configurations.

Figure 12A: Gross: Nodular tumor Fungating through the skin surface.

Figure 12B: Cut section of A showing grey white circumscribed nodule involving epidermis and infiltrating into the dermis and subcutaneous fat

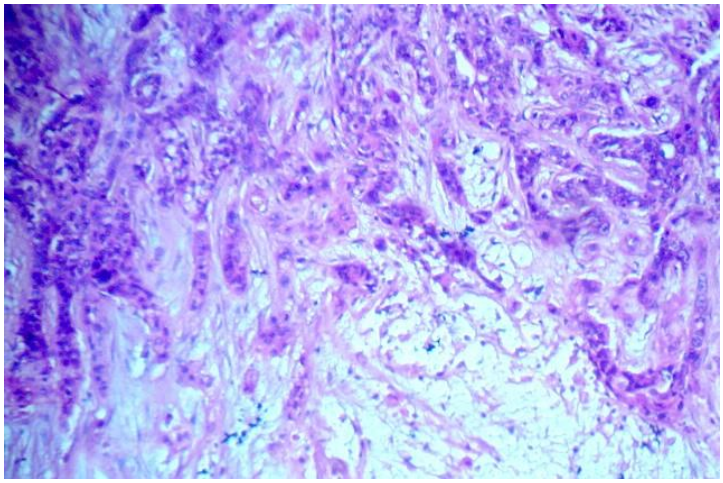

Figure 13: Mucoepidermoid carcinoma-HP: Islands of squamoid cells intermingled with pools of mucin which contain cuboidal mucin secreting cells. (100X)

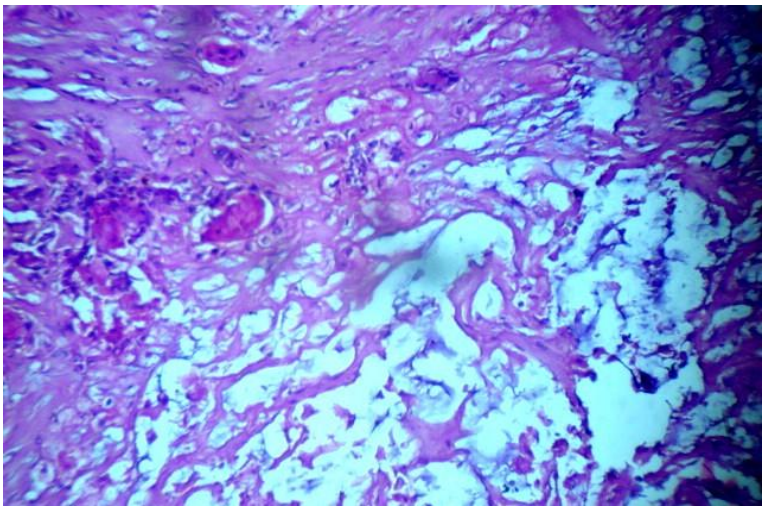

Figure 14: Mucoepidermoid carcinoma-HP: Squamous eddies with pools of mucin (100X)

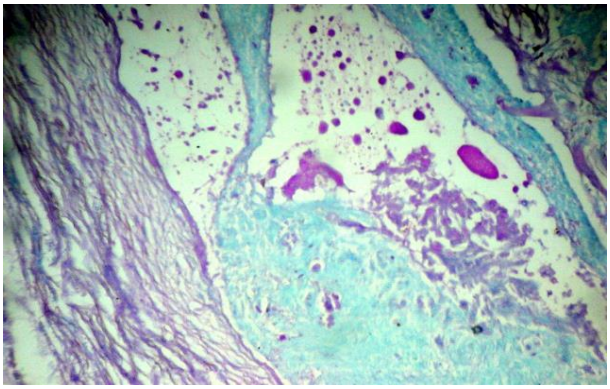

Figure 15: PAS stain of Mucoepidermoid carcinoma (100X)

Malignant Melanoma

In this study, five cases of malignant melanoma were encountered. All the lesions occurred over lower extremity with a peak incidence in seventh decade and showed a male preponderance.

Table 15: Age incidence of malignant melanoma

Age	Number of cases	Percentage
50-59	2	40
60-69	1	20
70-79	2	40

Table 16: Sex incidence of malignant melanoma

Sex	Number of cases	Percentage
Male	3	60
Female	2	40

Histologically, it showed marked junctional activity at the epidermo-dermal junction. Both epithelioid and spindle-shaped cells were seen, the former being more common. The individual cells were arranged in solid masses and sheets with pleomorphic nuclei and conspicuous nucleoli. Varying amount of intracytoplasmic pigment was also found.

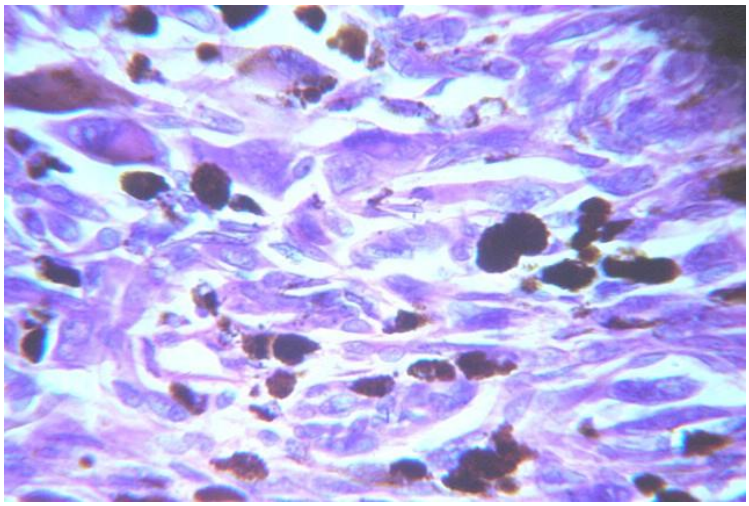

Figure 16: Malignant melanoma-HP: Mixture of epithelioid and spindle cells with melanin

Skin tumors constitute significant proportion of patients with cancer. Skin tumors are an ideal subject for study from clinical, morphological and therapeutic point of view and are so ubiquitous that they can affect people of all ages. In this study, the WHO classification of skin tumors[8] was followed. All non-neoplastic lesions and dermal tumors were excluded from this study. Total of 790 specimens of neoplasms were received, Out of these, tumors of epidermis, epidermal adnexae and melanogenic system were 54, constituting 6.83%. In the present study it was observed that malignant epidermal tumors were the most common (61%), followed by benign tumors of epidermal appendages (13%), benign tumors of epidermis (11%), malignant melanogenic tumors (9%), malignant adnexal neoplasms (4%) and benign melanogenic tumor

(2%). Of these 54 cases studied, the ratio of benign (14) to malignant tumors (40) was 1:2.85. The ratio of benign epithelial and adnexal tumors (13) to malignant counterparts (35) was 1:2.69 and ratio of benign tumors of melanogenic system (1) to malignant counterparts (5) was 1:5. Skin cancer incidence for the United States in 1994released by Cancer Society, predicted that there would be 32,000 new melanomas diagnosed and more than 5,00,000 NMSCs, making up about third of all cancers diagnosed.[9] In India, skin cancers constitute about 1-2% of all diagnosed cancers. Various cancer registries in India reported cumulative incidence of skin cancer varying from 0.5 to 2 per 1, 00,000 population.[10]

Table 8: Incidence of malignant neoplasms of skin in hospital based studied with respect to all malignant neoplasms

Hospital	Author	Percentage of skin tumors
Chittaranjan Cancer Hospital, Calcutta	Chakravarthy RC et al.[11]	1.87
Medical College, Jammu	Kapur R et al.[12]	8.16
JRTR Medical College, Ambojali	Kulkarni PV et al.[13]	5.79
JIPMER, Pondicherry	Budharaja et al.[14]	2.08
Present study	Karnataka	6.83

The malignant neoplasms of skin in different hospital based studies in India ranged from 1.87% to 8.84%. Observation obtained in the present study is near to that of study conducted by Kulkarni PV et al.[13]

Table 9: Incidence of malignant neoplasms of skin with respect to malignant tumors all over body as per National Cancer Registry[15]

Place	Male	Female
Bangalore	1.95%	1.28%
Bombay	1.05%	0.93%
Madras	1.92%	0.53%

Population based cancer registries from Bangalore, Bombay and Madras indicate that skin tumors account for between 0.5% to 1.95% of all cancers. In this study, skin tumors constituted 6.8% of total tumors received during this period. The incidence appears to be higher than the registry based incidence for the following reasons.

1. Registry is population based and our records are hospital based.
2. Inclusion of penile skin cancers in the present study.

As per cancer registries of Bombay, Bangalore and Madras malignant tumors were more in men with a male to female ratio of 1.9:1. In our study higher male incidence with a ratio of 4.6:1 was found. This may be due to small number studied and hospital based statistics could not be compared with population based registries. In the present study, squamous cell carcinoma

accounted for maximum number (67.5%) followed by basal cell carcinoma and malignant melanoma (12.5%). Squamous cell carcinoma accounted for maximum number of cases of skin cancer by Chakravarthy RC et al., [11] Budharaja SN et al.[14] and Deo SV et al.[10] as in the present study.

Table 10: Comparative incidence of different malignant tumors of skin in India

Type of tumor	Budhraja SN et al.[14]	Chakravarthy RC et al.[11]	Deo SV et al.[10]	Present study
Squamous cell carcinoma	49.02%	64.3%	55.8%	67.5%
Basal cell carcinoma	17.65%	16.5%	18.1%	12.5%
Malignant melanoma	29.41%	8.69%	26.1%	12.5%
Hidradenocarcinoma	-	-	-	2.5%
Mucoepidermoid carcinoma	-	-	-	2.5%

In the present study, most patients were males – 23 patients (85%) compared to females – 4 patients (15%). Even when penile cancers were excluded, the incidence in males was higher in the present study than those reported by Chakravarthy RC et al.[11] and Reddy DJ and Rao KV.[16] In the present study, 57% of squamous cell carcinomas occurred over the genitalia. This figure is high when compared to the series of Chuang CY et al.[17] When anogenital cancers were excluded, squamous cell carcinoma occurred commonly over the extremities, which was consistent with findings of Reddy DJ and Rao KV,[16] Chakravarthy RC et al.[11] Most squamous cell carcinomas of the skin are well differentiated.[18] The present study correlate with above studies having max. number of squamous cell carcinomas (Grade I & Grade II) accounting for 82% of all cases.

Verrucous carcinoma

It is a low grade variant of squamous cell carcinoma. In the present study lesion is seen over penis in a 65 year old male. Histologically, the lesion showed endophytic growth with blunt shaped projections into the dermis, and deeper sinuses with keratin filled cysts. Similar observations have been made by Schwartz RA.[19]

Basal cell carcinoma

Basal cell carcinoma accounted for 12% of all malignant neoplasms of the skin in the present study. The incidence of basal cell carcinoma in Indian literature ranges from 12-30%. The incidence of basal cell carcinoma in the present study is lower compared to the study done by Solanki RL et al.,[20] Budhraja SN et al.[14] and Deo SV et al.[10]

Table 11: Comparison of incidence in basal cell carcinoma with respect to malignancies of skin

	Percentage of basal cell carcinoma

Budhraja SN et al.[14]	16.52
Deo SV et al.[10]	18.10
Solanki RL et al.[20]	28.00
Present study	12

In the present study, all the lesions occurred over the face, which was consistent with the findings of Solanki et al.[20] and Raasch et al.[21] In the present study male to female ratio was found to be 4:1. Solanki RL et al.[20] found a male:female ratio of 1.26:1., Budhraja SN et al.[14] found a male:female ratio of 2.6:1. In the present study, the average age was 63 years and the peak incidence was seen in the 7th decade. The average age in the present study was corresponding to that of Sprawl CW et al.[22]

Table 12: Comparison of histological types in basal cell carcinoma (percentage)

Histological pattern	Solanki RL et al.[20]	Present study
Solid	60	-
Keratotic	9.3	20
Pigmented	7	40
Basi squamous	3.4	20
Basal cell carcinoma with mucin and squamous differentiation	-	20

Histologically, maximum number of cases, observed was of pigmented type. Solanki RL et al.[20] and Sprawl CW et al.[22] encountered solid type as the most common.

Neuroendocrine carcinoma with areas of squamous differentiation

It wasan uncommon tumor, one case was encountered in this study. The patient was a 55 year old male, presented with an ulcerated growth over the penis. Histologically, it showed sheets and nests of tumor cells with foci areas of squamous differentiation, which was consistent with findings of Cerroni et al.[23] and Iacocca MV et al.[24] There were seven patients with appendageal tumors. Four (57.1%) had hair follicle origin and three (42.9%) had sweat gland origin.

Malignant Melanoma

Malignant melanoma accounted for 13% of all malignant lesions of the skin. In Indian studies, malignant melanoma accounted for 8.8% to 29.4% of all skin cancers. The present study was near to the study of Reddy DJ et al.[16]

Table 13: Comparison of incidence of malignant melanoma with respect to all skin cancers

	Incidence (%)
Budhraja SN et al.[14]	29.40
Chakravarthy RC et al.[11]	8.85
Reddy DJ et al.[16]	15
Present study	13

All the cases occurred over the foot. The observations in this study are higher to those by Budhraja SN et al.,[14] Reddy DJ et al.[16] and Chakravarthy RC et al.[11]

Table 14: Comparison of location in malignant melanoma

	Foot (%)
Budhraja SN et al.[14]	85.33
Reddy DJ et al.[16]	80
Chakravarthy RC et al.[11]	80
Present study	100

In the present study, incidence of melanoma was more in males which was consistent with findings of Chakravarthy RC et al.[11] and Sampath MB et al.[25] Most cases of melanoma occurred in the sixth and seventh decade. In the studies conducted by Sampath MB, Sirsat MV[25] and Reddy DJ et al.[16] the maximum incidence of melanoma was in the fifth decade. This difference may be due to small number of cases that were available for the present study. Histologically, lesions showed pronounced junctional activity, large atypical melanocytes in nests and sheets with dust like melanin, hyperchromatic nuclei and large nucleoli. Both epithelioid and spindle cells were seen with epithelioid cells being predominant which is consistent with the findings of various authors.[26,27]

CONCLUSION

In India threre are significant proportion of patients with Skin cancer. Unlike in the Western countries, SCC is the commonest histologic variety. Increase in amount of Ultraviolet radiations involved in tumor induction and also co-carcinogen, ionizing radiation, nitrogen mustard, electron beam irradiation, chemical carcinogen. Viral infections acting as direct carcinogens or as promoting agentsare predisposed to cutaneous malignancies. These are some of the reasons for cutaneousmalignancies. Histopathological study is one of the most valuable means of diagnosis in dermatology and diagnosis of skin tumors.In some cases rare problems of differential diagnosis encountered may be solved with the help of histochemical and/or electron microscopic studies.

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