ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 2, 2025

ORIGINAL ARTICLE

AN OVERVIEW OF HISTOPATHOLOGY OF NEOPLASTIC LESIONS OF SKIN

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ABSTRACT

Introduction- Skin is the largest organ in the body performing multiple functions. There is a wide spectrum of skin tumors. The skin tumors are broadly divided into surface epidermal tumors and tumors of epidermal appendages.

Aim - To study varies neoplasms of skin and classify them accordingly to WHO classification.

Methods -The present study consisted of analysis of tumors of skin received in the histopathology section of department of pathology from January 2018 to July 2021. The material comprised of biopsies and excision specimens. The clinical and histopathological details were noted and analyzed.

Results - During the study period we found 116 neoplastic skin lesions and majority were benign. Squamous cell carcinoma was the most common malignant tumor. Benign tumors were common in younger age group while malignant in older age group.

Conclusion-Benign tumors are more common than malignant tumor. Histopathological examination of skin tumors remains the gold standard for precise diagnosis.

Keywords: Appendageal tumor, Benign skin tumor, Skin neoplasm, Squamous cell carcinoma, Verruca

INTRODUCTION:

Skin is the largest organ of the body and represents a window to the internal wellbeing or disease. It is a complicated protective covering with diverse functions like mechanical photoprotection, immune surveillance, nutrient metabolism and repair. [1]

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The spectrum of skin disease varies greatly according to the age, gender and other factors. It is very difficult to define a benign or malignant skin lesion clinically. Hence, histopathological examination remains the gold standard for helping the clinician to overcome the diagnostic dilemma.

Skin tumors comprises a wide variety of neoplasms of skin and subcutis that are classified as keratinolytic, melanocytic, appendageal, hematolymphoid and soft tissue tumors. Skin tumor incidence shows significant geographic variability worldwide. Cutaneous squamous cell carcinoma and other skin carcinomas exhibit diverse incidence rates across regions, with a general upward trend observed since the 1960s, estimated to increase annually by 3–8%. The elevated occurrence of cutaneous squamous cell carcinoma and basal cell carcinoma is predominantly attributed to sun exposure and the mutagenic impact of ultraviolet (UV)radiation.[2]

Benign tumors can occasionally present clinical features that mimic malignancy, especially when displaying pigmentation, ulceration, or inflammation. In such cases, histological analysis of biopsy specimens becomes essential to definitively diagnose the condition. Therefore, histomorphological examination remains the gold standard for precise diagnosis and prognostic evaluation of the patient. Understanding histopathological patterns of skin tumors is crucial for predicting outcomes and devising effective management strategies[2].

This study aimed to assess the frequency distribution of various histopathological types of skin tumors, analyze their clinicopathological characteristics, and determine the staging of malignant tumors to mitigate associated mortality and morbidity risks.

MATERIAL AND METHODS:

The present study is a retrospective and prospective study. The material comprised of biopsies and excision specimens of skin tumors received in the histopathology section of department of pathology from January 2018 to July 2021.

All lesions of the skin of genitalia were excluded. The specimens were received in 10% formalin and fixed for 12 to 24 hours in the same.

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A thorough gross examination was conducted according to standard protocols. Representative tissue bits were taken. Tissue samples were processed and embedded in paraffin wax, followed by cutting of 3–4-micron thick sections using a rotary microtome. These sections were then stained with hematoxylin and eosin and examined under a light microscope. Clinical data, including patient age, sex, location and duration of swelling, as well as other relevant clinical history and investigations, were retrieved from requisition forms. A detailed analysis of clinical, gross, and microscopic findings of skin lesions was performed.

RESULTS:

During the study period of 3 year and 6 months, 400 skin biopsies were received at our institution and this represented 5.57% of all the surgical specimens received at the histopathology laboratory. The skin lesions were received in the form of either excisional biopsies (84%) or incisional and punch biopsies (16%). Among the 400 skin lesions, 116 were neoplastic skin lesions. Thus, the frequency of skin tumors out of total skin specimens received at our institute was 29%. Out of total surgical specimens received, frequency of skin tumors constitutes 1.6%.

Neoplastic skin tumors are broadly classified as benign, borderline and malignant. (Table-1)

Table 1 : Broad classification of skin tumors

Type	Number of cases	% of cases
Benign	74	63.79 %
Borderline	1	0.86 %
Malignant	41	35.34 %
Total	116	100%

Benign skin lesions were more common than malignant one while we found a case of borderline tumor.

Among total 116 neoplastic skin lesions, youngest patient was 6 days old with myrmecia of right thumb while

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oldest patient was 89 years old who had squamous cell carcinoma of right ear pinna. Maximum number of cases were found in 21-30 years age group. In both benign and malignant skin tumors, males were affected more than females.

Depending upon cell of origin, skin tumors are classified as keratinocytic, melanocytic, appendageal, soft tissue, neural or vascular tumors etc according to WHO classification of skin tumors 2018. (Table-2)

Table no 2 : Distribution of various skin tumors

Tumors	Type	Lesions	No:	M	F	Total
Benign	Keratinocytic	Verruca	22	14	8	27
		Seborrheic keratosis	04	1	3	
		Squamous papilloma	01	1	0	
	Melanocytic	Intradermal naevus	01	0	1	01
	Appendageal	Hidradenoma	03	1	2	15
		Hidradenoma Papilliferum	01	0	1	
		Cylindroma	01	0	1	
		Syringocystadenoma papilliferum	01	0	1	
		Pilomatrixoma	03	1	2	
		Chondroid syringoma	01	0	1	
		Folliculosebaceous cystic hamartoma	01	1	0	
		Eccrine angiomatous hamartoma	02	2	0	
		Eccrine Spiradenoma	01	0	1	
		Apocrine hidrocystoma	01	0	1	
	Soft tissue and neural tumors	Hemangioma	22	12	10	31
		Dermatofibroma	02	2	0	
		Schwannoma	02	2	0	
		Fibrolipoma	05	1	4	
Borderline		Papillated bowen disease	01	1	0	01
Malignant	Keratinocytic	Squamous cell carcinoma(SCC)	18	15	3	25
		Basal cell carcinoma(BCC)	07	2	5	
	Melanocytic	Malignant melanoma(MM)	08	6	02	08
	Appendageal	Malignant chondroid syringoma	02	1	1	04
		Porocarcinoma	02	1	1	
	Fibrous	Dermatofibrosarcoma Protuberans(DFSP)	03	3	0	03
Metastatic		Metastatic signet ring cell carcinoma	01	1	0	01

Among benign tumors, maximum number of cases were of soft tissue and neural origin followed by keratinocytic and appendageal tumors. We found a case of intradermal naevus.

In benign keratinocytic tumors, verruca was the most common lesion and males were affected more than females. There was a female predilection among adnexal tumor. Among soft tissue tumors, hemangioma was the most common

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skin lesion and males were affected more than females.

There was a case of borderline tumor which was of papillated bowen disease.
Among malignant tumors, keratinocytic tumors were most common followed by melanocytic tumors. Squamous cell carcinoma was the most common malignant skin tumor and males were affected more than females.

Malignant melanoma was more common in males than in females.

Benign tumors - were more common in 3rd decade of life and showed male preponderance. The least affected age group was 81-90 years where only single case was identified.

Verruca and hemangioma were the most common benign tumor with male preponderance. Seborrheic keratosis showed female preponderance with M:F ratio of 1:3.

Age group 21-30 had highest incidence of hemangioma and verrucae which constituted 31.8% and 27.2% respectively.

Verruca- Among benign keratinocytic tumors, verruca was the most common lesion with a peak frequency in the third decade (31.8%) and with a significant male preponderance (63.6%). The extremities were the most common affected site.

On histopathology, epidermis showed hyperkeratosis, acanthosis and hypergranulosis with rete ridges displaced laterally and their tips pointing towards the centre. The squamous cells showed abundant refractile appearing eosinophilic cytoplasmic inclusions- keratohyaline bodies. (Fig 1A, 1B)

Seborrhoeic keratosis –

Four cases were found with male to female ratio of 1:3. Three were located on the back and one on the scalp. Histopathological examination revealed proliferating epidermis with acanthosis, hyperkeratosis and papillomatosis. Tumor was composed of basaloid cells with varying amount of squamoid cells. Few horn cysts and squamous eddies were seen. (Fig 1C)

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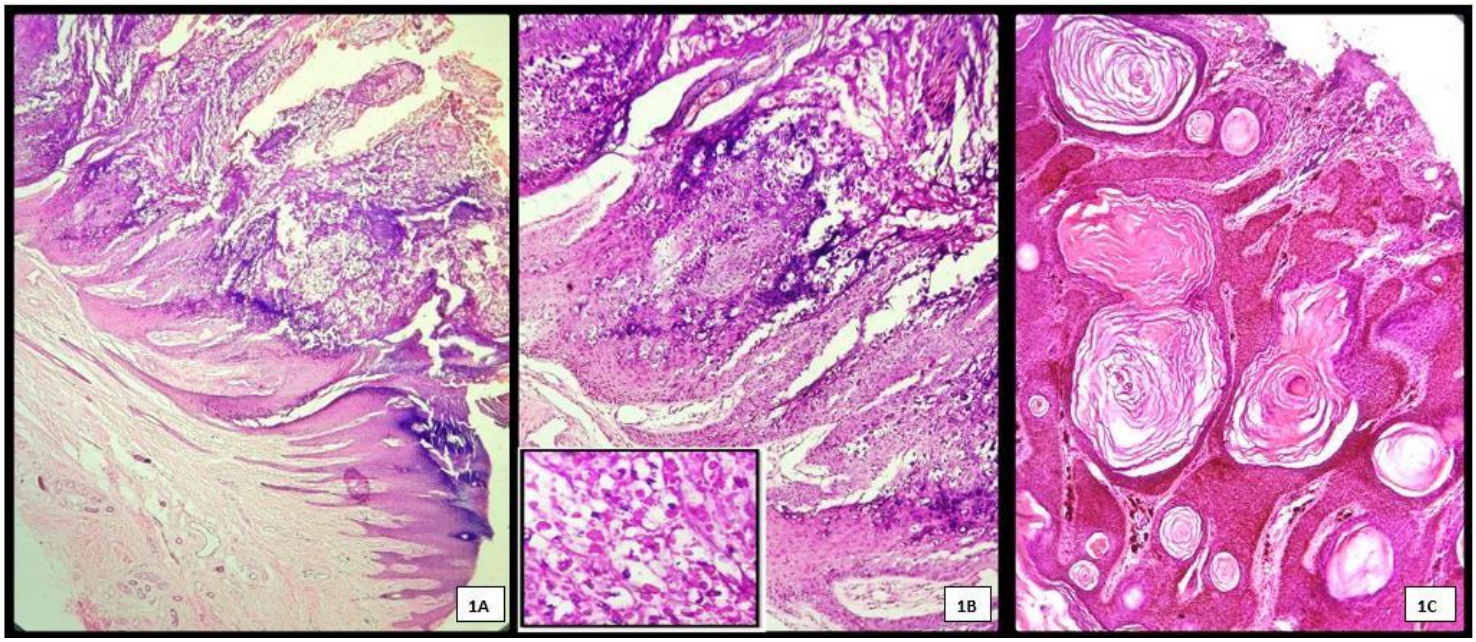

Fig-1-A-Myrmecia-Photomicrograph showing hyperkeratosis, acanthosis, papillomatosis and elongation of rete ridges (H & E 100x)

Fig -1-B- Myrmecia- showing koilocytic change and inset showing eosinophilic cytoplasmic inclusions (H & E 100x)

Fig-1-C- Seborrhoeic keratosis- Microphotograph showing horn cyst formation (H&E 100x)

Borderline tumor-

A 37-year-old male presented with verrucous thigh growth since 10 years. Grossly an elevated nodular growth arising from skin was seen which on histopathology showed an exophytic papillary mass composed of proliferating epidermis. The epidermis showed increased cellularity and full thickness squamous atypia with multinucleation, mitotic figures and apoptotic bodies. (Fig 2 A, 2B) Diagnosis of Papillated bowen disease was rendered.

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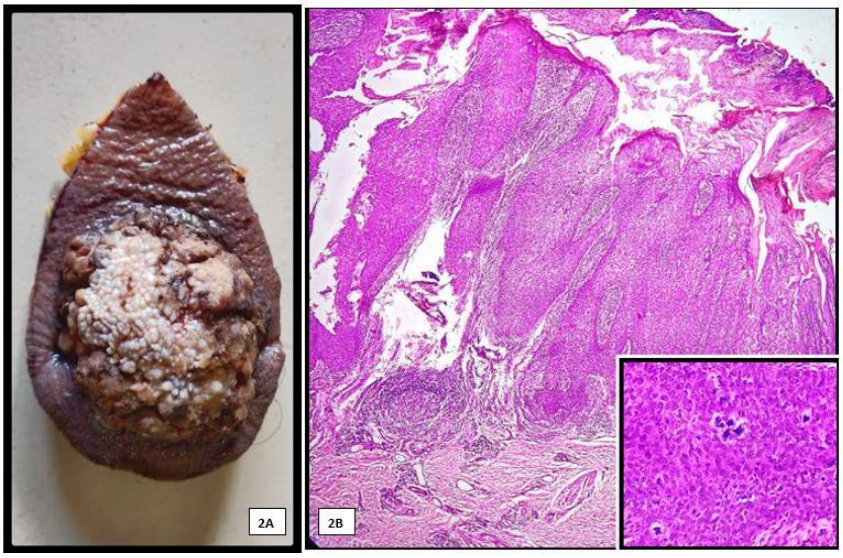

Fig-2 A - Gross photograph of papillated bowen disease

Fig 2-B- Papillated bowen disease displaying papillomatosis and full thickness atypia upto the basal layer with inset showing cytological atypia (H & E 40x)

Malignant tumors –

We found 41 cases of malignant skin tumors which includes SCC, BCC, DFSP, MM, Porocarcinoma and others. They were commonly found in 5^{th}, 6^{th} and 8^{th} decades. Malignant tumors were more common in males (65.8%) than in females (34.1%)

Anatomical distribution: Extremities was the most common site of presentation of malignant tumors of skin (58.5%) followed by head and neck region (26.8%). Inguinal region and back were least common sites (2.4% each) affected. (Table-3)

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Table no 3: Frequency and sex wise distribution of various malignant skin tumors.

Tumors		M	F	Total no: of cases	%
Keratinocytic	**SCC**	15	3	18	43.9
	BCC	2	5	7	17
Melanocytic	**MM**	6	2	8	19.5
Soft tissue and neural	**DFSP**	3	0	3	7.3
Appendageal	**Malignant chondroid syringoma**	1	1	2	4.8
	Porocarcinoma	1	1	2	4.8
Metastatic	**Metastatic signet ring carcinoma cell**	1	0	1	2.4
	Total	**29**	**12**	**41**	**100**

Keratinocytic category had the maximum number of cases (25 cases). SCC was more common and showed male preponderance with M:F ratio of 5:1 while BCC was common in females.

Malignant melanoma showed male preponderance with M:F ratio of 3:1.

Grading of SCC - In 1920, Broder introduced a formal grading system based on keratinocytic differentiation which is used even today. Tumors are graded from one to four grades based on increasing percentage of undifferentiated cells.

On histopathological examination, 13 cases (72.3 %) were Well differentiated, 3 (16.6%) were moderately differentiated and rest 2 (11.1%) were poorly differentiated. (Fig 3A,3B)

In the present study, we found two variants of SCC - Keratoacanthoma and acantholytic SCC.

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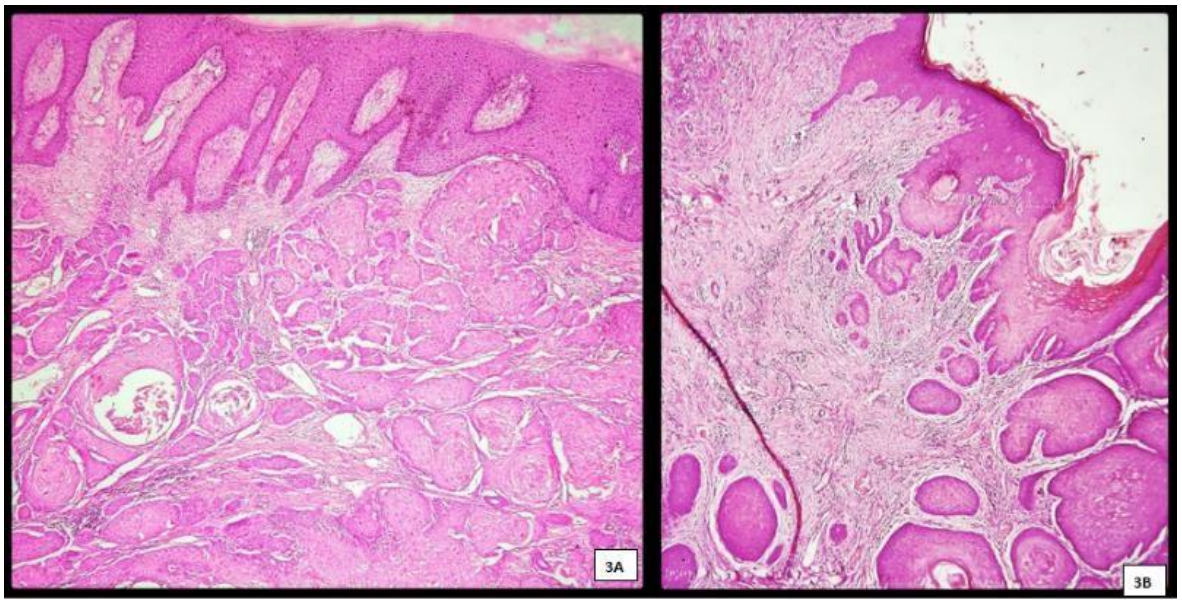

Fig -3A & 3 B- Squamous cell carcinoma- Microphotograph showing tumor arising from epidermis and invading the dermis (H & E 100x)

Keratoacanthoma:

A 78 years man presented with mass on the right side of neck since 6 months. On histopathology, skin with a central crateriform lesion filled with keratotic plugs and flasked by epidermal buttresses was noted. The margins were free. (Fig 4)

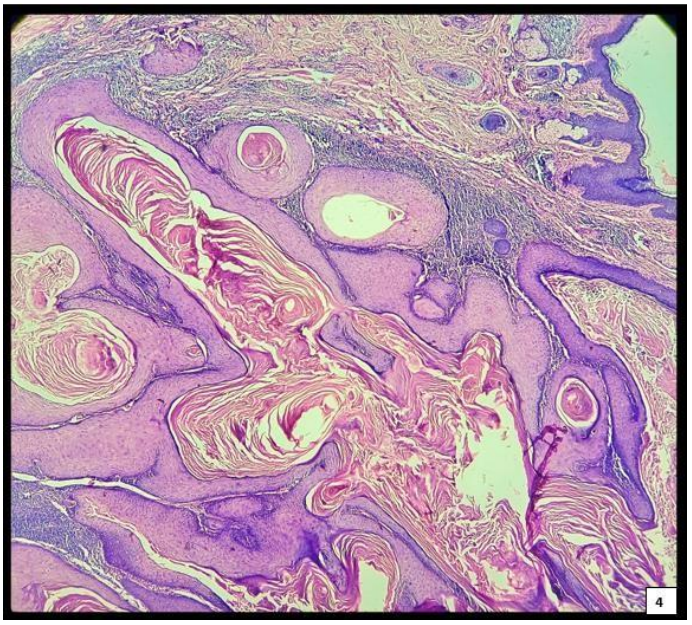

Fig 4 - Keratoacanthoma- Whorl of laminated keratin present within invagination of squamous cells (H & E 100x)

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Acantholytic SCC:

A 77 years male presented with ulcer at canthus of left eye. Biopsy showed a tumor composed of round to polyhedral cells arranged in sheets, cords and in adenoid pattern where the tumor cells showed loss of cohesion forming clefts like spaces lined by cuboidal cells. Many dyskeratotic cells were seen in cleft.

Basal cell carcinoma

In the present study, 7 cases of BCC were found including 2 variants- basosquamous and pigmented.

BCC was commonly found in 71-80 years age group with female preponderance and maximum on head and neck region. (Fig 5A,5B,5C)

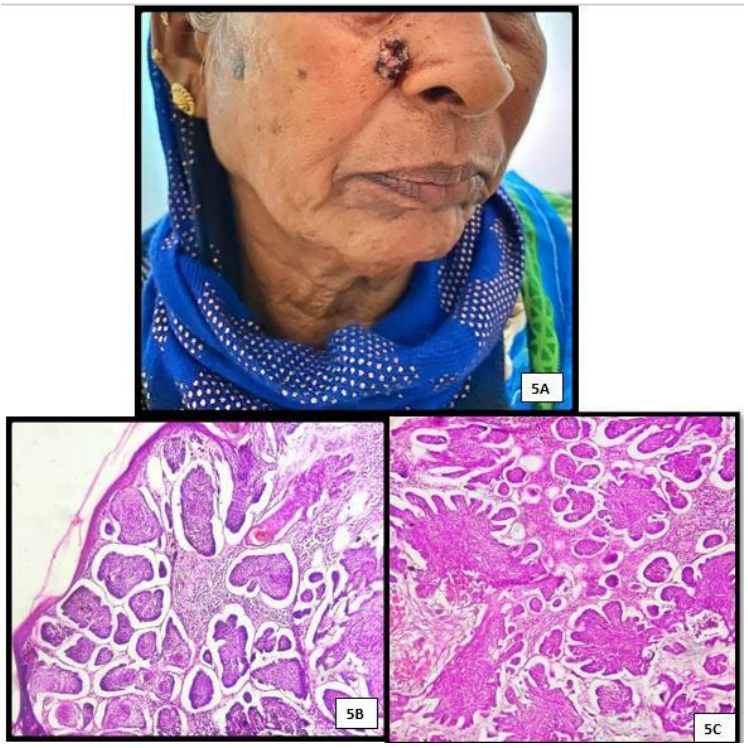

Fig -5 A- Gross photograph of Basal cell carcinoma

Fig- 5-B- Basal cell carcinoma- Microphotograph showing irregular proliferation of basaloid cells infiltrating the dermis with clefting artifact (H & E 100x view)

Fig-5-C- Basal cell carcinoma- Microphotograph showing basaloid cells and clefting artifact (H & E 100x view)

Malignant Melanoma

Eight cases were observed in our study. Age group 41-50 years and 71-80 years had the maximum number

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of cases with male preponderance. (Fig 6A,6B)

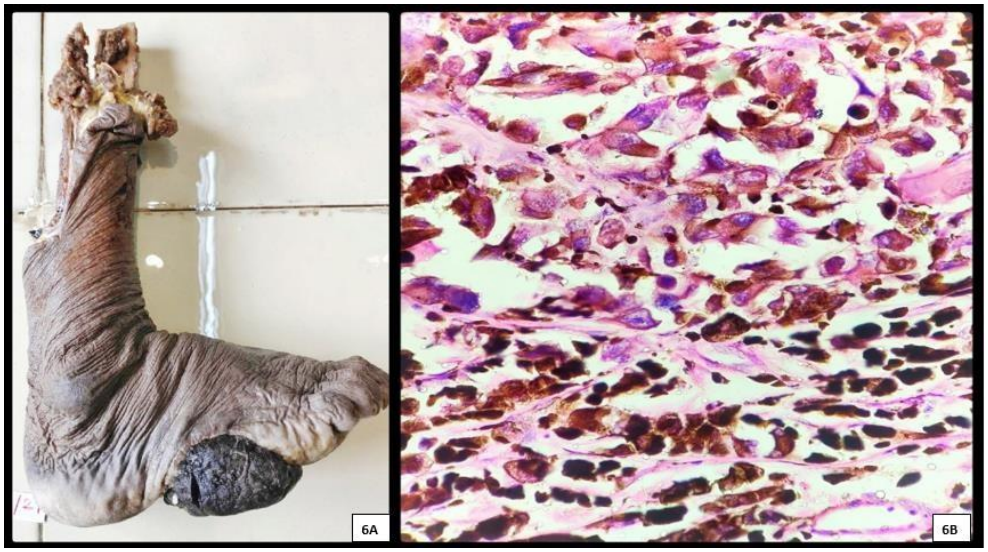

Fig- 6 A- Malignant melanoma- Gross photograph of amputed specimen of leg showing nodular growth at the foot

Fig-6-B-Malignant melanoma-Microphotograph showing tumor cells having pleomorphic nuclei, prominent nucleoli and intracytoplasmic melanin (H & E 400x)

Appendageal tumors

In the present study, benign appendageal tumors were more common than malignant. Maximum being in the third decade. Pilomatrixoma and hidradenoma were the most common appendageal tumors found. (Fig 7 A, 7B, 7C, 7D)

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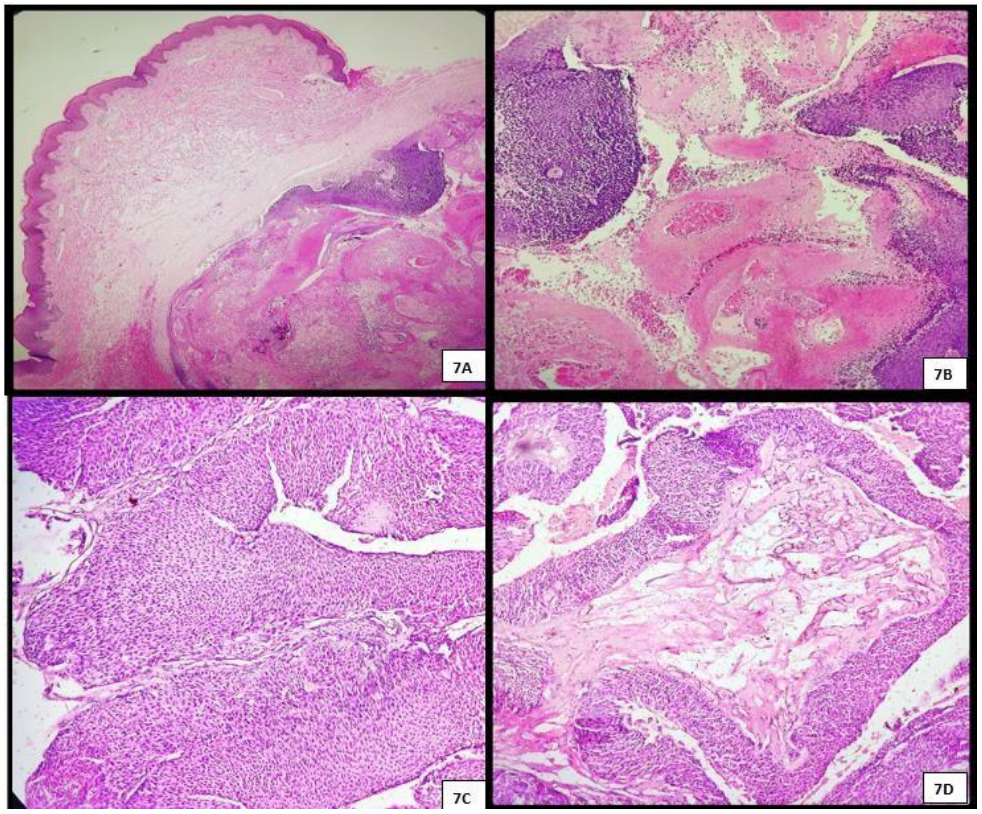

Fig-7- A- Pilomatrixoma- Microphotograph of dermal based tumor showing two types of cells- peripheral basophilic cells and central shadow cells (H & E 40x)

Fig- 7-B- Pilomatrixoma- Microphotograph of tumor showing two types of cells- peripheral basophilic cells and central shadow cells (H & E 100x)

Fig –7C,7D- Solid cystic Hidradenoma – A and B- Polyhedral basophilic cells around cystic space (H & E 100x)

Malignant chondroid syringoma-

Histopathology revealed small groups as well as scattered pleomorphic epithelial cells having hyperchromatic nuclei and scanty cytoplasm with one to two mitotic figures per high power field and surrounded by abundant basophilic chondromyxoid stroma. (Fig 8A,8B)

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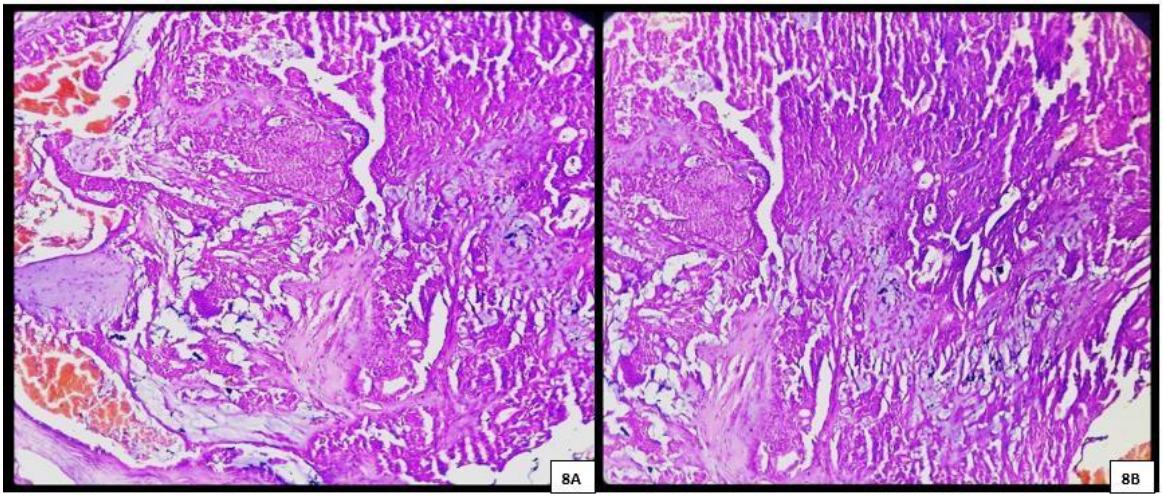

Fig – 8A & 8 B- Chondroid syringoma- photomicrograph showing epithelial tubules and ducts embedded in fibromyxoid stroma (H & E 100x)

Porocarcinoma:

A 55 year old female presented with lump over nipple areolar region of right breast since 10 years with recent ulceration. The patient gave history of similar swelling at same site 17 years back which was excised.

Histopathology showed an infiltrative high-grade tumor connected to the epidermis with partial lobular growth architecture. The tumor had an endophytic growth pattern with invasion of the deep reticular dermis and subcutaneous tissue. (Fig 9A, 9B, 9C)

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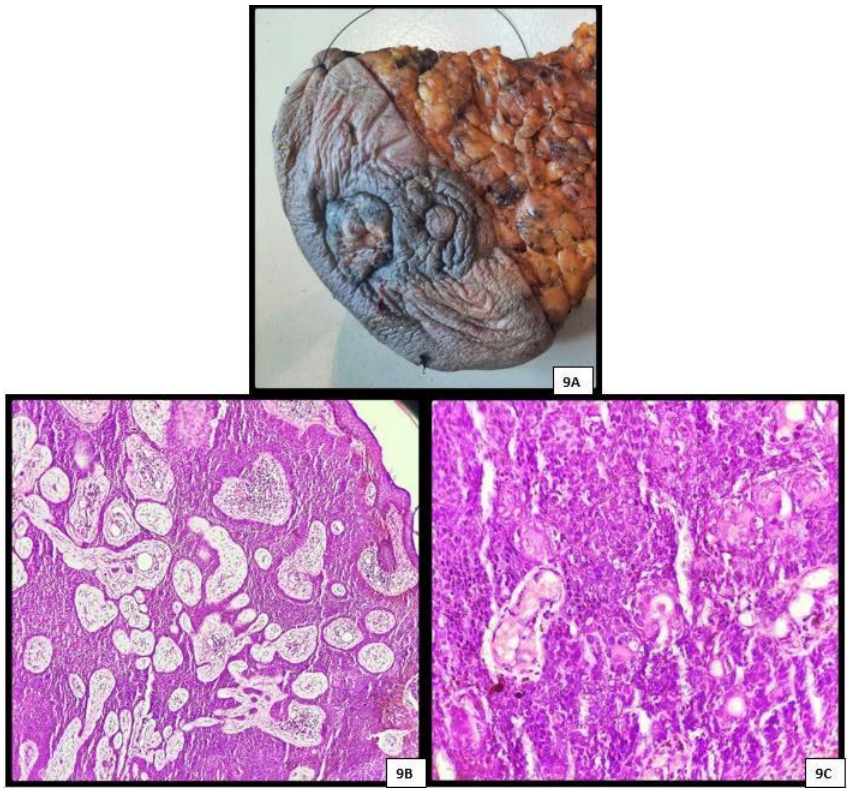

Fig-9 A- Porocarcinoma - Photograph of gross specimen showing a ulcernodular growth in the areolar region of the breast

Fig- 9-B- Porocarcinoma- Microphotograph shows an infiltrative tumor arising from the epidermis and composed of basaloid cells arranged in cords (H & E – 100x)

Fig- 9-C- Porocarcinoma- Microphotograph showing collection of tumor cells showing cytological atypia and squamous differentiation (H & E - 400x)

Dermatofibrosarcoma Protuberans

Dermatofibrosarcoma protuberans (DFSP) is a fibrohistiocytic tumor of intermediate malignant potential.

Three cases of DFSP in 44, 69 and 70-year-old males were encountered.

Metastasis to skin:

An unusual case of Metastatic signet ring cell carcinoma was found in 30 year old male presented with respiratory distress and multiple nodules on chest, neck, upper back and arms. Punch biopsy from the upper arm showed presence of round tumor cells with peripherally pushed nucleus and intracytoplasmic mucin- signet ring cells. (Fig 10A, 10B)

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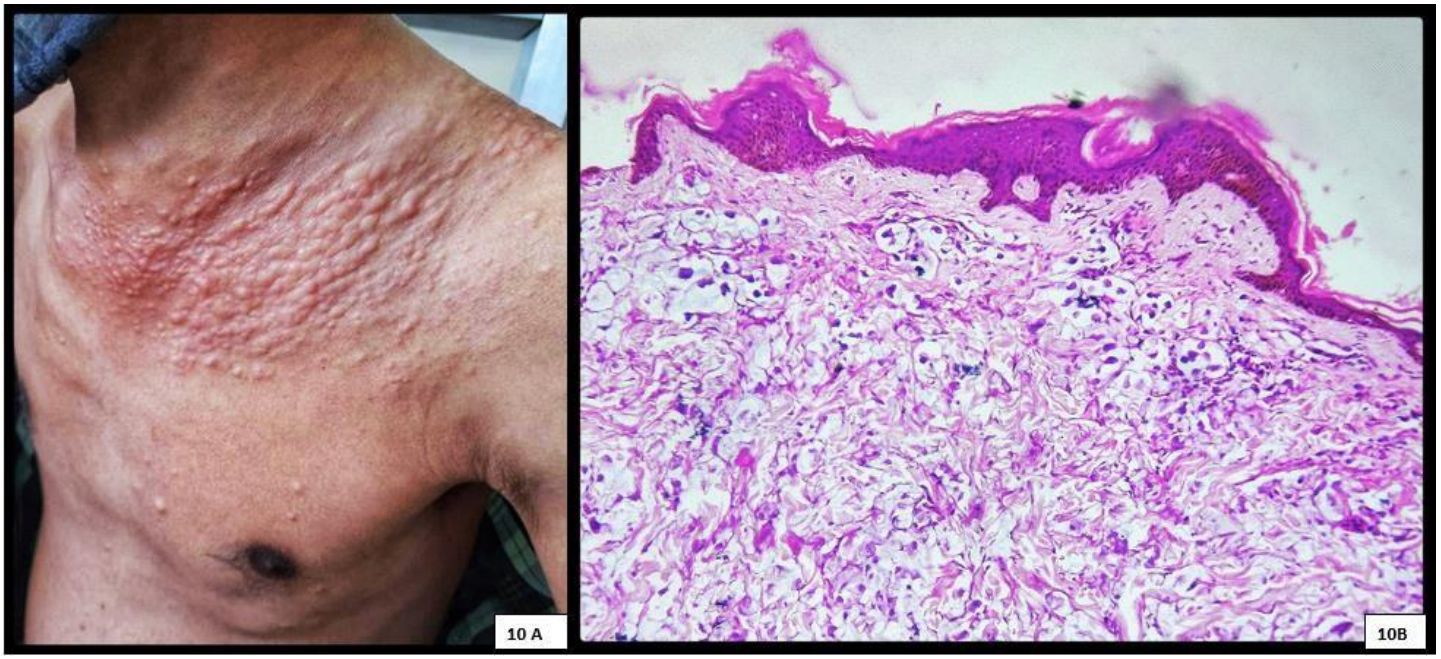

Fig-10 A- Clinical photograph showing metastatic nodules on the skin in a patient with metastatic signet ring cell carcinoma

Fig-10-B- photomicrograph showing metastatic signet ring cells in the dermis (H & E 40x)

DISCUSSION:

Dermatological disorders are frequently encountered health disorders in tropical countries like India with varied spectrum depending on the geographical area. Skin tumors constitutes 1.6% among total surgical specimen received and 29% among total skin specimens received at our institute. In a study by Kaur R et al, skin tumors constituted 27.5% of all skin specimens and 0.6% of all the surgical specimens received.[3]

Benign tumors were more common than malignant which is comparable with studies done by Sajad P et al[4], Sherpa et al[5] and Pappala et al[6].

Benign tumors:

Benign tumors were commonly seen in 21-30 years with male preponderance which is concordant with study done by Sherpa et al[5] and Goel et al[7]. While Gundalli et al [8] and Kaur R et al [3] showed females predominance. Goel et al[7] in their study found that verruca (20.1%) were the most common benign

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keratinocytic tumor followed by seborrheic keratosis (19.5%) which is comparable with the present study.

Borderline Tumors:

Bowen disease(BD) is an in-situ SCC of epidermis and is usually occurs on sun exposed area but in our study we found Papillated variant of BD on thigh.[9] Papillated variant is characterized by prominent koilocytosis as found in our case and is considered to be associated with human papillomavirus (HPV) infections. Miolo et al[10] also found similar case in their study. About 3-5% of all bowen disease progress to invasive SCC.

Malignant tumors:

Total 41 malignant lesions were observed and were commonly seen in older age group which is concordant with the study by Gundalli et al[8], Miolo et al[10] and Goel et al[7].

The frequencies of malignant tumors were greater in male than female which is comparable with studies by Gundalli et al[8], Kaur R et al[3], Shrivastava et al[11]. This may be because of increased risk factors like increased outdoor activity leading to prolonged sun exposure and other factors like trauma and occupation associated factors[10]

SCC: SCC was the predominant (43.9%) malignant tumor with maximum cases in 6th decade which is comparable with studies done by Gundalli et al[8], Kaur R et al[3], Sherpa et al[5] , Pappala et al[6].

Males were affected five times more than females. Rajbhar et al[12] also found similar male preponderance. This can be attributed to the prolonged sun exposure in men encounter while doing outdoor activities.

There were 2 cases of SCC arising in marjolin ulcer in 42 year and 49 year female. Both of them gave history of burn at the same site of lesion.

Marjolin's ulcer is a rare, aggressive condition that arises on chronic skin lesions. In 1828, the French physician Jean Nicholas Marjolin first described the ‘warty ulcer' that occurred on scars and termed it ‘cancroidal ulcer'. In 1903, Da Costa reported 2 cases of malignant ulcers on lower extremities with a history of venous ulcers and considered them to be consistent with the ulcers described by Marjolin.

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Subsequently, the malignant ulcers occurring on chronic wounds or scars gradually began to be referred to 'Marjolin ulcers[12].

The pathological types of marjolin ulcer include SCC, BCC, MM, sarcoma etc; majority being SCC. They are classified as acute and chronic based on the latency period[9].In our study both the cases were of SCC arising on chronic marjolin ulcer.

In the present study, SCC was most commonly found over the lower extremity which is consistent with the observations of Chalya PL et al[13] and Rajbhar et al[12].

In the present study, maximum case of SCC were well differentiated and is consistent with study by Laishram RS et al[14]. We found a case of keratoacanthoma and acantholytic SCC.

Keratoacanthoma is a well differentiated variant of SCC with distinctive clinical behavior. It is locally destructive with very little potential to metastasize. Many keratoacanthomas eventually undergo resolution, but central facial giant keratoacanthoma and subuncal keratoacanthoma may be locally aggressive.[15]

Acantholytic SCC is a more aggressive variant of SCC. The acantholytic variant has shown decreased expression of desmoglein 3 and E- cadherin which is responsible for the acantholytic pattern.[15]

BCC

In our study, BCC was most commonly found in the 71-80 years age group (57.1%) similarly Kaur R et al[3] found maximum number of cases > 70 years of age. There was a female preponderance which is consistent with observations of Rajbhar et al[12] and Raina RK[16] et al .

Maximum number of cases of BCC were found in the head and neck region, which is consistent with studies done by Kumar S[18] et al , Raina RK[16] et al, Rajbhar et al[12]

Nodular or solid type was the predominant form in the present study as observed by all the other studies.[17]

We had a case of basosquamous variant which has high metastatic rate compared with conventional BCC.[19]

Malignant melanoma

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Melanoma results from the interplay of genetic, environmental, and host factors.[20] The present study is comparable with the studies by Supekar BB et al[21] and Panda S et al[22] where males were affected more than females.

Women has incomplete inactivation of one X chromosome leading to mosaicism and hence better protection against melanoma. A higher number of missense mutations were noted in men, in turn increasing the risk. Also female hormones and immune system is said to be protective against melanomas.[22]

Appendageal tumors

In this study, benign appendageal tumors were more common than malignant which is comparable with studies conducted by Gundalli et al[8], Pujani M et al[24] and Goel P et al[7]. Maximum cases were seen in the third decade which is comparable with Pujani M et al.[24]

Kaur K et al[25], Goel P et al[7] also found maximum cases of pilomatrixoma and hidradenoma

Chondroid syringoma and malignant chondroid syringoma:

Chondroid syringoma represents the cutaneous counterpart of mixed tumor (pleomorphic adenoma) of salivary glands, therefore it is also termed mixed tumorof the skin.

Malignant chondroid syringoma is a malignant eccrine neoplasm that is rarely encountered in clinical practice. Unlike the benign variety which occurs most often on the head and neck, malignant chondroid syringomas are most often found on the trunk and extremities as found in our case.[25]

Porocarcinoma:

Eccrine porocarcinoma is an invasive carcinoma of the eccrine sweat glands, with an acrosyringeal origin. Other names are epidermotropic eccrine carcinoma, poroepithelioma, malignant eccrine poroma.[25]

Eccrine porocarcinoma can arise de novo or evolve from a benign poroma. In our study, one case was considered to be malignant evolution of poroma as there was past history of similar lump at the same site.

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Metastasis to skin:

Metastatic skin cancers form rare dermatological malignancies and constitute 2% of all skin tumors.[29]

In present study, a case was clinically diagnosed as histioid leprosy and histopathological study helped in unmasking the diagnosis of Metastatic signet ring cell carcinoma.

Signet ring cells are usually associated with malignancies like gastric, prostatic, breast cancers etc.

However in our case, before further investigations patient succumbed to death and the primary origin of the tumor could not be revealed.

Since skin metastases can be observed as the first sign of clinically-silent malignancy, a detailed medical history should be taken and a thorough physical examination must be conducted to find out the underlying malignancy.

CONCLUSION:

The study revealed a wide spectrum of neoplastic lesions of skin. Majority of cases were benign tumors verrucae being most common and among the malignant tumors, squamous cell carcinoma was the predominant.

Benign tumors were common in younger age group whereas skin cancers exhibit an ascending trend in age. Maximum numbers of tumors were found predominantly in male. Morphologically, skin tumors manifest as papules, nodules, plaque or ulcer and is very difficult to define it as a benign or malignant clinically, hence histopathological examination remains the gold standard method to overcome the diagnostic dilemma.

ACKNOWLEDGEMENT-

Authors acknowledge the support received from the institution in promoting research and scientific papers

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