

Clinicopathological spectrum of Keratinocytic tumors of skin in a tertiary care centre

Sujatha R¹, Tricha Kulhalli^{2,*}, Manjunatha Y.A³

¹Associate Professor, ²Post Graduate, ³Professor and HOD, Dept. of Pathology, Dr. B.R. Ambedkar Medical College, Bangalore, Karnataka, India

***Corresponding Author: Tricha Kulhalli**

Email: drsujatha02@gmail.com

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Abstract

Introduction: Skin is the largest organ in the body and tumors can arise from any part of the skin. Skin cancer represents the most common form of malignant disease in the world.¹ In India, malignant skin tumors constitute about 1-2% of all cancers. National Cancer Registry Programme, Indian council of medical research- Consolidated report of the Population based cancer registries reported cumulative incidence of skin cancer varying from 0.5 to 2 per 100000 population.² Non melanoma skin cancers are associated with substantial morbidity, including loss of function and disfigurement and their treatment is costly. Early diagnosis can reduce morbidity and cost. There is a definite role of pathologists in the management of tumors.

Aim: To study the different Clinicopathological features of Keratinocytic skin tumors and analyze the tumors according to age, sex, site and incidence.

Materials and Methods: This is a prospective study from June 2015 to August 2017 for a period of 26 months. Excision biopsy specimens and skin punch biopsies sent for histopathological evaluation to the Department of Pathology, Dr. B. R. Ambedkar Medical College, were studied.

Results: Out of the 140 skin tumors studied, 130 were benign and 10 were malignant. Incidence of benign tumors was most common in the younger age groups. Premalignant tumors were more common in the 4th decade. These tumors showed an overall male preponderance. However, malignant tumors were found to be more common in females and in the older age groups. The sun exposed areas were the most common site of both benign and malignant Keratinocytic tumors. Squamous cell carcinoma was found to be more common than Basal cell carcinoma.

Conclusion: We studied, 140 cases of Keratinocytic tumors of skin. 87.2% were benign, 5.7% were Pre-Malignant and 7.1% were malignant. Most common benign tumor in our institution was verruca vulgaris and the most common malignant tumor in our institution was squamous cell carcinoma. Although malignant tumors were seen in older age group, benign tumors showed prevalence in younger patients. Our findings mostly correlate with the published Indian literature.

Keywords: Non melanocytic skin tumors, Keratinocytic tumors, Keratoacanthoma, Bowen's disease, Pre-malignant skin tumors.

Introduction

Skin is the largest organ in the body and tumors can arise from any part of the skin. Skin cancer represents the most common form of malignant disease in the world.¹ The ability to properly diagnose and treat tumors is a vital skill for all clinicians.

In India, Malignant skin tumors constitute about 1-2% of all cancers.² Despite growing public awareness of harmful effects of sun exposure, incidence continues to rise. Non melanoma skin cancers are associated with substantial morbidity, including loss of function and disfigurement and their treatment is costly.

Early diagnosis can reduce morbidity and cost. There is a definite role of pathologists in the management of tumors. But due to diversity of these tumors, there can be confusion regarding nomenclature of these tumors.³ As a result, the study of skin tumor is perhaps more interesting and challenging than any other tumors.

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.⁴

Hence, the aim was to study the different histopathological features of Keratinocytic skin tumors and to study the variations of skin tumors and analyze the tumors according to age, sex, site and incidence.

Materials and Methods

This study was undertaken in the department of Pathology at the Histopathology division of Dr. B.R. Ambedkar Medical College and Hospital, Bangalore, from June 2015 to August 2017. All specimens were fixed in 10% formalin, processed and embedded in paraffin. Three to five microns thick sections were taken and then stained with Haematoxylin and Eosin stains and evaluated under light microscopy. All Keratinocytic tumors of the Skin classified as per the WHO classification were included in the study. Hematolymphoid tumors, soft tissue tumors, neural tumors, metastatic tumors of skin, inherited tumor syndromes, adnexal and melanocytic tumors were excluded from the study. Relevant clinical data was retrieved and gross findings were noted. A total of 140 Keratinocytic tumors were diagnosed during a period of 26 months.

Results

140 Keratinocytic tumors of the skin were analyzed. These tumors were found to have a slight Male preponderance [Table 1]. Of all the tumors studied 122 were benign, 8 were Premalignant and 10 were malignant cases [Table 2]. In our study, Keratinocytic tumors were found to be common in all age groups. Incidence of Benign tumors was more common in the younger age groups, Pre-malignant was more common in the 4th decade whereas the malignant tumors were more common in the older age groups. Among the 122 benign Keratinocytic tumors, 107 were verruca vulgaris and the peak age incidence was found in the 2nd to 3rd decade [Table 3] and male to female ratio was 1.22: 1 [Table 4]. Squamous cell carcinomas were more common than the Basal cell carcinomas and were also found to be more common in the females [Table 5]. Majority of the benign tumors were that of Verruca vulgaris for which extremities was the most common site [Table 6]. Sun exposed areas like the head and neck, thorax, back and abdomen and extremities was the most common site for both Premalignant and Malignant lesions.

Discussion

Keratinocytic tumors comprise a large spectrum of lesions ranging from benign proliferations to malignant squamous cell carcinomas which show aggressive growth and have a metastatic potential. Keratinocytic tumors are very frequent. Despite their low mortality rate, they pose a significant public health problem, the

main etiologic factor is UV radiation which causes, DNA alterations, which during DNA replication may lead to CC: TT mutations in the TP53 tumor suppressor gene.¹

Three most frequent primary skin cancers are Basal Cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC) and malignant melanoma. Together SCC and BCC are referred to as Non-Melanoma Skin Cancers (NMSC).

The current study was done for a period of 26 months and shows the histopathological findings of 140 Keratinocytic tumors diagnosed in the Pathology Department of Dr. B. R. Ambedkar Medical College, Bangalore.

Keratinocytic tumors were found to have a slight Male preponderance. 74 (52.8%) were males and 66 (47.2%) were females. [Table 1]. 122 were benign, 8 were Premalignant and 10 were malignant cases [Table 2]. As per National Cancer Registry Programme, Indian council of medical research. Consolidated report of the Population based cancer registries incidence of skin malignancies is 0.5-2% and our study showed incidence of 7.1% (10 out of 140) this variation is probably due to the duration of our study, the representative population in the different studies available and the limited sample size. Keratinocytic tumors were found to be prevalent in all age groups. [Table 3]. Study by Nandyal et al⁵ also showed similar age range benign in the 3rd to 5th decade and malignant in the 5th to 7th decade with a male preponderance of 71.91%.

Table 1: Age & gender specific distribution in keratinocytic tumors

Age(years)	Males	Females	Total
<10	5	3	8
11-20	13	15	28
21-30	12	13	25
31-40	13	9	22
41-50	12	10	22
51-60	9	7	16
61-70	3	3	6
>70	7	6	13
Total	74 (52.8%)	66 (47.1%)	140

Table 2: Distribution of the different types of tumors

	Total
Benign	
Verruca vulgaris	107
Squamous papilloma	7
Seborrhoeic keratosis	8
Premalignant	
Bowen's Disease	2
Actinic Keratosis	4
Keratoacanthoma	2
Malignant	
Basal cell Carcinoma	3
Squamous cell carcinoma	7
Total	140

Table 3: Age wise distribution of different tumors of skin

Histopathological tumor types	Age group (years)								Total
	<10	11-20	21-30	31-40	41-50	51-60	61-70	>70	
Benign									
Verruca vulgaris	8	27	21	17	13	11	3	7	107
Squamous papilloma	-	-	3	2	-	1	1	-	7
Seborrhoeic keratosis	-	1	1	-	1	-	2	3	8
Premalignant									
Bowen's Disease	-	-	-	-	1	1	-	-	2
Actinic Keratosis	-	-	-	-	4	-	-	-	4
Keratoacanthoma	-	-	-	1	1	-	-	-	2
Malignant									
Basal cell Carcinoma	-	-	-	-	-	1	-	2	3
Squamous cell carcinoma				2	2	2	-	1	7
Total	8	28	25	22	22	16	6	13	140

In the present study the most common benign Keratinocytic tumor was Verruca Vulgaris (81.5%) which correlates with the studies conducted by Muhammad Usman Shams et al (78%)⁶ and Bari V et al (72%).⁷ Here, the skin exhibits hyperkeratosis, koilocytic change of keratinocytes along with prominent keratohyaline granules.

The most common site of involvement of verruca was the extremities (43.9%) [Table 6] which correlates with the study done by Young R et al⁸ who also showed extremities to be the most common site (61.9%) comparing verruca vulgaris with other keratinocytic lesions, no comparative reference could be found. In our study, verrucas were the commonest nonmalignant keratinocytic lesion comprising and this may be due to the fact that viral warts are quite frequent in children and adolescents.³

Squamous papilloma [Fig. 1] showed increased incidence in 2nd and 3rd decade with female preponderance. [Table 3 & 4] The tissue shows a polypoidal structure exhibiting acanthosis,

hypergranulosis, hyperkeratosis, papillomatosis, along with dense fibrovascular core.



Fig. 1: Microphotograph of Squamous papilloma showing a papillary lesion with arborizing fibrovascular cores lined by keratinizing mature squamous epithelium (H & E at 40x)

Table 4: Sex wise distribution of benign tumors of skin

Histological tumor type	Incidence	Male	Female
Bowen's Disease	2 (1.5%)	0	2
Actinic Keratosis	4 (3.07%)	3	1
Verruca vulgaris	107(81.5%)	59	48
Seborrhoeic keratosis	8 (6.15%)	5	3
Keratoacanthoma	2 (1.5%)	1	1
Squamous papilloma	7 (5.3%)	2	4
Total	130	70	60

Seborrhoeic keratosis was diagnosed in 8 (6.15%) cases in our study and was the second most common benign tumor with slight female preponderance [Table 3 & 4]. The skin tissue exhibits small cuboidal keratinocytes without cytologic atypia. Usually has "horn pseudocysts" these are round intralesional cysts

of loose keratin and the lesion extends to a uniform depth and one could draw a horizontal line parallel to the epidermal surface underlying the lesion.

Rajesh G et al.⁹ observed a male to female ratio of 1:1.04 and the most common age group affected was 60 years. The most common variant of Seborrhoeic

keratosis is the acanthotic type¹. In our study too, acanthotic type [Fig. 2] was the most commonly observed variant.

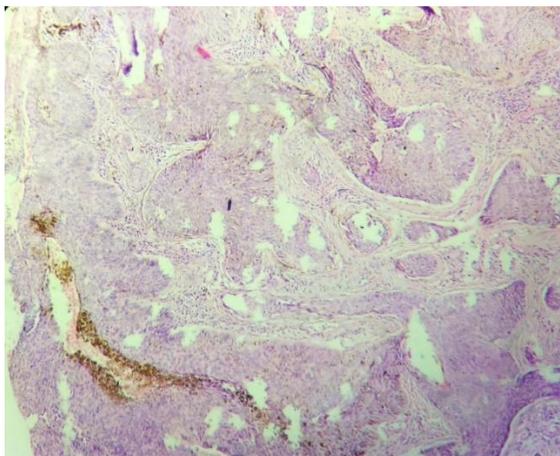


Fig. 2: Microphotograph of seborrheic keratosis-acanthotic type showing thick layer of basal cells mixed with pseudohorn cysts (H & E at 10x)

The occurrence of NMSCs is closely linked to ultraviolet irradiation, as they are diagnosed on chronically sun-exposed skin, occur among older individuals, and in lighter skin.¹⁰ Actinic keratosis are

believed to be precursor lesions to invasive squamous cell carcinoma. Few also believe it to be a low-grade SCC in situ.¹¹ They are induced by ultraviolet radiation and can develop into squamous cell carcinoma, and they are the most common pre-malignant lesions in humans the other being Bowen's disease.¹² In one of the patients, coexistence of Bowenoid actinic keratosis and minimally invasive Squamous cell carcinoma was reported by us [Fig. 3]. This finding directly implies the premalignant nature of this condition.

Skin in actinic keratosis shows, Basal cell and squamous layer atypia and disorderly maturation, with hyperkeratosis and parakeratosis with absence of granular layer and dermis showing elastosis and dense chronic inflammatory cell infiltrate.

In our study, 4 cases of actinic keratosis were reported, all of which were in the fourth decade and were more common in males (75%) with sun exposed areas as the most commonly involved site [Table 6]. These findings correlate with the study done by Kennedy C. et al who concluded the same.¹³

We also reported 2 cases of Bowen's disease both in females between the 4th to 6th decades, one in the vulval area (also called currently as vulval intraepithelial neoplasia) [Fig. 4] and the other in the breast region [Fig. 5].

Table 5: Sex wise distribution of malignant tumors of skin

Histopathological tumor types	Incidence	Male	Female
Basal cell carcinoma	3 (30%)	2	1
Squamous cell carcinoma	5 + 2 (70%)	2	5
Total	10	4	6

Table 6: Site wise distribution of the Keratinocytic tumors

Histopathological tumor types	Site				Total
	Head and neck	Thorax, Back and Abdomen	Genital area	Extremities	
Benign					
Verruca vulgaris	18	26	16	47	107
Squamous papilloma	2	2	-	3	7
Seborrhoeic keratosis	1	5	-	2	8
Pre-Malignant					
Bowen's Disease	-	1	1	-	2
Actinic Keratosis	1	1	-	2	4
Keratoacanthoma	-	2	-	-	2
Malignant					
Basal cell Carcinoma	2	1	-	-	3
Squamous cell carcinoma	1	1	2	3	7
Total	25	39	19	57	140

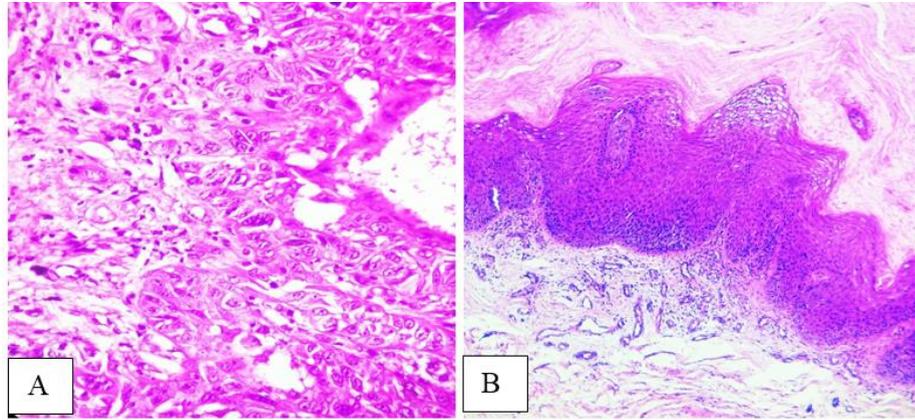


Fig. 3: Microphotograph showing; A: SCC with minimal invasion (H & E at 40x); B: The same patient showing Bowenoid actinic keratosis in another lesion. (H & E at 10x)

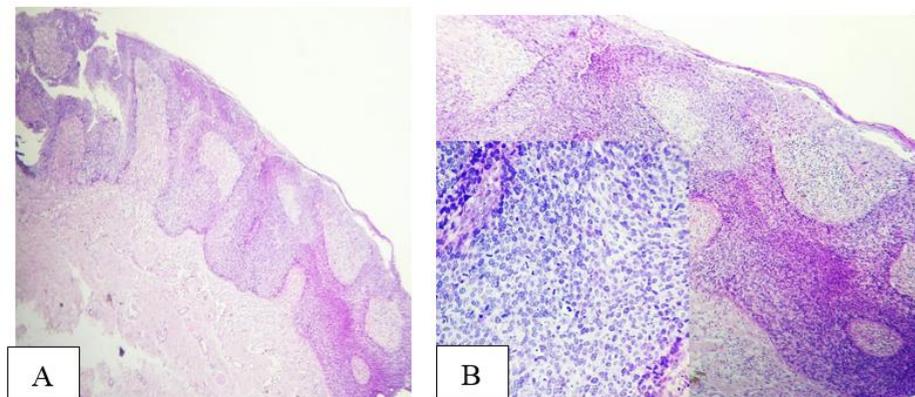


Fig. 4: Microphotograph of Vulval Intraepithelial neoplasia III showing; A: Hyperkeratosis and parakeratosis, Acanthosis with club shaped rete ridges; B: Disorientation of the cells above the basal cell layer with variable extension to the surface, Intact basement membrane inset shows numerous mitotic figures.(H & E 40 X)

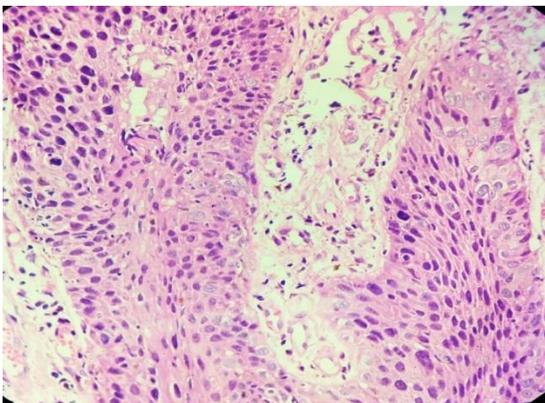


Fig. 5: Microphotograph of Bowen's disease showing atypical squamous cells proliferating through the whole thickness of the epidermis. The entire lesion is confined to the epidermis and does not invade into the dermis. The cells in Bowen's disease are highly atypical. (H & E, 10X)

We reported two cases of Keratoacanthoma: both in the middle aged group and both were on the back with equal gender distribution [Fig. 5]. One of which also showed features of micro invasion. The tissue showed, a central crater filled with keratin without a granular layer it also exhibited irregular infiltrating squamous nests and islands, accompanied by marked inflammatory infiltrate.

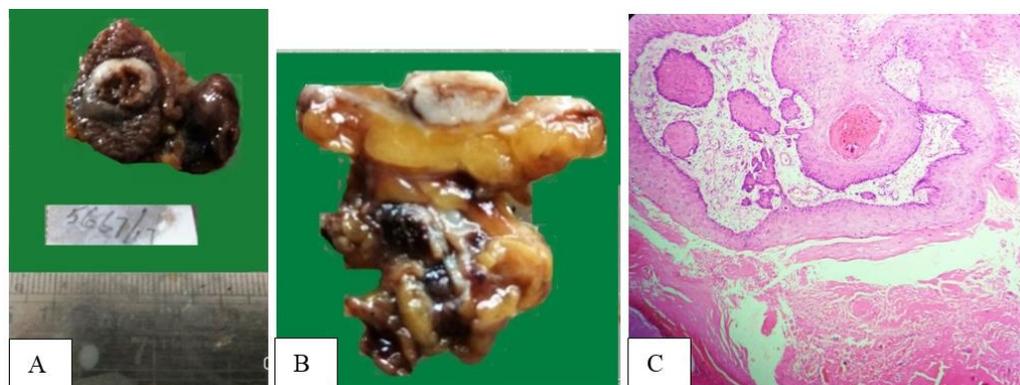


Fig. 6: A: Gross image of Keratoacanthoma; B: Cut surface of the same specimen showing a well formed crater; C Microphotograph showing central crater filled with keratin but no granular layer, irregular infiltrating squamous nests and islands, accompanied by marked inflammatory infiltrate. (H & E, 10X)

Basal Cell Carcinoma (BCC) shows a marked regional variation in incidence. Decreased incidence has been reported in northern Europe as opposed to extremely high incidence in Australia. BCC is very rare with dark skin colored individuals and has a slight male

preponderance and found majorly on the head and neck regions.^{1,3} Although BCC is the commonest form of skin cancer worldwide, various studies from India have reported SCC as the most prevalent skin malignancy.^{2,7}

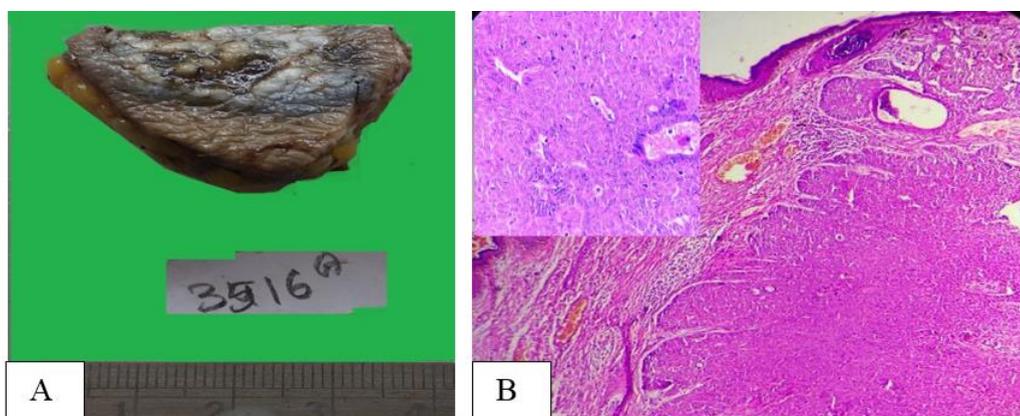


Fig. 7: A: Gross image of nodular BCC showing superficial ulceration with raised margins; B: Microphotograph of Basal Cell carcinoma showing nodular arrangement of atypical basaloid cells with peripheral palisading. Inset higher magnification of the same. (H & E, 40X)

The discrepancies in the presentations of skin cancers can be related to differences in exposure to sun either occupational or due to geographical latitudes or the various skin types. Unawareness and poor surveillance could also play a major role.^{1,9}

The most common variant of BCC in our study was the nodular type [Fig. 7], which shows large tumor nodules in the dermis that are generally circumscribed.

Similar to various studies from India, the current study shows the most common histologic type of skin cancers is SCC (70%) which is similar to the observations made by Chakravarthy RC et al,¹⁴ Deo SV et al,¹⁵ Budharaja SN et al¹⁶ and Bari V et al.⁷

We also recorded 2 cases of the verrucous variant of SCC, both in females, one of which was around the waist and another one the leg. Verrucous carcinoma is a less common variant of invasive squamous-cell

carcinoma. These were single, cauliflower-shaped tumors, like large warts. Microscopically it showed, epidermis with hyperkeratosis, papillomatosis, hypergranulosis, acanthosis, rete ridges were bulbous with "bulldozing" pattern and invaded deep dermis in a pushing manner.

The maximum number of malignant tumors were found in 4th to 7th decade which was similar to study by Bari V et al who also showed maximum malignant tumors in the 7th decade.⁷

Conclusion

We studied 140 cases of Keratinocytic tumors of skin. 87.2% were benign, 5.7% were Pre-Malignant and 7.1% were malignant. The most common benign tumor was verruca vulgaris and the most common malignant tumor was squamous cell carcinoma.

Although malignant tumors were seen in older age group, benign tumors showed prevalence in younger patients. Our finding mostly correlate with the published Indian literature.

Concluding our study in which age, sex, distribution and the morphologies of various Keratinocytic tumors were studied. Routine surveillance of skin is recommended to identify premalignant and precursor lesions of skin cancer to avoid them from turning into aggressive malignancies. This is especially so for certain syndromic disorders that have a tendency towards skin cancer for example xeroderma pigmentosum which has predilection towards squamous cell carcinoma.

Creating awareness about the effects of prolonged exposure to sun and the use of protective along with UV creams will prove to have important health implications since the incidence of skin tumors continues to rise.

Hence, early diagnosis can reduce morbidity, cost and overall prognostic outlook. Pathologists hence play a major role in the management of Keratinocytic tumors.

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