

SPECTRUM OF MALIGNANT SKIN LESION IN PATIENTS ATTENDING NEPALGUNJ MEDICAL COLLEGE AND TEACHING HOSPITAL

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ABSTRACT

Introduction

Clinical diagnosis of dermatological manifestation of neoplastic skin lesion can pose a diagnostic difficulty at times. Histopathological diagnosis is mandatory for accurate characterization of disease entity for proper and timely management of cases.

Objective

The aim of this study was to analyze malignant tumor of skin with respect to age, sex, clinical features and histopathological features and to evaluate the accuracy of clinical diagnosis with histopathological correlation.

Methodology

This is hospital based cross-sectional study conducted at Nepalgunj Medical College and Teaching Hospital, Kohalpur from February 2010 to January 2011. A total of 70 histopathological specimens of skin biopsies were studied and correlated with the clinical diagnosis. The data was entered into Microsoft office excel and analyzed using statistical package for social sciences (SPSS 17.0).

Results

Malignant tumor of skin constituted 21.4% of total cases. In malignant tumor, most common sites were head and neck regions followed by lower limb with keratinocytic tumors being in the majority. Most of the specimens (65.7%) were obtained as excisional biopsies. Seven cases diagnosed as benign lesions clinically, turned out to be malignant on histopathological examination. Out of 13 cases in which clinical diagnosis was of malignancy, only 8 turned out to be malignant, thus for malignant lesions, the clinical diagnosis had a sensitivity of 53.3%, specificity of 90.9% and a positive predictive value of 61.5%.

Conclusions

Squamous cell carcinoma was the most common malignant tumor in this study and histopathological correlation significantly modifies the overall management in dermatological disorders where clinical diagnoses are equivocal.

KEY WORDS

Histopathology, malignant lesion, skin

INTRODUCTION

The skin is affected by both internal and external conditions and other factors as it is exposed to a range of environmental hazards making it vulnerable to all manner of threats. Various lesions affecting the skin range from nonspecific inflammatory dermatoses, infective disease and neoplasms. This study was conducted in mid-western region of Nepal, which is a very hot and humid tropical region. Skin diseases are the common problems in such region. Among skin diseases, skin cancer if diagnosed in later stages, causes significant morbidity and mortality. Clinical diagnosis of dermatological manifestation of neoplastic skin lesion can pose diagnostic difficulty at times. The clinician in many cases suggest differential diagnosis which forms the basis for the pathologist to evaluate the particular skin biopsy.¹ Histopathological diagnosis is mandatory for accurate characterization of disease entity for proper and timely management of cases. The aim of this study was to analyze malignant tumor of skin with respect to age, sex, clinical features and histopathological features and to evaluate the accuracy of clinical diagnosis with histopathological correlation.

METHODOLOGY

This is hospital based cross-sectional study conducted at Nepalgunj Medical College Teaching Hospital, Kohalpur from February 2010 to January 2011. A total of 70 histopathological specimens of skin biopsies were studied and correlated with the clinical diagnosis. The study was conducted after obtaining approval from Nepalgunj Medical College and Teaching Hospital. The personal details of the patient, clinical findings, laboratory reference number, gross and microscopic descriptions and final histopathological diagnosis were noted. Hematoxyline and Eosin stain (H&E) was done routinely for histopathological examination. The skin tumors were classified according to World Health Organization classification of skin – 2006.²

Inclusion criteria: Skin biopsies sent to the pathology department.

Exclusion criteria: Inadequate skin biopsies without clinical details.

The data was entered into Microsoft office excel and analyzed using statistical package for social sciences (SPSS 17.0).

RESULT

Out of 70 cases only 15 cases were malignant skin tumors comprising 6 cases (40%) of SCC, followed by 4 cases of Malignant Melanoma (26.6%) and three cases of BCC (20%). One case each of Dermatofibrosarcoma protuberance (6.6%) and Mucinous Eccrine Carcinoma (6.6%). Benign tumor of the skin were more common than malignant tumor in this study period. The histological categorization according to the frequency of the cases are given in table 1 and 2.

Table.1: Distribution of benign tumor (n = 22)

Benign Tumors	Number of Cases
Palimatixoma	2
Eccrine cylindroma	1
Keratinous cyst of pilar type	2
Keratinous cyst of epidermal type	2
Dermoid cyst	2
Dermatofibroma	3
Angiomyofibroblastoma	1
Plexiform neurofibroma	1
Capillary hemangioma	3
Pyogenic granuloma	4
Intradermal nevus	1

Table 2: Distribution of malignant tumor (n = 15)

Malignant Tumors	Number of Cases
Keratinocytic malignant lesions Squamous cell carcinoma (SCC) = 6 Basal cell carcinoma (BCC) = 3	9
Melanoma (MM)	4
Dermatofibrosarcoma protuberans (DFSP)	1
Mucinous eccrine carcinoma	1

In this study the malignant lesion were common in head/neck region and then in lower limbs.

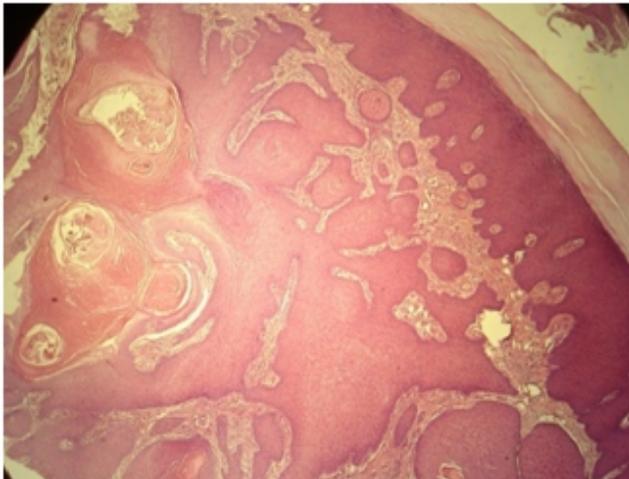
All the malignant lesions presented clinically as localized lesions and maximum of it were ulcerated followed by nodular lesion. Malignant lesions were more common in the 51 to 60 years age group followed by age group of 21- 30 years as shown in table 3. Maximum number of specimens (65.7%) were obtained as excisional biopsies.

In our study, among the six cases of squamous cell carcinoma, five were well differentiated microscopically and one was of verrucous type (an extremely well-differentiated rare variant of SCC) in a 65 year old female which was present for 6 months on the right foot. The case had clinical diagnosis of pyogenic granuloma which turn out to be malignant in histopathological examination. The microphotograph of the lesion is shown in figure1.

Table 3 : Histopathological groups of disease according to age distribution

Age group (years)	Inflammatory dermatoses of known etiology	Other dermatoses	Malignant tumor	Benign tumor				Total
				Adnexal	Dermal	Vascular	Nevus	
1-10	2	1	-	1	1	-	-	5
11-20	-	1	1	4	1	2	1	10
21-30	7	7	3	1	1	3	-	22
31-40	4	2	1	-	-	-	-	7
41-50	1	3	2	1	1	-	-	8
51-60	1	-	4	-	-	1	-	6
61-70	2	1	2	1	-	-	-	6
71-80	-	1	1	1	1	1	-	5
81-90	-	-	1	-	-	-	-	1
TOTAL	17	16	15	9	5	7	1	70

Figure 1: Verrucous carcinoma: endophytic, pushing growth pattern of well differentiated squamous cells. Minimal atypia and no foci of the usual squamous cell carcinoma (H & E × 10).

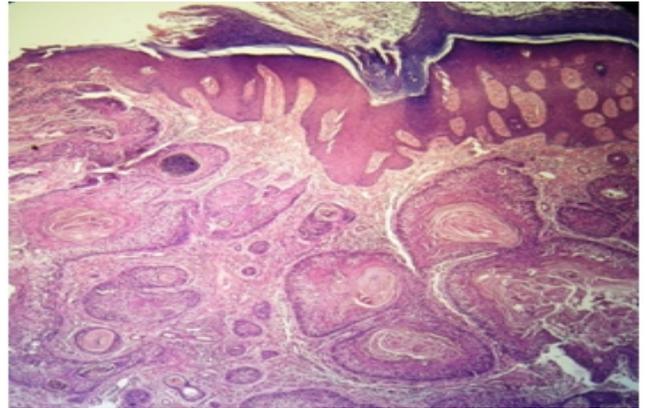


Photograph showing clinical presentation of one of the case of SCC with its photomicrograph is shown in Figure 2a, 2b.

Figure 2a: Squamous cell carcinoma, developing in the scar tissue of the right knee in a 26 year old male.



Figure 2b: Photomicrograph of the same, showing invasive well differentiated SCC, hyperkeratosis, acanthosis, and tumor nests with keratin pearls (H&E× 10).



Malignant melanoma is the second most common malignant tumor of skin in this study and the histopathological findings revealed clark level IV in all the cases as shown in table 4 and photomicrograph is shown in Figure 3a, 3b.

Table 4: Histopathological findings in the cases of Malignant Melanoma

Case	Epidermis	Malignant cell	Dermis	Clark level
1 st Case	Normal in thickness	Largely spindle shaped cell with melanin pigment	Desmoplastic reaction noted	IV
2 nd Case	Atrophic	Irregular clusters, nestoid pattern melanin pigment in cytoplasm Some spindle shaped cells	Lymphocytes and plasma cell present	IV
3 rd Case	Atrophic with marked ulceration	Lots of melanin pigment in epithelial cell and in histiocytes Spindle cell pattern	Area of myxoid change Intense lymphoplasmacytic infiltrate	IV
4 th Case	Hyperkeratosis, parakeratosis Focal acanthosis With surface ulceration	Round to oval Basophilic to clear cytoplasm Some with blackish brown pigment	Focal necrosis Foci of marked desmoplasia	IV

Figure 3a: Melanoma, hyperkeratosis, epidermal atrophy and atypical spindle shaped cells with melanin pigment occupying whole of the dermis, (H&E×10).

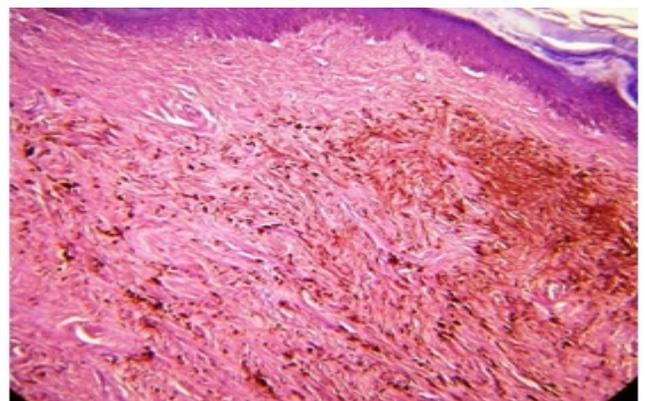
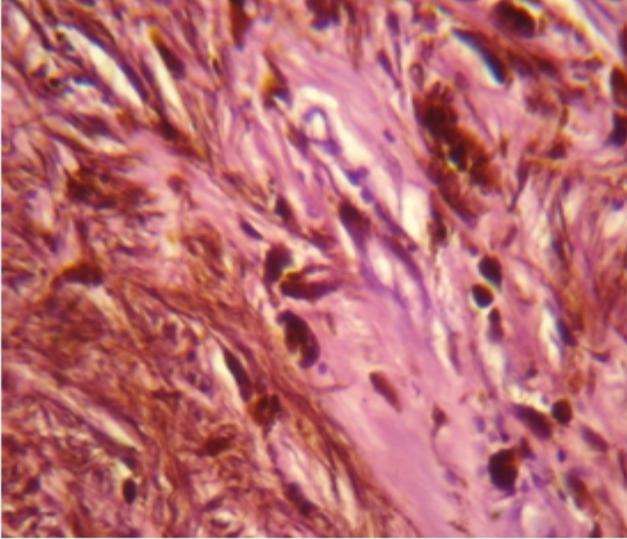


Figure 3b: Bizarre, spindle shaped melanin containing malignant cells, (H & E ×40)



Histomorphological findings of BCC and Adenoid basal cell carcinoma is shown in Figure 4 and Figure 5 respectively.

Figure 4: Basal cell carcinoma, nests of basaloid cells in the dermis with hyperchromatic nuclei and peripheral palisading. Artifacts clefting around tumor nests, (H&E×10)

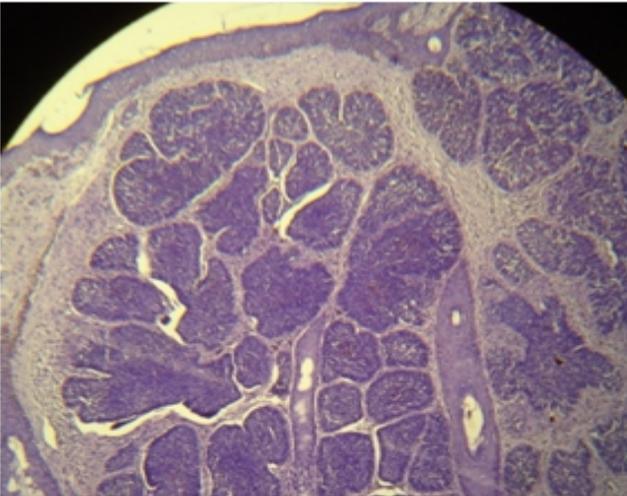
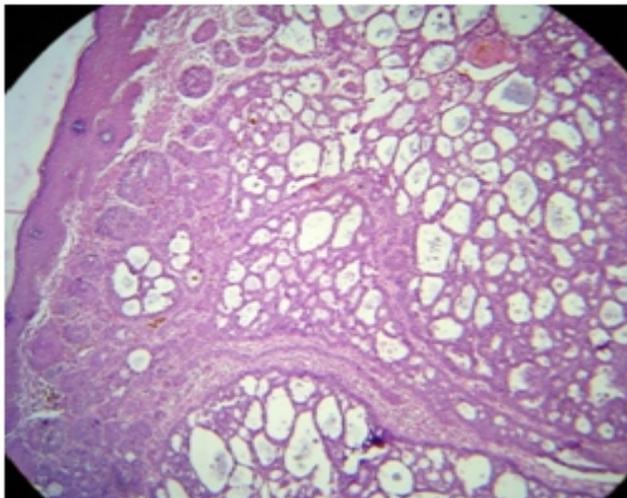


Figure 5: Adenoid Basal cell carcinoma basaloid cells in a reticulate pattern with stromal mucin (H&E×10)



Photomicrograph of mucinous eccrine carcinoma is shown in Figure 6a, 6b.

Figure 6a: Mucinous Eccrine carcinoma, pale mucin surrounding nests of moderately anaplastic epithelial cells, (H&E×40)

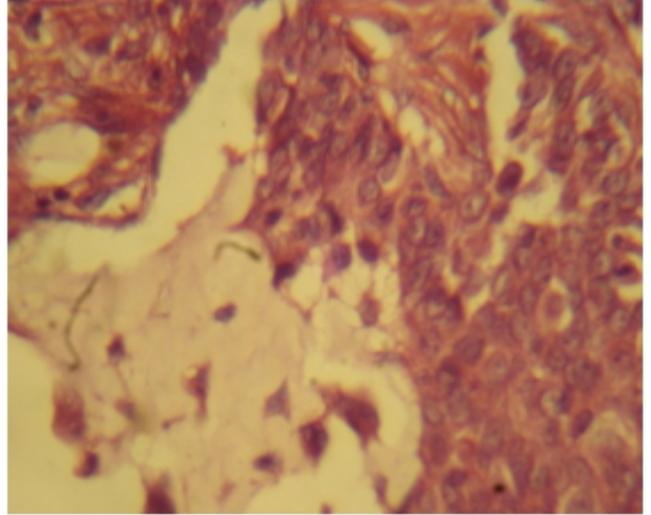
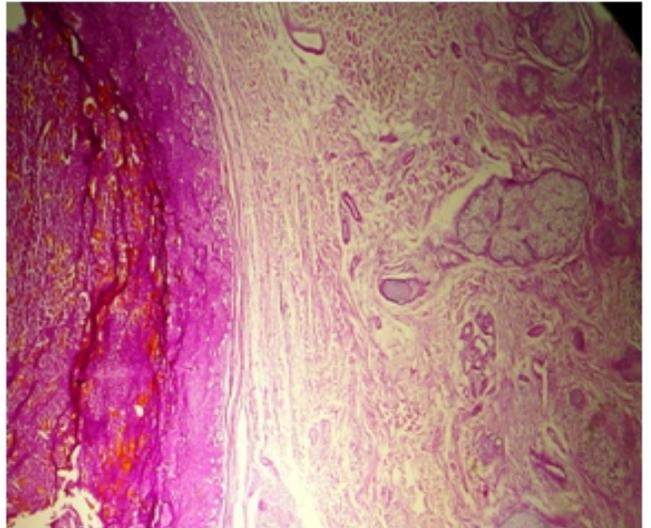


Figure 6b: PAS stain of the same case which shows lack of extracellular mucin (arrow), (PAS ×10).



Gross picture and photomicrograph of dermatofibrosarcoma protuberans is shown in Figure 7 a, 7b.

Figure 7a: Dermatofibrosarcoma protuberans Gross: ulceronodular growth (arrow) involving the skin and the subcutis

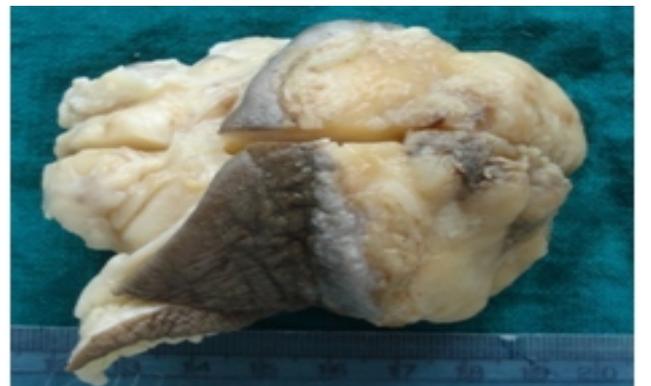
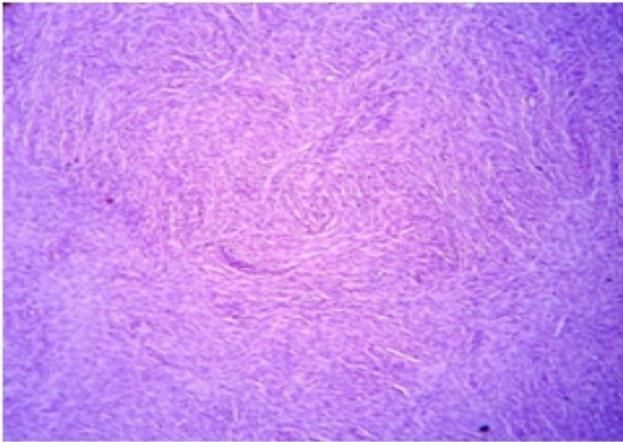


Figure 7b: Photomicrograph Dermatofibrosarcoma protuberans, densely packed, monomorphous, plump spindle cells arranged in a storiform pattern, (H&E×40)



Seven cases diagnosed as benign lesions clinically turned out to be malignant on histopathological examination. Out of 13 cases in which clinical diagnosis was of malignancy, only 8 turned out to be malignant. Thus for malignant lesions, the clinical diagnosis had a sensitivity of 53.3%, specificity of 90.9% and a positive predictive value of 61.5%. Cross tabulation of these cases is shown in table 5.

Table 5: Cross tabulation of Histopathological and Clinical diagnoses

	Histopathological diagnosis		
	Types of lesion	Malignant	Benign
Clinical Diagnosis	Malignant	8	5
	Benign	7	50
	TOTAL	15	55

DISCUSSION

Skin is the largest organ of the human body making 15% of the total body weight and dermatological manifestations are of varied nature. Very few studies have described and correlated the clinical diagnosis and histopathological results in skin diseases in Nepal. The current study describes the pattern of skin diseases referred for histopathological examination at Nepalgunj Medical College Teaching Hospital, Kohalpur, Nepalgunj. Out of the 1440 different kinds of surgical specimens submitted during the study period of one year from February 2010 to January 2011, only 70 cases were of skin biopsies contributing 4.86% of total surgical pathology load of the histopathology department. In a similar study performed in a pediatric population, skin biopsies constituted 7.29% of the total surgical load in a general tertiary care hospital.³

In 15 malignant lesions, from our study (5 were males and 10 females) and SCC was more in number than BCC. Several studies reveal a preponderance of SCC in Africa whereas in North America and Europe, 80% of invasive skin cancers are BCC while 20% are SCC. This reversal of SCC/BCC incidence

in Africa could well be due to chronic inflammatory diseases, malnutrition and possibly parasitic infestations.⁴

In our study, head and neck regions were the most common site of malignant tumor and similar findings were noted in other study and also predicted the sun exposure could be the major etiological factor.⁴⁻⁶ One of our case of SCC was in a scar tissue in the right knee, patient had history of road traffic accident 12 years back (Figure 2a and 2b). One case of SCC was present on the left forearm as ulcerated lesion in patient of albinism. These findings were similar to a study reported from Nigeria.⁷

Incidence of SCC were 20% more common than BCC in black patient according to the information gathered from Tumor registry of Charity Hospital of Louisiana in New Orleans. The most common sites of involvement were face, lower extremities, non-sun exposed areas, and the most common predisposing conditions were scarring processes.⁸ The incidence of skin tumors varies geographically and is relatively well documented for melanoma and to a lesser extent for SCC and BCC in different international samples of the general population.⁹⁻¹¹

All the four cases of melanoma were present in female in our series and similar sex predilection was noted in other studies.¹² Three cases presented as nodular swelling and was black in color while other one case was ulcerated type. Lesion was present in foot in two cases and one case each in neck and eyelid margin. Primary melanomas of the eyelid have a nodular pattern and account for less than 1% of all eyelid malignancies.¹³

Salient morphological features of these four cases are tabulated (Table 4) and microscopic morphology shown in Figure 3a & 3b.

In all the three cases of basal cell carcinoma, lesions were ulcerated, and present on the nose, lateral canthus and post auricular area and in all of them excisional biopsy was done. Two cases were solid type of basal cell carcinoma, with nodular masses of basaloid cells extending into the dermis in relation to a delicate specialized tumor stroma (Figure 4). One of the case was adenoid basal cell carcinoma which is a rare variant of BCC. Microscopically, it showed keratinized stratified squamous epithelium with follicular plugging and dermis showing basaloid tumor cells in lobular and glandular patterns with an edematous loose fibromucinous stroma. Cribriform areas, mucin filled glandular structures and pigment laden macrophages were also seen in the stroma (Figure 5).

Ten cases of skin tumor were arising from adnexal structures comprising 14.2% in which one case was of malignant mucinous eccrine carcinoma and rest were benign tumor. Similar finding was noted by Paudyal et al, in which benign appendageal tumor were more common than malignant appendageal tumor.¹⁴

In this study the eccrine carcinoma was present in 60 years old male patient, on right cheek and was clinically diagnosed as pyogenic granuloma. Microscopically, epidermal ulceration was continuous with a growth occupying the dermis and getting into the subcutis. This growth showed solid as well as

a reticulate pattern with mucus lakes in which atypical epithelial cells with moderately acidophilic, finely granular cytoplasm and nucleus with prominent nucleoli were trapped (Figure 6 a and b). A chronic inflammatory response with foreign body giant cells was also seen in the margins to extravasated mucinous material. However, eccrine carcinoma has been reported most frequently in lower extremity (44%), trunk (24%) and head (18%) and only few cases have been reported in the upper extremity (8%) and hand (3%).¹⁵ A case with dermatofibrosarcoma protuberans in our study was present in 11 year old girl on right ankle and was nodular ulcerated type. These are fibrous histiocytic tumors of intermediate (border line) malignant potential. The tumor is typically centered in the dermis, lacks circumscription, and show high cellularity and storiform pattern of growth (Figure 7a,b). Studies have shown that majority of cases in young adults and presentation during childhood being rare.¹⁶

In our study, sensitivity of clinical diagnosis of malignancy was 53.3%, specificity 90.9% and a positive predictive value of 61.5%. Seven cases which were given the clinical diagnosis of benignity turned out to be malignant on histopathological examination. The cases clinically diagnosed as malignant were also proven benign by histopathological examination and the specific diagnosis and categorization of a particular malignancy could not be made clinically. One case of DFSP and melanoma were sent for histopathological examination with the clinical diagnosis of SCC. Histopathological examination thus remains the mainstay for correct diagnosis categorization and for proper management. Sensitivity of clinical diagnosis of malignancy varies widely in the literature with rates ranging from 73 to 91%. Sensitivity for diagnosis

of individual malignancies varies with rates of 95.4% for BCC, 68% for SCC, and 67.3% for MM. Clinicians had a tendency to misclassify benign lesions as malignant, but were less likely to do the reverse.¹⁷

CONCLUSION

This study concludes that histopathological examination of the skin lesion is extremely important for categorization of skin tumor. Squamous cell carcinoma is the most common malignant tumor followed by malignant melanoma.

RECOMMENDATION

This study was conducted in the Mid-Western region of Nepal. It is recommended to conduct such studies throughout the country to have an overall picture and understanding of malignant skin lesions in Nepalese population.

LIMITATION OF THE STUDY

This is a hospital-based study conducted during the course of one year, and hence, includes the data collected only during that period. The study is based on the cases that were registered in the Hospital, and does not include other probable cases that never reached the Hospital for treatment or diagnosis.

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CONFLICT OF INTEREST

There are no conflict of interest.

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