DOI: 10.7860/NJLM/2023/58359.2697

Original Article

Pathology Section

A Histopathological Study on Primary Cutaneous Malignancies of Surface Epidermis

MUNI BHAVANI ITHA[1], SATYANARAYANA VEERAGANDHAM[2], KRISHNA BHARATHI YARLAGADDA[3], RAMESWARY KORATA[4]

ABSTRACT

Introduction: Skin is a complex organ, it's intricacy allows for a wide range of malignancies. Skin types, geographical latitudes, occupational exposure, sun exposure, and skin protection behaviours may all contribute to skin cancer trends and rates. Some cancers are easily recognised clinically, whereas others require a combination of clinical and histopathological correlation.

Aim: To determine the spectrum and frequency of various primary cutaneous malignancies of the surface epidermis based on histomorphological characteristics, Guntur, Andhra Pradesh, India.

Materials and Methods: The present retrospective study was conducted in the Department of Pathology at Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India. The study covered a total of 30 cases of primary cutaneous malignancies of surface epidermis with histopathological confirmation. The study samples included from January 2019 to June 2021 over a 30-month period and the data was collected and analysed in the month of August 2021 and September 2021 from the histopathology records. Typing of these tumours was done by using Haematoxylin and Eosin (H&E) stained sections. All the cases were analysed and divided according to the patient's age, gender, and tumour location, as well as the tumour's histological characteristics. Descriptive statistics were used and data was tabulated in frequency and percentages.

Results: A total of 30 cases of primary cutaneous malignancies of surface epidermis, were studied, of which 21 (70%) cases were keratinocyte derived cancers and 6 (20%) cases were melanocyte derived cancers. The most frequent keratinocyte tumour was squamous cell carcinoma followed by Basal cell carcinomas. Present study documented three cases of melanocarcinomas, of which two were basomelanocytic tumours and one case was squamomelanocytic tumours. There was slight male preponderance with male to female was 3:2. Most cases distributed in the age group of 61-80 years, followed by 41-60 years. The most frequently involved anatomical site was the head and neck region followed by the trunk region.

Conclusion: Skin cancers, at times, may be difficult to diagnose clinically. Hence, histopathological examination is a must for definitive diagnosis. This study highlighted the critical role of histopathology in accurately classifying tumours into distinct morphological types which enables the clinician to make the correct diagnosis and formulate appropriate treatment plan.

Keywords: Basal cell carcinoma, Malignant melanoma, Squamous cell carcinoma, Skin

INTRODUCTION

The skin is a heterogeneous organ, which has a variety of elements with ectodermal and mesodermal origins that work together to protect the body. Instead of being considered a simple organ serving only as a protective covering for the body's more delicate and functionally sophisticated internal organs, the skin has been recognised as a surprisingly complex organ, largest in the body. In which, numerous essential processes are controlled by highly precise cellular and molecular interactions. It is composed of three layers, epidermis (the outermost layer), dermis (the middle layer), and hypodermis (the innermost layer). The epidermal layer is composed primarily of keratinocytes (greater than 90%) with a modest population of langerhans cells, melanocytes and merkle cells (neuroendocrine cells). Most of these individual components are capable of producing skin cancers [1-3].

Due to prolonged exposure to sunlight, climatic changes, as well as personal and societal factors, the incidence of skin cancer is rising globally [4,5]. Skin cancers as a whole include Cutaneous Melanoma (CM) and Non Melanoma Skin Cancer (NMSC), which is primarily represented by basal cell carcinoma, Squamous Cell Carcinoma (SCC) and Merkel Cell Carcinoma (MCC) [6,7].

The incidence and mortality rates of Malignant Melanoma (MM) and Non Melanoma Skin Cancers (NMSC) in different parts of the world vary greatly. The Global Cancer Statistics 2020 report states that NMSC accounts for more than one million new cases (1,198,073) excluding basal cell carcinoma and 64,731 fatalities worldwide, while melanoma of the skin accounts for 3,24,635 new cases and 57,043 deaths worldwide [8].

Skin cancer incidence has increased over the last several decades. A wide range of tumours is encountered in clinical practice and the majority of these conditions are diagnosed based on the findings of the clinical examination and the patient's medical history. Skin neoplasms, on the other hand, might be difficult to distinguish because of their similarity in gross appearance. In such cases, skin biopsy aids in the diagnosis of the patient's condition and directs the course of the treatment. Also, it is critical to accurately identify skin lesions to ensure that malignancies are not ignored and that they are treated as soon as possible to minimise morbidity and mortality.

Of all skin cancers, surface epidermal skin cancers are the most common to progress and become potentially fatal, if neglected may be locally and functionally destructive. The current study is primarily concerned with the study of the primary cutaneous malignancies of surface epidermis observed at tertiary care hospital in Guntur.

The aim of the present study was to determine the spectrum and frequency of the various primary cutaneous malignancies of the surface epidermis, which have been observed in and around study region based on histomorphological criteria. It also aspires to examine the distribution of these lesions in terms of age, gender and the primary anatomical site that has been affected.

MATERIALS AND METHODS

The present study was a retrospective study conducted in the Department of Pathology at Katuri Medical College and Hospital, Chinnakondrupadu, Guntur, Andhra Pradesh, India, and data was analysed between August 2021 and September 2021. The study period covered the 30 months from January 2019 to June 2021 and all primary cutaneous malignancies of the surface epidermis (Tumours of keratinocytes, melanocytes, merkel cells and langerhan's cells) were studied. The approval of the Institutional Ethics Committee was obtained (F.No. IEC/KMCH/2021/38). Of 120 skin biopsies investigated, primary cutaneous malignancies of the surface epidermis were 30 cases.

Inclusion criteria: Primary cutaneous malignancies of the surface epidermis (Tumours of keratinocytes, melanocytes, merkel cells, and langerhan's cells) and the cases that were self-reported to the hospital were included in the study.

Exclusion criteria: Benign tumours of the surface epidermis, tumours of epidermal appendages, dermis and hypodermis (skin appendageal tumours and soft tissue tumours) were excluded from the study.

Study Procedure

Relevant clinicopathological data such as age, sex, anatomical location and histopathological features were obtained from the histopathology request forms and histopathology records. The corresponding histopathology slides were retrieved, reviewed and the tumours were classified based on the type of surface epidermal cell origin. The primary anatomical sites of involvement were classified into the following groups and studied:

- Head and neck (scalp, face and neck);
- Upper extremity (shoulder, arm, forearm, wrist and hand);
- Lower extremity (buttock, thigh, leg and foot);
- Trunk;
- Others (abdomen, back chest wall and genital region).

STATISTICAL ANALYSIS

Descriptive statistics were used and the results were tabulated and expressed in frequencies and percentages by using Statistical Package for the Social Science (SPSS) software version 20.0.

RESULTS

During the study period, 120 skin biopsies were received, of which 30 (25%) cases were primary cutaneous malignancies of surface epidermis. The maximal number of cases were reported in the age group of 61-80 years (13 cases, 43.33%) followed by 41-60 years (10 cases. 33.33%). The distribution of primary cutaneous malignancies of surface epidermal cells concerning age was shown in [Table/Fig-1]. In the present study, majority of cases showed male preponderance accounting for 18 cases represents 60% of total cases and females were 12 cases accounting for 40% of total. The male to female ratio was 3:2. The head and neck region (12 cases, 40% of total) followed by the trunk region (06 cases, 20% of total) was the most often affected region by these lesions, shown in [Table/Fig-2]. [Table/Fig-3] depicts the distribution and frequency of malignant cutaneous tumours originating from surface epidermal cells. Skin cancers of keratinocyte origin (21 cases, 70%) were the most common presentation followed by cancers of melanocyte origin (06 cases, 20%) and three cases of combined tumours involving keratinocyte and melanocyte origin have been reported [Table/Fig-4] depicts the distribution of various histopathological types of cutaneous malignancy of the surface epidermis.

Age group (Years)	n (%)
21-40	6 (20)
41- 60	10 (33.33)
61-80	13 (43.33)
>80	1 (3.33)
Total	30 (100)

[Table/Fig-1]: Age distribution of primary cutaneous malignancies of surface epidermis.

Site of tumour presentation	n (%)
Head and neck	12 (40)
Upper extremity	5 (16.67)
Lower extremity	4 (13.33)
Trunk	6 (20)
Others	3 (10)
Total	30 (100)

[Table/Fig-2]: Site distribution of primary cutaneous malignancies of surface epidermis.

Cell of origin	n (%)
Keratinocyte	21 (70)
Melanocyte	6 (20)
Merkle cell	0
Langerhans cell	0
Others	3 (10)
Total	30 (100)

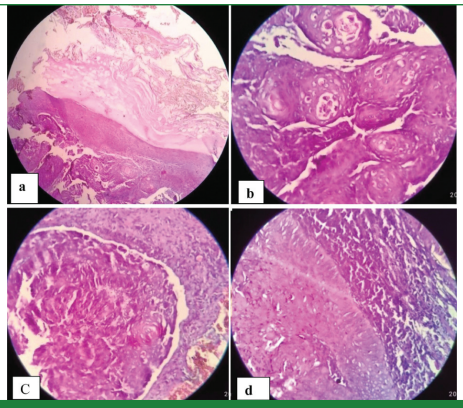
[Table/Fig-3]: Distribution and percentage frequency of primary cutaneous malignancies of surface epidermis.

Histopathological types	n (%)
Keratinocyte origin	21 (70)
Basal cell carcinoma and its variants	9 (30)
Cutaneous squamous cell carcinoma and its variants	12 (40)
Melanocyte origin	6 (20)
Cutaneous malignant melanoma and its variants	6 (20)
Merkle cell origin	0
Langerhans cell origin	0
Others*	3 (10)

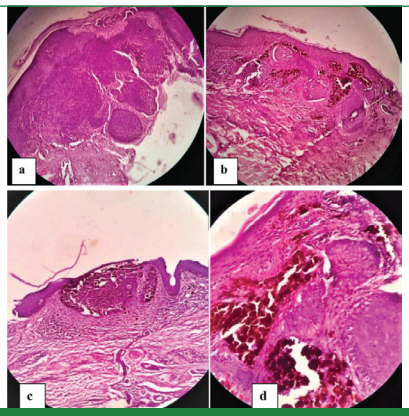
[Table/Fig-4]: Histopathological types of primary cutaneous malignancies of surface epidermis (N=30).
*Combined tumours involving keratinocytes and melanocytes), one case of squamomelanocytic tumour and two cases of basomelanocytic tumours

Of all keratinocyte tumours, squamous cell carcinoma and its variants were the most common (12 cases, 40% of all reported cases), the majority cases were conventional squamous cell carcinomas except each one case of an acantholytic and verrucous variant of squamous cell carcinoma. The second most common keratinocyte malignancies were Basal cell carcinomas (Nine cases, 30%), of which most cases were nodular variant (Six cases), two cases of basosquamous variants, and one case of an infiltrative variant of Basal cell carcinoma [Table/Fig-5] depicts the photomicrograph of a case of Basosuamous carcinoma. In the present study, tumours of melanocyte origin were the second most common accounting for six cases (20% of total malignant epidermal tumours). The superficial spreading melanoma accounts for five cases, followed by one case of lentigo malignant melanoma. In the present study, no cases were reported concerning primary cutaneous malignancies of the Merkle cell and Langerhan cell origin. Present study reported three cases of combination tumours, two of which had Malignant Melanoma and Basal Cell Carcinoma (MM-BCC) basomelanocytic features and one of which had Malignant Melanoma and Squamous Cell Carcinoma (MM-SCC) squamomelanocytic features.

Histologically malignant basomelanocytic tumours composed of nests of proliferating basaloid cells with peripherally palisaded nuclei that extended the papillary dermis, associated with a proliferation of atypical melanocytes located in the epidermis and within the basaloid proliferation shown in [Table/Fig-6].

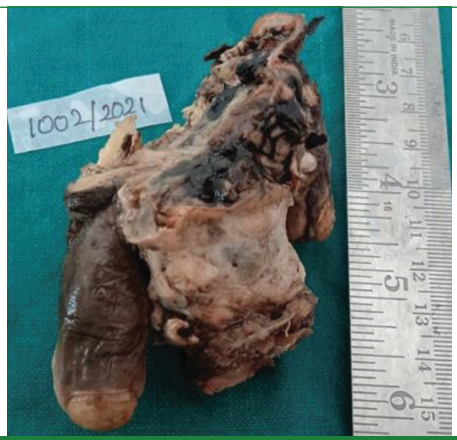


[Table/Fig-5]: Photomicrograph of basosquamous carcinoma: a, b) Tumour cell islands with squamoid differentiation, atypical squamous cells and keratin pearls and individual cell keratinisation (H&E stain, 4X); c, d) Tumour cells exhibiting basaloid morphology with nuclear peripheral palisading and retraction artifacts (H&E stain, 10X).



[Table/Fig-6]: Photomicrograph of basomelanocytic carcinoma: a, b, c) Atypical melanocytes, melanin pigment admixed with basaloid lobules (H&E stain, 4X); d) Tumour cell nests with peripheral nuclear palisade, cleft formation, atypical melanocytes with pigment melanin (H&E stain, 10X).

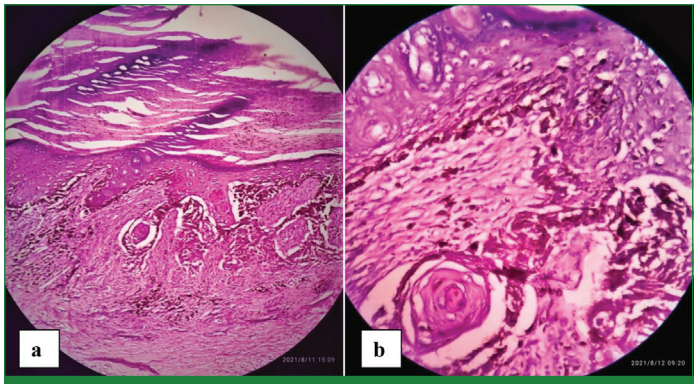
Macroscopic picture of squamomelanocytic tumour involving left foot was shown in [Table/Fig-7]. Histologically malignant squamomelanocytic tumours composed of atypical squamoid cells, some with abundant eosinophilic cytoplasm giving rise to individual cell keratinisation and squamous peal formation admixed with atypical melanocytes with melanin pigment shown in [Table/Fig-8].



[Table/Fig-7]: Macroscopic examination of squamomelanocytic tumour: Ulceroproliferative growth on the dorsum of left foot involving the 3rd, 4th and 5th metatarsals.

DISCUSSION

Skin cancer is becoming an increasingly important public health problem. Skin malignancies constitute a significant proportion of all malignancies and there has been an increase in the prevalence of cutaneous malignancies in the past several years [9]. Cutaneous malignancies account for 1-2% of all the diagnosed cancers in India. Worldwide BCC is the most common cutaneous malignancy, but in India, SCC is reported to be the most common with prevalence of 30-60% followed by BCC with prevalence of 15-25% [3].



[Table/Fig-8]: Photomicrograph of squamomelanocytic tumour: a) Epidermis with tumour tissue shows melanin pigment and keratin pearls (H&E Stain, 4X); b) shows tumour cell nests with squamoid differentiation with keratinization and atypical melanocytes with melanin pigment (H&E stain, 10X).

Of 120 skin biopsies studied, present study reported a total of thirty cases of primary cutaneous malignancies of surface epidermis. The age range of 61-80 years was the one with the greatest number of cases (13 cases, or 43.33%), followed by the age range of 41-60 years (10 cases, 33.33%) and the lowest number of cases reported in those between the ages of 21 and 40 years, as well as those over the age of 80 years. There were no cases reported in those under the age of 20 years. In the present study, the majority of cases (18 cases, 60%) were male and the male to female ratio was 3:2.Similar findings were observed in study by Jina A et al., [10].

Among those who were affected by these lesions, the head and neck region was the most frequently affected (12 cases, 40%), followed by the trunk (6 cases, 20%). There were no significant differences between the upper and lower extremities involvement by these lesions. Similar findings were observed with the study by Rajbhar R et al., and Supekar BB et al., [11,12]. Of all the primary cutaneous malignancies of surface epidermal cell origin, tumours of epidermal keratinocyte origin were the first most common accounting for 21 cases representing 70% of total cases, followed by tumours of melanocytes accounting for six cases, representing 20% of total cases and three cases of combined tumours involving keratinocytes and melanocytes have been reported.

Of all keratinocyte tumours, cutaneous squamous cell carcinoma and its variants were the most common (12 cases, 40% of all reported cases), the majority cases were conventional squamous cell carcinomas except each one case of an acantholytic and verrucous variant of squamous cell carcinoma. The second most common keratinocyte malignancies were basal cell carcinomas (nine cases, 30%), of which most cases were nodular variant (six cases), two cases of basosquamous variant, and one case of an infiltrative variant of Basal cell carcinoma. A case of basosquamous carcinoma in a 65-year-old male on the anterior chest wall is shown in [Table/Fig-5].

In the present study, six cases (20%) were primary cutaneous melanocyte malignancies. The most common variant was superficial spreading melanoma (five cases), followed by one case of lentigo malignant melanoma. In the present study, no cases were reported concerning primary cutaneous malignancies of the Merkle cell and Langerhan cell origin.

The present study findings were compared to the study by Sherpa P and KC SR in which out of 410 cases of skin biopsies studied 39 cases were malignant, of which 25 cases were of keratinocyte origin and three cases were of melanocytic origin, and no merkle and langerhans cell origin cases were reported. Also, in their research, similar to present study findings, squamous cell carcinoma was the most common malignant neoplasm followed by basal cell carcinoma [13]. Similar findings were observed in various studies by Kaur R et al., Gundalli S et al., Nandyal SS and Puranik RB, Bari V et al., and, Shrivastava V et al., where the incidence of squamous cell carcinoma was the greatest among malignant neoplasms, followed by basal cell carcinoma and in contrast to the study by

Shilpa V et al., where among all keratinocytic malignancies, basal cell carcinoma was the most frequent presentation than squamous cell carcinoma [14-19].

Various keratinocyte-melanocyte-tumour combinations have been described in dermatopathology [19]. These tumours are classified as basomelanocytic or squamomelanocytic tumours depending on the cellular make-up. Melanocarcinoma is another name for these malignancies. However, that phrase has been criticised because it was initially used to describe melanoma. Numerous theories exist to explain how these tumours develop. These theories have been classified into three categories: Collision between nearby neoplastic processes, dual differentiation of one neoplastic cell line and divergent differentiation of pluripotent stem cells [20].

Tumours composed of cutaneous malignant epithelial and melanocytic populations are rare [21]. Despite the rarity of these tumours, present study reported three cases of combination tumours, two of which had malignant melanoma and basal cell carcinoma (MM-BCC) basomelanocytic features and one of which had MM-SCC squamomelanocytic features. A case of basomelanocytic carcinoma in a 60-year-male presented with pigmented, ulcerative lesion over the trunk is shown in [Table/Fig-6]. The present study findings were compared with study conducted by Pierard GE et al., who retrieved 78,000 excisions of primary cutaneous malignancies, of which 11 were collision tumours of MM with basal cell carcinoma and 106 were basosquamous carcinoma, but no relationship between MM and SCC was found [22].

Combined tumours that have features of malignant melanoma and squamous cell carcinoma are extremely rare. However, in the present study, a case of squamomelanocytic tumour in a 70-year-old male patient was reported. This patient presented with a three-month history of ulceroproliferative growth over the dorsal aspect of his left foot involving the 3rd, 4th, and 5th metatarsals [Table/Fig-7,8].

Limitation(s)

As this was a retrospective study, in-depth and long-term prospective studies are required to produce accurate data on skin malignancies. Immunohistochemistry (IHC) and other molecular studies like Polymerase Chain Reaction (PCR), which are crucial for comprehending the nature of the lesion, were not part of the study.

CONCLUSION(S)

Because of complexity of the skin, a wide range of cancers can develop from the skin. Of all skin cancers, epidermal skin malignancies are more likely to turn fatal. Skin cancers, at times, may be difficult to diagnose clinically, hence histopathological examination is a must for definitive diagnosis. This study highlights the critical role of histopathology in accurately classifying tumours into distinct morphological types which helps in diagnosing the cases correctly and to establish appropriate treatment plan. The present study reported that tumours of keratinocyte origin were the most common followed by melanocyte origin. Also highlights various rare tumour combinations such as basomelanocytic or squamomelanocytic tumours of epidermis. Majority of cases were males and the maximal numbers of cases were reported in the age group of 61-80 years followed by 41-60 years. Head and neck region was the most predominant anatomic site involved in the indexed study.

REFERENCES

[1] Elder DE, Elenitsas R, Johnson BL, Murphy GF, Xu X. Lever's Histopathology of the Skin. 10th ed. Histology of skin. Philadalphia: Lippincott Williams and Wilkins. 2009:7-66.
[2] Kumar V, Abbas A, Aster J. Robbins and Cotran pathologic basis of disease. South asia ed. The skin. Reed Elsevier. 2014;1141-78.
[3] Gloster Jr HM, Neal K. Skin cancer in skin of color. J Am Acad Dermatol. 2006;55(5):741-60.
[4] Veisani Y, Jenabi E, Khazaei S, Nematollahi S. Global incidence and mortality rates in pancreatic cancer and the association with the human development index: Decomposition approach. Public Health. 2018;156:87-91.
[5] Zaar O, Gillstedt M, Lindelöf B, Wennberg-Larkö AM, Paoli J. Merkel cell carcinoma incidence is increasing in Sweden. J Eur Acad Derm Venereol. 2016;30:1708-13.
[6] Emerging trends in the treatment of advanced basal cell carcinoma. Public Health. 2017;64:01-10.
[7] García JB, Suárez-Varela MM, Vilata JJ, Marquina A, Pallardó L, Crespo J, et al. Risk factors for non-melanoma skin cancer in kidney transplant patients in a Spanish population in the Mediterranean region. Acta Derm Venereol. 2013;93:422-27.
[8] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209-49.
[9] Apalla Z, Nashan D, Weller RB, Castellsagué X. Skin cancer: Epidemiology, disease burden, pathophysiology, diagnosis, and therapeutic approaches. Dermatol Ther (Heidelb). 2017;7(Suppl 1):05-19.
[10] Jina A, Singh V, Saini S, Chotan N, Rajan M. Clinicopathological profile, diagnosis and treatment of skin cancers at a tertiary care center: A retrospective study. Int Surg J. 2017;4:2549-55.
[11] Rajbhar R, Anvikar A, Sulhyan K. Clinicopathological correlation of malignant skin tumors: A retrospective study of 5 years. Int J Health Sci (Qassim). 2020;14(3):18-25. PMID: 32536845; PMCID: PMC7269623.
[12] Supekar BB, Tomar SS, Wankhade VH, Bhushan R, Singh RP, Bhat DM, et al. Clinical spectrum of cutaneous malignancies in central India: A retrospective study. Indian J Dermatol. 2021;66:284-90.
[13] Sherpa P, KC SR. Histopathological Evaluation of Skin Neoplasms. Nep Med J. 2018;1(2):89-93.
[14] Kaur R, Kumar V, Mehra K, Gupta N, Singh A. Histopathological evaluation of Skin Tumours. Indian J Pathol Oncol. 2016;3(4):627-31.
[15] Gundalli S, Kolekar R, Pai K, Kolekar A. Histopathological study of skin tumours. Int J Healthcare Sci. 2015;2:155-63.
[16] Nandyal SS, Puranik RB. Study of demographic profile of skin tumors in a tertiary care hospital. Int J Curr Res Rev. 2014;6:24-28.
[17] Bari V, Gosavi A, Murarkar P, Sulhyan K. Skin tumours-histopathological review of 125 cases. Indian Medical Gazette. 2014;148(11):418-27.
[18] Shrivastava V, Tangde A, Joshi A, Bindu R. Clinicopathological study of skin tumours. Int J Res Med Sci. 2019;7(5):1712-19.
[19] Shilpa V, Uplaonkar, Mandakini Tengli, Syeda Farheen, Pratima S. Histopathological study of tumours of epidermis and epidermal appendages. Indian J Pathol: Res Prac. 2017;6(2):460-66.
[20] Satter EK, Metcalf J, Lountzis N, Elston DM. Tumors composed of malignant epithelial and melanocytic populations: A case series and review of the literature. J Cutan Pathol. 2009;36(2):211-19.
[21] Kochoumian E, Kazlouskaya V, Mangold A, Lal K, Maia-Cohen S, Elston DM. Tumor with the features of both squamous cell carcinoma and melanoma (melanocarcinoma). Indian Dermatol Online J. 2015;6(3):217.
[22] Pierard GE, Fazaa B, Henry F, Kamoun MR, Piérard-Franchimont C. Collision of primary malignant neoplasms on the skin: The connection between malignant melanoma and basal cell carcinoma. Dermatology. 1997;194(4):378-79.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India.
2. Professor and Head, Department of Pathology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India.
3. Professor, Department of Pathology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India.
4. Assistant Professor, Department of Pathology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rameswary Korata,
Assistant Professor, Department of Pathology, Katuri Medical College and Hospital, Katuri Nagar, Guntur, Andhra Pradesh, India.
E-mail: drbhavanikm@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 25, 2022
- Manual Googling: Aug 30, 2022
- iThenticate Software: Sep 22, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jun 10, 2022**
Date of Peer Review: **Jul 28, 2022**
Date of Acceptance: **Sep 23, 2022**
Date of Publishing: **Jan 01, 2023**