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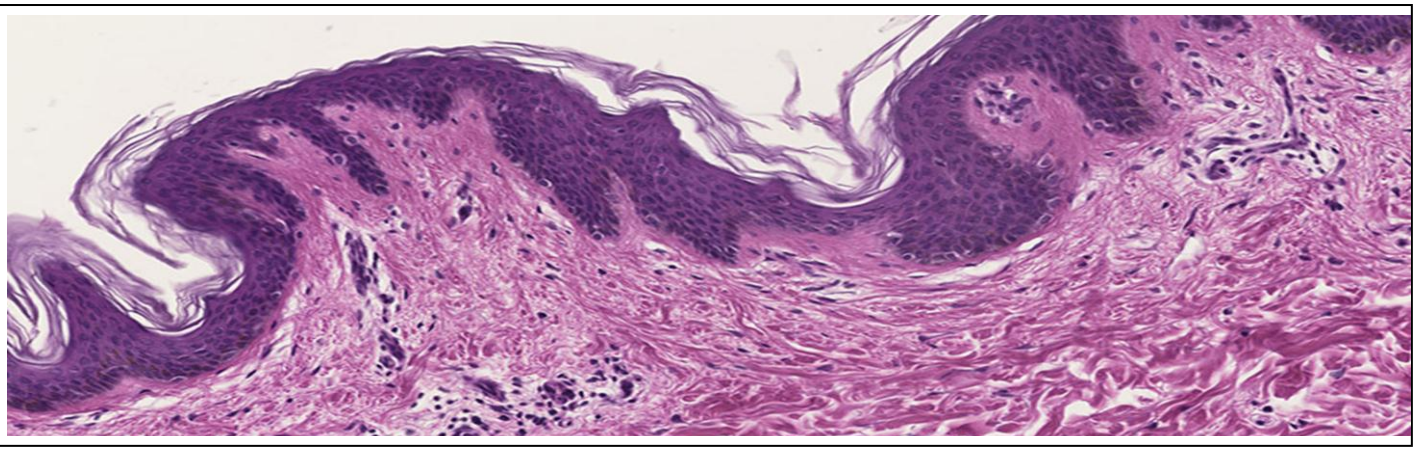

Histomorphological spectrum of hyperpigmented skin lesions: Are all of melanocytic origin? - A retrospective study

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NAME OF THE AUTHOR

Sushma K L
*** Manjunath H K**
Bhargavi Mohan
Dharani V C
Sushma T A
Vinitra K

[1]Assistant professor, BGS Global Institute of Medical Sciences, BGS health & education city, Uttarahalli main road, Kengeri, Bangalore, India

[2]Professor and Head, BGS GIMS, Bangalore, India
[3,4] Associate Professor and Head, BGS GIMS, Bangalore, India
[5] Professor and Head, BGS GIMS, Bangalore, India
[6] Tutor, BGS GIMS, Bangalore, India

ABSTRACT

Background: Hyperpigmented skin lesions include both melanocytic as well as non-melanocytic lesions. Hyperpigmentation of the skin reflect underlying benign or malignant lesions more than just being a cosmetic deformity. Histopathology acts as a cornerstone in diagnosing these lesions. **Aims and Objective**: In the present study, we intend to categorize the hyperpigmented skin lesions based on the divergent histomorphological features and to differentiate melanocytic lesions from its non-melanocytic mimickers. **Materials and Methods:** This was a retrospective, descriptive study conducted from January 2017 to December 2019 on 80 cases of hyperpigmented skin lesions, at BGS Global Institute of Medical Sciences. **Results:** A total of 80 cases were studied. Of the 80 cases, 38 (48%) were melanocytic and 42 (52%) were non-melanocytic lesions. Age group commonly affected was between 31-40 years (25%); with male to female ratio being 1:1. The most common site of involvement was the extremities 46 (58%). Most common pigmented skin lesion in our study was melanocytic nevi (n=33) (41%) among the melanocytic lesions and Erythema dyschromicum perstans (n=13) (16%) among the non-melanocytic lesions. **Conclusion:** Pigmented skin lesions are one of the most common causes for dermatological consultation. Majority are benign, while a small minority are malignant. Therefore, all clinically pigmented skin lesions should be submitted for histopathological evaluation so as to not miss a small percentage of malignant lesions.

KEYWORDS: melanocytic lesions, pigmented lesion, cutaneous melanocytic, nevus.

CITATION OF THE ARTICLE

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** Corresponding Author*

I. INTRODUCTION

Hyperpigmentation refers to the presence of increased melanin pigment in the epidermis, dermis and/or mucus membrane to the extent that the person seeks medical intervention.[1] Increased proliferation of melanocytes or increased melanin pigment in the epidermis is characterized by 'Brown hyperpigmentation' whereas that in the dermis is known as 'blue hyperpigmentation' or 'Ceruloderma'.[2] Benign melanocytic naevi and malignant melanomas are close mimickers and clinically challenging to diagnose.

II. MATERIALS AND METHODS

This retrospective study comprised of skin biopsies from patients received in the Department of Pathology, BGS GIMS, Bengaluru for a duration of 3 years from January 2017 to December 2019.

Inclusion criteria: All neoplastic and non-neoplastic pigmented skin lesions were included in the study.

Exclusion criteria: Inadequate biopsy specimen, specimen sent in saline and skin biopsies other than clinically diagnosed pigmented lesions were excluded from the study.

Punch biopsy of 0.3 mm was done for smaller lesions while excision biopsy was done for larger lesions. The tissue was fixed in 10% formalin and 3-5 µ thick sections were stained with haematoxylin-eosin. Serial sectioning, step deeper, reverse embedding along with special stains were done wherever necessary. Patients' clinical details such as age, sex, and site of lesion were documented from the histopathology requisition form, clinical case sheets and other medical records. Relative frequency of various lesions along with age and site distribution of the lesions were analysed.

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III. STATISTICAL ANALYSIS

The collected data were entered and analysed using Microsoft excel. The data were expressed in percentages (%).

IV. RESULTS

Out of the 80 cases evaluated, 38 cases (47.5%) were melanocytic lesions which include 33 cases (41.2%) of benign naevi and 5 cases (6.2%) of malignant melanoma (Figure 1). Other 42 cases (52.5%) were cutaneous non-melanocytic lesions which include erythema dyschromicum perstans 13 (16.2%), lichen planus pigmentosus 11 (13.7%), post inflammatory hyperpigmentation 7 (8.7%), pigmented basal cell carcinoma 5 (6.2%), pigmented seborrheic keratosis 3 (3.2%), lentigo simplex 1 (1.2%) and pigmented dermatosis 2 (2.5%) (Table 1).

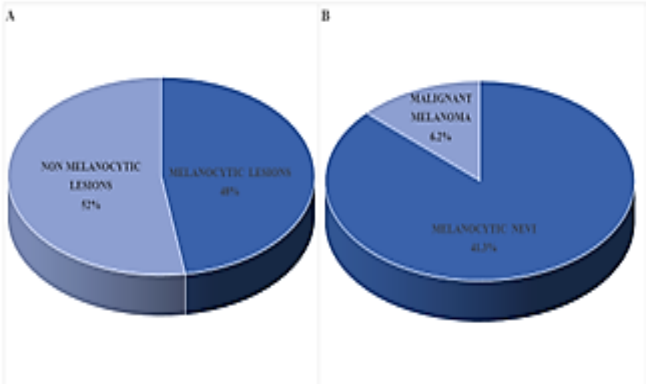

Figure 1 : (A) Distribution of melanocytic and non melanocytic lesioins. (B) Distribution of melanocytic lesioins.

In our study, among the melanocytic lesions, benign melanocytic nevi (41.2%) was the most common lesion and among them intradermal nevi was the most common. Erythema dyschromicum perstans was the most common lesion among the pigmented non-melanocytic lesions (Figure 2).

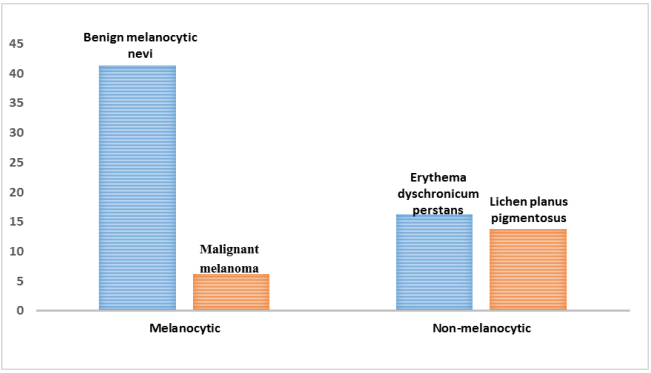

Figure 2: Common Pigmented lesions

These cases are distributed in the age group of 5 years to 77 years with overall equal male to female incidence except for melanoacanthoma where only one case was found in a male. Most common age group affected was between 31- 40 years (25%). Both melanocytic and non-melanocytic lesions are seen equally in all the age groups where are malignant melanomas were seen in elderly individual >45 years, with male preponderance (60%).

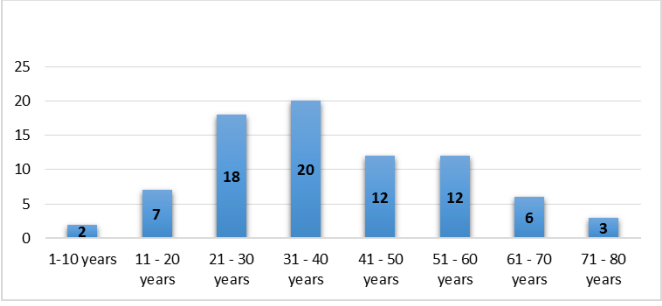

Figure 3: Age wise distribution of hyperpigmented

skin lesions

Most common site of involvement was extremities 46 (57.5%) of which 24 (30%) cases were seen in upper limbs and 22 (27.5%) cases in lower limbs followed by head and neck region 23 (28.7%). 5 (100%) cases of malignant melanomas were found in the lower limbs whereas 3 (60%) cases of pigmented basal cell carcinoma and a single case of melanoacanthoma were found in head and neck region.

Of the 38 cases of melanocytic lesions, 33 (41.3%) were melanocytic nevi which included 19 (23.7%) intradermal nevi, 3 (3.7%) blue nevi, 2 (2.5%) nevus of oto, 2 (2.5%) congenital melanocytic nevi, 2 (2.5%) nevus sebaceous, 1 (1.2%) melanoacanthoma, 1 (1.2%) compound nevus, 1 (1.2%) nevus verrucosus, 1 (1.2%) Ancient nevus and 1 (1.2%) bakers nevus. 5 (6.2%) cases were malignant melanoma of which 4 (5%) were superficial spreading type and 1 (1.2%) was nodular type.

Of the 42 cases of non-melanocytic lesions, 13 (16.2%) were erythema dyschromicum perstans followed by 11 (13.7%) lichen planus pigmentosus, 7 (8.7%) post inflammatory hyperpigmentation, 5 (6.2%) pigmented basal cell carcinoma, 3 (3.7%) pigmented seborrheic keratosis, 2 (2.5%) pigmented purpuric dermatoses and 1 (1.2%) lentigo simplex. Among the malignant pigmented lesions; malignant melanoma and pigmented basal cell carcinoma were seen in equal incidence.

Table 1: Distribution of Melanocytic and Non-melanocytic lesions

LESIONS		No of cases (n=80) (%)
MELANOCYTIC	Intradermal Nevus	19 (23.7%)
	Malignant Melanoma	5 (6.2%)
	Blue nevus	3 (3.7%)
	Nevus of oto	2 (2.5%)
	Congenital melanocytic nevus	2 (2.5%)
	Nevus sabeceous	2 (2.5%)
	Melanoacanthoma	1 (1.2%)
	Compoud nevus	1 (1.2%)
	Nevus verrucosus	1 (1.2%)
	Ancient nevus	1 (1.2%)
	Becker nevus	1 (1.2%)
NON MELANOCYTIC	Erythema dyschromicum perstans	13 (16.2%)
	Lichen planus pigmentosus	11 (13.7%)
	Post inflammatory hyperpigmentation	7 (8.7%)
	Pigmented basal cell carcinoma	5 (6.2%)
	Pigmented seborrheic keratosis	3 (3.7%)
	Pigmented purpuric dermatosis	2 (2.5%)
	Lentigo simplex	1 (1.2%)
TOTAL		80 (100%)

V. DISCUSSION

Hyperpigmented skin lesions are a group of heterogeneous disorders associated with alterations in the intensity and patterns of pigmentation of skin. Most of these are genetic while others can be inflammatory, degenerative, endocrine, toxic and immunologically mediated.[3] Some of the histomorphological differences and overlapping features between melanocytes, nevus cells and melanoma cells are discussed in table 2:

Table 2: Histomorphological differences and overlapping features between melanocytes, nevus cells and melanoma cells

Feature	Melanocytes	Nevus Cells	Melanoma Cells
Contour	Dendritic	Rounded or spindle shaped	Rounded or spindle shaped
Arrangement of Cells	Singles	Clusters	Clusters, large sheets
Nuclei	Small, regular	Small, regular	Large, irregular, hyperchromatic
Mitosis	Rare	Rare	Present
Ihc	Mel - 5	S-100, MART-1	HMB-45, Melan A

Melanocytic lesions refer to the proliferation of neural crest derived melanocytic cells in the skin. This includes melanocytic nevus and malignant melanoma. Melanocytic nevus are benign hamartomatous or neoplastic proliferation of melanocytes. Three types of nevus cells have been identified, Type A, Type B and Type C. Type A cells are present as small nests in the upper dermis. They are round to cuboidal, have abundant cytoplasm and contains moderate amount of melanin. Type B cells are present in mid dermis and are seen in aggregates and cords. They are smaller than type A cells, have less cytoplasm and less melanin. Type C cells are present in lower dermis, resemble schwann cells and hence called "neurotized nevus" and they rarely contain melanin.[3]

In our study, benign melanocytic nevi was the most common lesion (33 cases) which was concordant with the study conducted by Parvathi et al [4] and the commonest site of involvement of these pigmented lesions was extremities which was similar to the study conducted by Shushan Shweta Jayker [5]and was non concordant with the study conducted by Shilpa M shetty [6] which showed head and neck region as the most common site of involvement. These lesions show an overall equal male to female incidence whereas in a study conducted by Shushan Shweta Jayker [5], females were more commonly affected than males.

Intradermal nevus unlike melanoma enlarge to a point, stabilize and then involute. It is composed of nevus cells in nests and cords in the upper dermis (Figure 4A). In our study, among the melanocytic lesions, benign melanocytic nevus was the most common lesion (33 cases) and among them intradermal nevus was the most common (19 cases) which was concordant with the study conducted by parvathi et al [4], shilpa M Shetty [6] and Rajendra Prasad Jagannadham.[7] These lesions were common in females (11 cases) which correlated with the study conducted by Shilpa M Shetty[6] and Rajesh Singh Laishram.[8]

Blue nevus is a benign pigmented skin lesion which appears blue in colour. Blue colour is caused by the pigment being present deeper in the dermis than in ordinary nevus. The lesions in our study showed presence of pigmented spindle and dendritic melanocytes in reticular dermis with alteration in the dermal collagen (Fig 4B) which was similar to the histopathological features described by Nozomi Yonei[9]. Blue nevus must be differentiated from spitz nevus in which spindled cells are arranged in fascicles, perpendicular to epidermis and epithelioid cells are dispersed individually in dermal papillae. Eosinophilic hyaline bodies along the dermo-epidermal junction known as kamino bodies are characteristic of spitz nevus. In our study, the lesion was commonly seen in females which was concordant with the study conducted by de Lorenzi et al[10] whereas it was non concordant with the study conducted by Erik S. Cabra[11] which showed male preponderance.

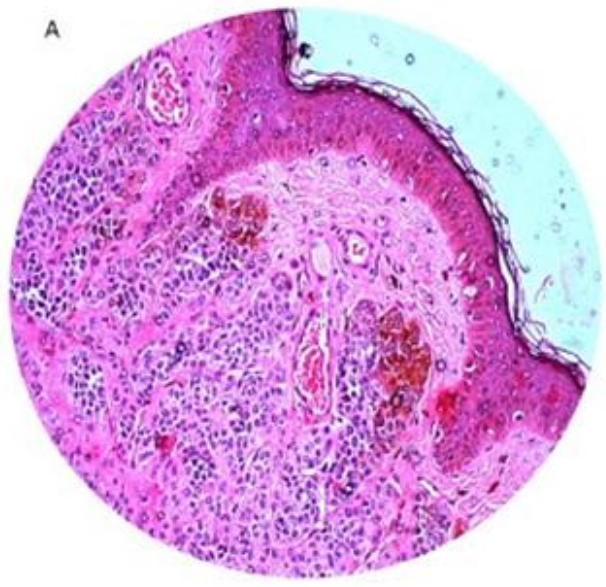

Figure 4 : (A) Intradermal nervus showing nests and cords of nervus cells with pigmentation in the upper dermis (H and E); 10x

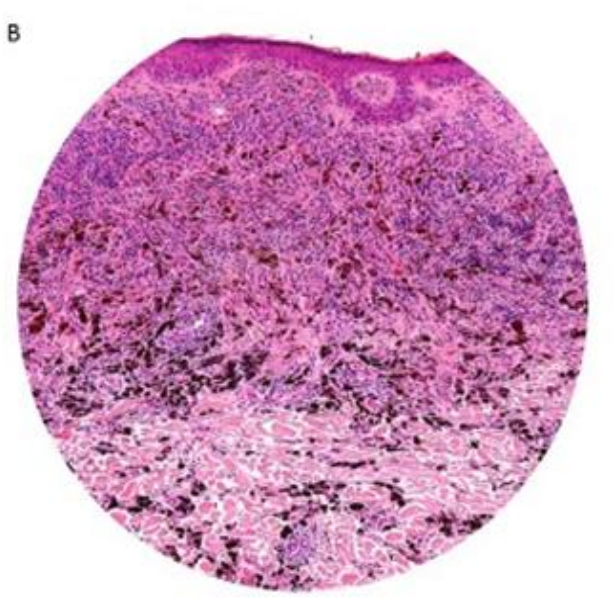

Figure 4 : (B) Blue nervus showing pigmentated spindle and dendritic melanocytes in reticular dermis with alteration in the dermal collagen (H and E); 10x

Nevus of Oto is a type of dermal melanocytosis which commonly involves the face and is distributed along the ophthalmic, maxillary, and mandibular divisions of the facial nerve.[12] It is characterised by increased concentration of dermal melanocytes in the upper dermis. In our study, out of the 2 cases, one was seen on the face and the other was seen on the arm. 100% of the cases were seen in females which was concordant with the study conducted by shanmuga sekar. [12]

Becker's melanosis was described as “concurrent melanosis and hypertrichosis in the distribution of nevus unius lateris” by S. William Becker in 1949.[13] It is characterized by a well-defined hyperpigmented patch with irregular margins and associated hypertrichosis over the upper half of trunk and upper extremities.[14],[15] It is characterized by increased melanocytes in the basal cell layer along with acanthosis, irregular elongation, and fusion of rete ridges.

Compound nevus possesses the features of both junctional nevus and intradermal nevus. In our study, a single case of compound nevus was seen which showed nests of nevus cells in the epidermis, dropping off into the superficial dermis. In junctional nevus, nests of nevus cells are present in the epidermis or bulging into the dermis but still present in contact with the epidermis.

Congenital melanocytic nevus is a lesion of nevus cells usually present at birth and is usually more than 1.5 cm. When the size of the lesion exceeds 20 cm, it is termed as congenital giant melanocytic nevus. These

lesions have a greater risk of transforming into malignant melanomas as compared to smaller-sized nevi according to Meshram G.G.[16] In our study, 2 cases were seen which showed the presence of nests of nevomelanocytes in the basal layer of the epidermis and deeper dermis.

Malignant melanomas arise in the epidermis and these lesions can be in situ or invasive. There are 4 major subtypes, superficial spreading melanoma, lentigo maligna melanoma, Nodular melanoma and Acral lentiginous melanoma (Figure 5).

In our study, superficial spreading type was the most common lesion which was similar to the study conducted by Rajendra Prasad Jagannadham[7] and Rajesh Singh Laishram[8]

All the 5 cases seen were in lower limb which was in concordance with the study conducted by Isha Bohra et al[17], Rajendra Prasad Jagannadham[7] and Rajesh Singh Laishram. [8] It was seen in patients above 40 years of age which is similar to study by Isha Bohra et al[17] and Dafe Forae G et al.[18] Malignant melanomas were seen in males more commonly than in females which was concordant with the study conducted by Rajendra Prasad Jagannadham. [7]

Figure 5 : (A) Malignant melanoma presenting as an ulceroproliferative growth on the sole of left lower limb.

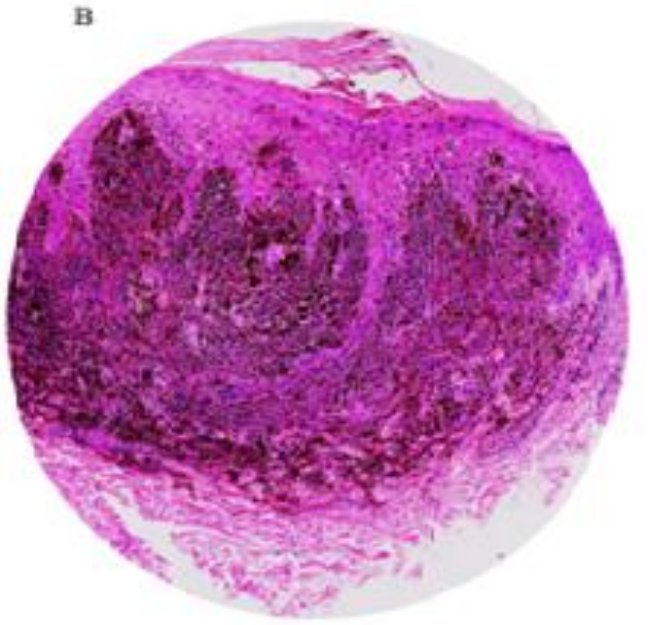

Figure 5 : (B) Malignant melanoma – Nodular variant with dermis showing cohesive nodule of tumor cells (H and E; 40x)

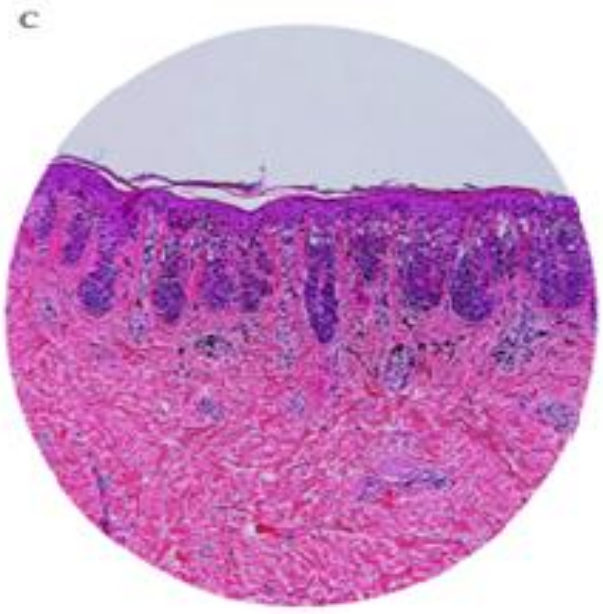

Figure 5 : (C) Malignant melanoma- Superficial spreading type showing pleomorphic tumor cells with abundant granular cytoplasm and pigmentation(H and E; 10x)

Erythema dyschronicum perstans (EDP) is very similar to ashy dermatosis except for the fact that erythematous border that is present in the active stage of EDP is not seen in ashy dermatosis.[19],[20] It is characterised by increased melanocytes in the upper dermis, basal cell degeneration and perivascular lymphocytic infiltrate. In our study EDP was the most

common pigmented non-melanocytic lesion which was non concordant with the studies conducted by Sushan Shweta Jayker et al.[5]

Lichen planus pigmentosus (LPP) is a characterised by macular pigmentation of uncertain aetiology.[19],[21] Our case showed lichenoid dermatitis, focal epidermal hyperkeratosis, hypergranulosis, basal vacuolization, perifollicular lymphocytic Infiltration with perifollicular fibrosis and pigment incontinence which was similar to study conducted by Suthinee Rutnin. [19] It was the second most common pigmented lesion among non melanocytic lesions in our study which was concordant with the study conducted by Sushan Shweta Jayker et al[5] whereas it was the most common lesion according to the study conducted by Rakesh Saha.[22]

Post inflammatory hyperpigmentation (PIH) can occur as a consequence of injury or inflammation to dark skin, after laser therapy for other pigmented skin lesions, and may be transient or long lasting.[23] 17% of the cases in our study were PIH and was not a common lesion, whereas it was the second most common pigmented lesion in the study conducted by Rakesh Saha.[22]

Basal cell carcinoma (BCC) is a common malignancy among skin cancers worldwide comprising of 80% of non-melanoma cancers.[24],[25] Pigmented basal cell carcinoma is a rare histological variant of basal cell carcinoma that exhibits increased pigmentation.

Our case showed nodular masses of basal cells with peripheral palisading, artifactual clefting between the epithelium and stroma and increased melanin pigmentation (Figure 6). In our study, incidence of pigmented BCC and malignant melanoma were similar which was concordant with the study conducted by Isha Bohra et al [17] and was not concordant with the study conducted by Rajesh Singh Laishram[8]. Pigmented BCC was commonly seen in head and neck which was in concordance with the study conducted by Isha Bohra et al[17], Rajesh Singh Laishram[8] and Rajendra Prasad Jagannadham[7] and was seen in patients above 40 years of age which is similar to study by Dafe Forae G et al [18] and Isha Bohra et al. [17] Majority of these cases were seen among females which was similar to the study conducted by Rajendra Prasad Jagannadham.[7]

Figure 6A - Case of BCC presenting as an ulcerative lesion on the left upper eyelid

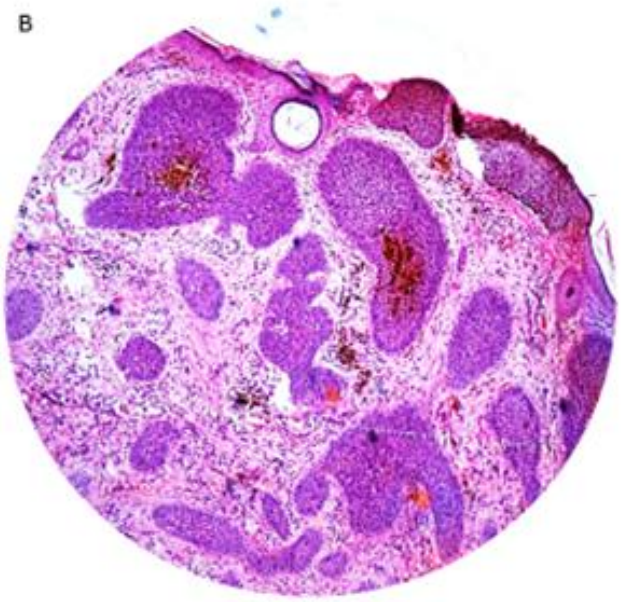

Figure 6B - Pigmented basal cell carcinoma showing nests of basaloid cells with peripheral palisading (H and E); 10x

Lentigo simplex is characterized by increased number of nevoid melanocytes present in focal contiguity with one another near tips and sides of elongated rete. A single case was seen in our study in a male patient while it was common in females in a study conducted by Rajesh Singh Laishram.[8]

Pigmented seborrheic keratosis is characterized by hyperplastic stratified squamous epithelium with multiple horn cysts and melanin pigmentation. In our study we had 3 cases and was not a common pigmented lesion whereas in a study conducted by Rajendra Prasad Jagannadham[7], this was the second most common lesion among the benign pigmented lesions.

Melanoacanthoma is rare variant of seborrheic keratosis presenting as a deeply pigmented benign proliferation of melanocytes and keratinocytes usually presenting over the head, neck and trunk of elderly people. In our study, a single case was seen in a male which was similar to the study conducted by Rajesh Singh Laishram. [8]

VI. CONCLUSION

Among the hyperpigmented skin lesions, non-melanocytic lesions were more common than the melanocytic lesions in our study. The most common pigmented melanocytic lesion was intradermal nevus. Erythema dyschromicum perstans was the most common lesion among the pigmented non-melanocytic lesions. Pigmented skin lesions were equally seen in both the sex groups. Histopathology remains a cornerstone for diagnosing these lesions and a detailed histopathological examination of all clinically pigmented skin lesions is a must to differentiate melanocytic lesions from its non-melanocytic mimickers.

VII. ACKNOWLEDGEMENT

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VIII. SOURCE OF FUNDING : None

IX. CONFLICT OF INTEREST: None

X. LEGENDS

Figure 1A - Distribution of melanocytic and non melanocytic lesioins

Figure 1B - Distribution of melanocytic lesions

Figure 2 - Common Pigmented lesions

Figure 3: Age wise distribution of hyperpigmented skin lesions

Figure 4A - Intradermal nevus showing nests and cords of nevus cells with pigmentation in the upper dermis (H and E);10x

Figure 4B - Blue nevus showing pigmented spindle and dendritic melanocytes in reticular dermis with alteration in the dermal collagen (H and E); 10x

Figure 5A - Malignant melanoma presenting as an ulceroproliferative growth on the sole of left lower limb

Figure 5B - Malignant melanoma - Nodular variant with dermis showing cohesive nodule of tumor cells (H and E; 40x)

Figure 5C - Malignant melanoma - Superficial spreading type showing pleomorphic tumor cells with abundant granular cytoplasm and pigmentation (H and E; 10x)

Figure 6A - Case of BCC presenting as an ulcerative lesion on the left upper eyelid

Figure 6B - Pigmented basal cell carcinoma showing nests of basaloid cells with peripheral palisading (H and E); 10x

Table 1: Distribution of Melanocytic and Non-melanocytic lesions

Table 2: Histomorphological differences and overlapping features between melanocytes, nevus cells and melanoma cell.

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