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Original Article

Benign melanocytic lesions with emphasis on melanocytic nevi – A histomorphological analysis

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ABSTRACT

Background: Melanocytic lesions are common and include both benign and malignant conditions. Benign melanocytic nevus may show varied microscopic features and should be differentiated from malignant lesions. In the present study, we analyse the histopathological pictures of different types of benign melanocytic nevi.

Materials and methods: This study was a hospital based retrospective study and all the cases reported as melanocytic nevus in the period from Jan 2014 to June 2018 in the Department of Pathology, Manipal Teaching Hospital were retrieved and analysed in the study.

Results: A total of 104 melanocytic lesions including 74 cases of benign melanocytic nevus were reported in the study period. Females were affected more with a female to male ratio of 1.8:1. The age range was 5 to 78 years with mean age of 28 years. Among the female patients, the commonest age group was 21-30 years while among the males; the most affected age group was 11-20 years. The commonest histopathological subtype was intradermal nevus comprising 73% cases followed by compound nevus. On analysis of the different sites involved, face, head and neck were found to comprise 92% cases. Epidermal changes including hyperkeratosis, acanthosis were common in intradermal nevus. In most cases, tumor cells were arranged in nests. Melanin pigment was noted in majority of the cases. Secondary changes noted were chronic inflammation, fibrosis and multinucleated giant cells.

Conclusion: Benign melanocytic nevus may present in varied age range and show wide spectrum of histological features. All pigmented lesions should be biopsied for its diagnosis and subtyping.

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INTRODUCTION

Melanocytic lesions are one of the most common skin lesions encountered by a dermatopathologist in day to day practice and they exhibit great morphological variations in their architecture and cytomorphological appearance.[1] Melanocytic proliferations are composed of one or more of three related types of cells viz., melanocytes, nevus cells and melanoma cells each of which may be located in the epidermis, the dermis and occasionally in subcutis.[2] Melanocytes are solitary dendritic cells that are usually separated from each other by keratinocytes or fibroblasts.[2] Benign tumors of melanocytes are known as melanocytic nevus and malignant tumors are called as malignant

Table 1: Age-wise distribution of melanocytic nevi (n=74) in males and females

	Age groups (in years)								
	<10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	TOTAL
Female	0	9	16	7	10	2	2	2	48
Male	1	10	8	4	1	1	1	0	26
Total	**1**	**19**	**24**	**11**	**11**	**3**	**3**	**2**	**74**

Table 2: Histomorphological subtypes of melanocytic nevi (n=74)

Diagnosis	Number of cases (%)	Female	Male
Intradermal nevus	54 (73%)	37	17
Compound nevus	17 (23%)	11	6
Junctional nevus	2 (3%)	-	2
Spitz nevus	1 (1%)	-	1
TOTAL	**74 (100%)**	**48 (65%)**	**2 (35%)**

melanoma and the cells of these lesions are known as nevus cells (or nevomelanocyte) and melanoma cells respectively.[2,3] Nevus cells are melanocytes that have lost their long dendritic processes as an adaptive response to formation of nests of cells.[3] Because these changes cannot be appreciated in routine hematoxylin and eosin stained sections, it has been suggested that all cells in melanocytic nevi should be referred to as melonocytes.[4] Melanocytic nevi may be present at birth (congenital melanocytic nevi) but the majority appear in childhood or adolescent and are known as acquired melanocytic nevi.[3] Various studies have been undertaken in recent years to ascertain the prevalence of nevi in different population groups and the role of environmental factors in its etiology.[5] In the current study we focus on the histopathological features of different types of benign melanocytic nevi.

MATERIAL AND METHODS

This study was a hospital based retrospective study carried out in the Department of Pathology, Manipal Teaching Hospital. All the cases reported as melanocytic nevus over a time period from Jan 2014 to June 2018 were analysed in the study. The entire of all the skin biopsy were processed in every case. They were routinely fixed in 10% buffered formalin and stained with hematoxylin and eosin stain. The outcome variables were melanocytic nevus and its subtypes while the explanatory variables were age, sex, site and different histopathological parameters as mentioned below. The data collected was analysed with the software SPSS v16 and a p value <0.05 was considered as statistically significant. Approval from the institutional ethical committee was taken and the study was conducted in accordance with the Helsinki Declaration.

RESULTS

A total of 104 melanocytic lesions were reported during the study period which comprised of 74 cases of benign melanocytic nevus, 3 cases of Becker's nevus syndrome, 3 cases of epidermal nevus, 1 case of congenital hairy nevus, 1 case of large congenital nevus with malignant melanoma and 23 cases of malignant melanoma. In the current study, we analysed all the 74 cases of benign melanocytic nevus of which 48 cases (65%) were female and 26 cases (35%) were male with a female to male ratio of 1.8:1. Among the female patients, the commonest age group was 21-30 years followed by 41-50 years while among the males, the most affected age group was 11-20 years followed by 21-30 years. The age distribution in female and male patients has been shown in Table1. All the diagnoses and their distribution in female and male patients have been summarised in Table 2.

The commonest histopathological subtype was intradermal nevus (n=54; 73%) followed by compound nevus (n=17; 23%). Both these types were more common in females in a ratio of 2.2:1 and 1.8:1 respectively. We also came across 2 cases of junctional nevus and 1 case of spitz nevus which were reported in males. The involved sites of all the cases have been correlated with subtype and sex distribution in Table 3. Face, head and neck comprised of majority cases (n=68, 92%) followed by trunk (n=5; 7%) and arm (n=1; 1%). Cheek (n= 15) was the commonest site followed by lip (n=12) and eyelids (n=10). No statistical correlation could be established (p value >0.05) between diagnostic subtypes and age, sex and site distribution. Microscopic features including changes in the epidermis, tumor cell arrangement, tumor cell morphology, and other secondary changes have been analysed in different subtypes and summarised in Table 4.

Epidermal changes including hyperkeratosis, acanthosis were common in intradermal nevus. Junctional activity was present in all compound and junctional nevus as a part of diagnostic criteria. In most cases, tumor cells were arranged in nests. Melanin pigment was noted in majority of the cases. In only 1 case of intradermal nevus, majority of the tumor cells showed intranuclear pseudoinclusions. Secondary changes included chronic inflammation, fibrosis and multinucleated giant cells. One case each of nevus was associated with basal cell carcinoma, epidermal inclusion cyst and chalazion. The parameters which were statistically significant (p<0.05) included arrangement in nest pattern and presence of melanin pigment.

Table 3: Sites of distribution and its correlation with different subtypes and sex

Site	Total	Female (n=48)		Male (n=48)			
		IN	CN	IN	CN	JN	SN
Eyelid	10	7	1	1	1	-	-
Cheek	15	6	1	5	2	-	1
Ear	5	3	2	-	-	-	-
Eye brow	2	-	1	1	-	-	-
Nose	7	3	2	2	-	-	-
Conjunctiva	1	-	1	-	-	-	-
Scalp	8	6	-	2	-	-	-
Neck	5	3	-	2	-	-	-
Lip	12	5	2	1	2	2	-
Chin	2	1	-	1	-	-	-
Forehead	1	1	-	-	-	-	-
Arm	1	1	-	-	-	-	-
Trunk	5	1	1	2	1	-	-
TOTAL	74	37	11	17	6	2	1

IN: Intradermal nevus, CN: compound nevus, JN: Junctional nevus, SN: Spitz nevus

DISCUSSION

Melanocytic nevus is considered as a benign neoplastic proliferation of melanocytes leading to a pigmented or nonpigmented lesion. Melanocytic nevi are rarely present at birth and most appear in adolescent and early childhood.[2,6,7] With advancing age there is progressive decline which is especially marked after the age of 50 years. Occasionally new nevi may arise in midlife and rarely in later age.[2,3]

In our study, the age range was 5 years to 78 years with a mean age of 28 years which is similar to the study by Azam S et al[8] (mean age 27 years) while Hussein MR et al[9] and Pailoor K et al[1] found the mean age to be 33 and 44 years respectively. Interestingly, most of our cases presented beyond the adolescent age range. New nevus arising in mid-life or later is uncommon.[2] We had 19 cases above the age of 40 years including 8 cases of above 50 years who presented with a new lesion.

In other studies, benign nevus showed female preponderance with a female to male ratio of 1.3:1 and 2:1 which is similar to our result of 1.8:1.[8,9] However Pailoor K et al[1] in their studies noted equal sex distribution and Oliveria SAet al[10] in their study found prevalence of nevi to be higher in boys than in girls.

In our series, face along with head and neck were by far the most common site which is similar to Azam S et al[8] and Gundalli S et al[11] but in contrast to Pailoor K et al[1] and Cohen LM et al[12] who found forearm and back to be the commonest site respectively. In the study among adolescents by Darlington S et al, numbers of nevi were more in back and shoulder than in face and neck.[7]

Other than its cosmetic significance, benign melanocytic

Table 4: Histopathological findings in melanocytic nevi (n=74)

Microscopic features	Morphological findings	IN (n=54)	CN (n=17)	JN(n=2)	SN(n=1)	Total
Epidermis	Hyperkeratosis	29	12	1	1	43
	Parakeratosis	12	3	-	-	15
	Acanthosis	32	10	2	-	44
	Lentigenous proliferation	-	3	1	-	4
	Junctional activity	-	17	2	-	19
Tumor cell arrangement	Sheet	34	10	-	-	44
	Nests	54	17	1	1	73
	Cords	40	8	-	-	48
	Singly	-	-	-	-	0
Tumor cell morphology	Round	54	17	2	1	74
	Spindle	26	15	-	-	51
	Melanin	47	15	2	1	65
	Nuclear atypia	2	1	-	1	4
	Mitosis	-	-	-	-	0
	Necrosis	-	-	-	-	0
Secondary changes in stroma	Inflammation	38	11	2	-	51
	Fibrosis	13	5	-	-	18
	Multinucleated giant cell	9	1	-	-	10
	Cleft formation	24	5	1	-	30

IN: Intradermal nevus, CN: compound nevus, JN: Junctional nevus, SN: Spitz nevus

nevi are primarily important as 'simulant' to melanoma, as 'precursor' to melanoma and as 'risk markers' of an individual for development of melanoma.[2] Histopathological spectrum of melanocytic nevi shows significant variation.[5,8]

Nevus cells and melanoma cells both can be round to spindle shaped. Both can be arranged in nests but sheets of tumor cells are usually more seen in melanoma. Both nevi and melanomas may show scant to obscuring melanin pigment. In general, nevus cells are more commonly round, show nesting pattern at least in part of the lesion and have a propensity to retain pigment in their cytoplasm. Nevus cell show small and regular nuclei with rare mitosis while melanoma cells show large irregular and hyperchromatic nuclei with prominent nucleoli and mitosis.[2,3] However, several overlapping and common features can be seen in many cases of either types.

Histologically, nevi are subdivided into junctional, compound and intradermal nevi and perhaps denotes the life cycle of nevi from junctional to compound to intradermal and finally to involuting stage. This concept was however challenged by some authors.[13]

The most common subtype in our study was intradermal nevi comprising 73% of all cases which is similar to other authors.[1,3,8] They, by definition, do not show any junctional activity. In our series, 59% cases showed epithelial acanthosis which is similar to Pailoor K et al (54%) but higher than Azam S et al (26%).[1,8] Other epithelial changes included hyperkeratosis and parakeratosis. Commonest pattern of arrangement of the tumor cells was in nests followed by cords. Tumor cells in intradermal nevi can be of type A, B or C. Type A cells have visible cytoplasm, type B cells are small lymphocyte like while type C cells are spindly, surrounded by collagen and more seen at the base of the nevus.[3] Out of 54 cases, type A and spindly type C cells were noted in 54 and 26 cases respectively. Presence of melanin pigment especially in upper part of the lesion was observed in 87% cases which is concurrent with other similar studies.[1,8,11] Mild degree of nuclear atypia was noted in 2 cases as also noted by Klein LJ et al in their article on nuclear atypia in benign nevus.[14] Though intranuclear pseudoinclusions and multinucleated cells may be a common finding, we found them in 1 case and 9 cases respectively.[3] We did not find any site-specific unusual histopathological feature as mentioned by other authors except in 1 case from conjunctiva which showed worrisome atypia.[3,15] Stoma showed secondary changes including artifactual cleft formation in 24 cases as also mentioned by Sagebiel RW et al.[16] Association of other secondary lesions with nevus are known.[3] We have seen 1 case each of epithelial inclusion cyst and basal cell carcinoma as also noted by other authors.[17,18]

We had 17 cases of compound nevus all of which showed junctional activity and 3 cases showed lentigenous proliferation of nevus cells in the epidermis. Both these findings were absent in all case of intradermal nevus. Except these 2 parameters, no other parameters were found to be statistically significantly different between intradermal and compound nevi. In both cases of junctional nevus, tumor cells show junctional activity and bulged into the underlying dermis which showed inflammation and clefting.[19] We did not see any mitosis and necrosis in any of the cases as expected, though mitoses have been found in benign nevi by some authors.[20,21]

CONCLUSION

In the present study, the age range was wide and considerable numbers of patients were in their midlife or even later age group. Females were affected more than the males with head, neck and face being by far the most affected site. Commonest subtype was intradermal nevus. We found occasional mild nuclear atypia but none of our cases showed mitosis and necrosis. It is suggested that all pigmented skin lesions should be biopsied for subtyping and exact catergorization of the lesion.

Conflict of Interest: None

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