Original Article

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Pigmented Pre-malignant and Malignant Lesions of Skin with Special Reference to Atypical Presentations

Pathology Section

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ABSTRACT

Background: Cutaneous melanocytic proliferations are diverse both morphologically as well as in their behavioural patterns. Both dermatologists and pathologists regularly encounter diagnostic dilemmas while interpreting such lesions.

Aim: To study all cutaneous premalignant and malignant lesions with respect to their clinical features and histopathological findings.

Materials and Methods: A retrospective study was done in the Department of Pathology over a period of 10 years (2004-14) on all the clinically pigmented lesions that were biopsied or excised. Out of these only premalignant and malignant melanocytic lesions were analysed with respect to their important clinical and histologic features. Immunohistochemistry was carried out using HMB-45 and S-100 where indicated.

Results: A total of 338 skin cancers were reported, out of these 27, 7.9% were cutaneous malignant melanoma. Premalignant lesions were 33. The mean age for premalignant lesions and melanomas was 43 years and 50.7 years respectively with a male predominance in both groups. The sole of foot/ankle was the most common site of involvement by melanoma (n=8,29.6%) while sun exposed sites like face and scalp were common sites for development of premalignant lesions like dysplastic nevi, lentigo simplex, pigmented seborrheic keratosis and Bowens disease. One case presented as post-traumatic scar tissue which turned out to be desmoplastic melanoma. One case of amelanotic melanoma presented as recurrent painful penile ulcers. Both cases were confirmed on Immunohistochemistry.

Conclusion: All pigmented lesions should be regarded as tumours of uncertain malignant potential and treated with complete excision if possible with long term follow up.

Keywords: Cutaneous, Malignant melanoma, Pigmented lesions, Premalignant

INTRODUCTION

Malignant melanoma accounts for only 4% of all skin cancers however it is responsible for >75% of all skin cancer related deaths world-wide [1,2]. It is mostly seen in adults with only 2% melanomas occurring in persons younger than 20 years of age and 0.3% in children <14 years old [3]. All the pigmented lesions are assessed for being potentially malignant by ABCDE mnemonic which takes into account asymmetry, border irregularities, colour variation, diameter >5mm and evolution. Risk factors for developing melanomas are both genetic and environmental, specially sensitivity to sun, light coloured skin, excessive sun exposure, history of skin cancer, family history of melanoma, presence of multiple melanocytic nevi, dysplastic nevi and xeroderma pigmentosum [4]. Cutaneous malignant melanomas can occur de novo or in a pre-existing nevus, therefore close examination of all nevi is recommended [5]. Early detection plays a strong role in treating the disease and reducing mortality because only 14% of patients with metastatic disease survive beyond 5 years [6,7]. Complete excision of the lesion is the definitive treatment; however, postexcision treatment needs to be individualized.

Since Cutaneous Malignant Melanoma (CMM) is seen usually in light skinned western population, there are very few studies from India. The present study will highlight the incidence of pigmented lesions and CMM in patients presenting to a medical college hospital and tertiary referral centre of Northern India.

AIM

We aimed to estimate the hospital based prevalence of all cutaneous pigmented premalignant and malignant lesions. All these lesions are discussed with respect to their clinical features and histopathological findings.

MATERIALS AND METHODS

All the clinically pigmented skin lesions that were biopsied over a 10 year period (2004-2014) were studied retrospectively in the Department of Pathology. Of these only the premalignant pigmented lesions and cutaneous malignant melanomas were included in this study. The demographic characteristic of the patient and the presenting complains; the site of the lesion, its multicentricity, and duration were recorded from the hospital records.

Melanoma was determined according to Clark with the following subtypes: Superficial Spreading (SS), Nodular Melanoma (NM), Lentigo Malignant Melanoma (LMM) and Acral Lentiginous (ALM). Main histological parameters that were described were tumour ulceration, Breslows depth of invasion in mm, mitotic activity (>2/10HPF), ulceration and tumour associated lymphocytic response. Immunohistochemistry (IHC) using S-100 and HMB-45 antibody (Biogenex) was carried out on 4 cases preliminarily reported as dermatofibrosarcoma protruberans (n=2) and small round cell tumour (n=2). Supported by IHC, the cases were reported as desmoplastic and amelanotic melanomas respectively.

RESULTS

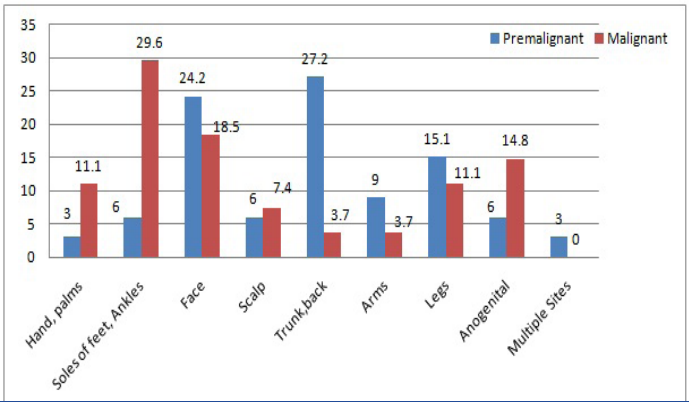
Over a duration of 10 years (June 2004-June 2014), 27 cases of cutaneous malignant melanomas were diagnosed out of a total of 338 skin cancers, thereby establishing the incidence of CMM to be 7.9% in our hospital. Pigmented premalignant lesions (n =33) were diagnosed by the clinical ABCDE mnemonic and histological WHO grade. The mean age for premalignant lesions was 43 years with a male to female ratio of 1.3:1 [Table/Fig-1]. Mean age for melanomas was 50.7 years with a male predominance (male: female =2.5:1) [Table/Fig-2]. The soles of feet and ankle were the most common site of development of CMM with 29.6% cases reported from this

Serial No.	Diagnosis	Mean Age (Range) years	M:F	No. of cases (%)
1	Dysplastic Nevus	59 (39-79)	1:1	4 (12.1)
2	Compound Nevus	42 (18-66)	1:2	10 (30.3)
3	Lentigo Simplex	28 (12-44)	1:2	6 (18.1)
4	Pigmented seborrheic keratosis	38 (21-55)	2.5:1	8 (24.2)
5	Bowen's disease	48 (32-64)	4:1	5 (15.1)

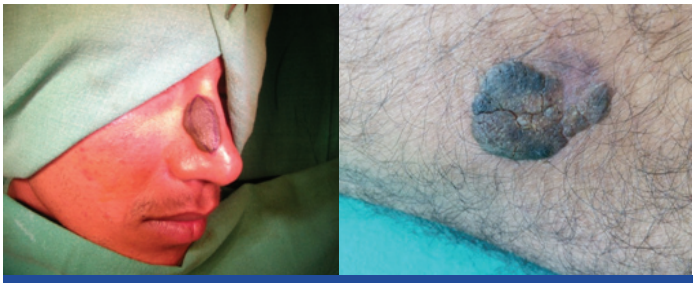
[Table/Fig-1]: Pigmented premalignant skin lesions (n=33)

Serial No.	Histologic type	Mean Age (Range) years	M:F	No. of cases (%)
1	Nodular	57 (46-68)	2:1	10 (37)
2	Acral lentiginous	61 (50-72)	3:1	8 (29.6)
3	Superficial Spreading	60 (37-83)	1:1	2 (7.4)
4	Lentigo maligna	63 (45-81)	1:1	2 (7.4)
5	Desmoplastic	46 (40-52)	2:0	2 (7.4)
6	Amelanotic melanoma	35 (31-39)	1:1	2 (7.4)
7	Melanoma arising from blue nevus	33	0:1	1 (3.7)

[Table/Fig-2]: Cutaneous malignant melanomas (n=27)

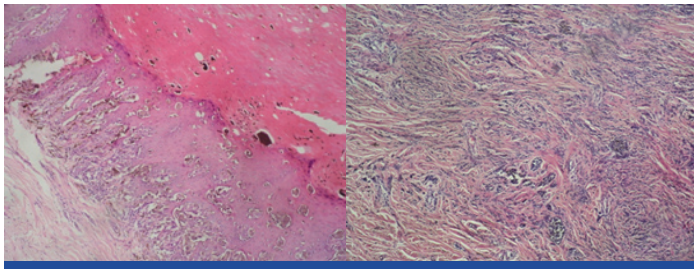


[Table/Fig-3]: Site wise distribution of pre malignant lesions and malignant melanomas (numbers represent percentages)

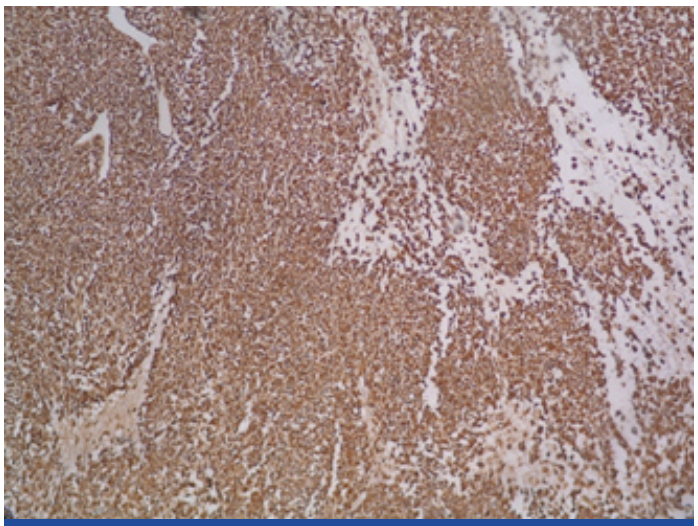


[Table/Fig-4]: Pigmented large nevus on face. **[Table/Fig-5]:** Bowens disease on lower limb

site; while trunk and back were seen in 27.5% cases of premalignant lesions, followed by face (24.2%) and scalp (6%) [Table/Fig-3-5]. Duration of symptoms ranged from 1 month to 18 years. Tumour ulceration was reported in 11 cases (40.7%), most of them were of Nodular type. Mixed population of epithelioid and spindle cells was the most common pattern histologically and was seen in 20/27 cases (74.1%) [Table/Fig-6]. Only spindle pattern was seen in five cases while only epithelioid pattern was present in two cases. Mitotic activity (>2/10 High Power Fields) was seen in five cases (18.5%). Breslows thickness ranged from 0.75 mm to 6.8 mm, mean thickness was 2.5mm. Most of the patients presented with Clarks level III (n=19,70.3%) followed by level IV(n=7, 25.9%), three cases each showed level I,II invasion while only one case infiltrated subcutaneous fat and qualified for Clark's level V invasion. Lymph node dissection was part of the surgical procedure in only 11/27 cases, out of which tumour metastasis without perinodal extension



[Table/Fig-6]: Malignant Melanoma on sole of foot showing predominantly radial growth phase (H&E: 200X:) **[Table/Fig-7]:** Desmoplastic melanoma showing tumour nests surrounded by dense fibrosis (H&E: 100X:)



[Table/Fig-8]: Immunohistochemistry: 200X: HMB-45 positivity in a case of amelanotic melanoma

was seen in six patients (22.2%). Systemic metastasis to liver was seen in one patient. One case presented with a thick scar on his right arm. He traced his scar formation to a fall at home. Wide local excision of scar tissue was done and sent for microscopy where it was diagnosed as desmoplastic malignant melanoma [Table/Fig-7]. Another case of amelanotic melanoma was seen in a middle aged male patient who presented with recurrent painful penile ulcers with right inguinal lymphadenopathy. All the cases were confirmed on immunohistochemistry (HMB-45+, S-100+) [Table/Fig-8]. Postprocedure follow-up records of 1-month duration could be retrieved; long-term follow up was not well documented in most of the cases.

DISCUSSION

Cutaneous malignant melanomas (CMM) can occur denovo or in a pre existent nevus. Studies have shown that the presence of dysplastic nevi considerably increases the risk of developing melanomas, which shows that these lesions are important risk markers besides being precursors to the disease [7]. Early detection has contributed greatly in improving the survival rate. The average estimated 5-year survival in developed countries being 73% and 56% in developing countries. The estimated world average is 69% [4].

The ABCD mnemonic for pigmented skin lesions was first devised in 1985 [8] and was modified in 2004 with the addition of 'E' to evolving lesions. ABCD stands for border irregularity, colour variation and diameter. The newly added 'E' or evolution of a lesion has been shown in some studies to be the most specific finding that may indicate melanoma [9]. The "ugly duckling sign" is another new addition to the terms used in describing melanomas. This is based on the fact that a melanoma may look different from other surrounding moles [10].

Any suspicious pigmented lesion should be biopsied. Methods of biopsy can be deep shave, punch and excisional. More important than the type of procedure is the depth of biopsy. Biopsy should be deep enough so that histologic depth of penetration of lesion

known as Breslows depth can be evaluated. This constitutes the most important prognostic parameter in evaluating the primary tumour [11,12]. Staging of melanoma is based on a combination of histologic and clinical features [13]. Breslows depth, ulceration and mitotic rate are three main features in the staging and ultimate prognosis of a patient's disease. Although presence of tumour ulceration increases the stage of a specific tumour, the Breslow depth and mitotic rate are the most powerful predictors of survival [13]. Dermoscopy as an aid to clinical features has shown to significantly increase the accuracy of diagnosis by 10 to 27% [11]. Dermoscopy was not done however in any of our patients. Saida et al., observed glaborous skin as the most common location for melanoma (50%) among the non-white Japanese population [14]. In our study, the soles of feet and the ankles were involved in 24.2% cases while trunk and back were the preferred site of involvement in 27.5% cases of premalignant lesions, followed by face (29.6%) and scalp (6%) .

Nodular melanomas were the most common type of CMM in our study as also found in the study by Chopra et al., [15]. These tumours do not have a radial growth phase and typically present as blue black nodules. Most of our patients presented with ulceration, bleeding and rapidly growing lesion. Acral lentiginous melanoma was the second most common type in our study however Khandpur et al., found this type of melanoma to be rare [16]. Our findings were similar to Vayer et al., who found this subtype of melanoma to be common [17]. Superficial spreading melanomas accounted for only 7.4% cases in our study while that by Mukhopadhyay et al., in Eastern India showed this type of CMM to be the commonest [18]. In our study, melanomas were preceded by a long standing indolent lesion in 33.3% cases as compared to another study in India by Sharma et al., where the incidence was 26% [19]. Most slow growing melanomas in our study were of Lentigo Maligna type.

Association of occurrence of melanoma with congenital nevus has not been validated; all the dysplastic nevi in our study too were sporadic. No case of familial dysplastic nevus was seen which carries a higher risk of transformation to malignant nevus. Compound nevi with focal atypia was the major group of premalignant skin lesion in our study (n=10, 30%).

Distant metastasis is commonly found in the liver, lungs, gastrointestinal tract, bone and central nervous system. In our series only one patient had visceral metastasis to liver at the time of presentation. Treatment of melanoma requires multimodality approach involving surgery, chemotherapy, radiotherapy and immunotherapy. Surgery includes optimum resection of the primary, lymph node dissection (LND), sentinel lymph node biopsy (SLNB) and resection of metastasis in selected cases. At many institutions SLNB has replaced elective LND and is done as a supplement to local excision to prognosticate the patients [20].

CONCLUSION

The high incidence of cutaneous malignant melanoma in our study cannot be extrapolated to the general population as the cases have been compiled from a tertiary center leading to a selection bias. However, high intensity sun exposure in this part of the world may have somewhat contributed to the prevalence. Long standing indolent lesions that occurred in a third of our cases reiterates detecting premalignant and malignant lesions requires improved screening and diagnostic practices.

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