

Clinical and Histopathological Characteristics of Malignant Melanoma of the Skin in Tertiary Care Centre

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Abstract: *The present study was a retrospective and prospective study of skin tumours during the period September 2004 to September 2011. Total 133 cases presented as skin tumours of these 53 cases (39.84%) were histologically diagnosed as benign and 80 cases (60.16%) were diagnosed as malignant lesions. The ratio of benign to malignant skin tumours was 0.66:1 indicating predominance of malignant lesions. Total 15405 specimens were received in the histopathology section during the study period from September 2004 to September 2011. Out of these 3200 were diagnosed as cancers of various sites in the body and cancers of skin accounted for 80(2.5 %) cases. In the present study the most common malignancy was squamous cell carcinoma with occurrence of 46.25% cases of total skin malignancies followed by basal cell carcinoma (26.25%), verrucous carcinoma (5%), adnexal carcinoma (7.5%) and malignant melanoma (11.25%) in the present study malignant melanoma was common in females, 33.34% of cases were grade 3, (44.4%) of cases the lesions were located over extremities.*

Keywords: skin tumours, malignant lesions, cancers, carcinoma.

1. Introduction

Understanding the normal histology of skin is essential in recognizing cutaneous pathology. The histology of the skin is amazingly complex. The color of the skin is influenced by the amount of melanin present in the skin.¹ Melanomas arise from epidermis and these may be in situ or may be invasive. All major types of melanoma originate almost invariably from melanocytes at the epidermal-dermal junction and can occur in pre-existing melanocytic nevi.² Malignant melanoma of skin is rare and has lower incidence among Indians.³ Melanomas show varied appearance which may mimic carcinomas, sarcomas, stromal tumours, lymphomas, plasmacytomas and germ cell tumours.

Incidence of Malignant melanoma of skin has increased dramatically over the last several decades at least in part as a result of increasing sun exposure necessitating vigorous surveillance.⁴ Malignant melanoma of skin at time pose a great challenge to surgeons as some of benign tumours can be confused with malignant tumours and it is vitally important to intervene as some can become metastatic resulting in morbidity and mortality. Most of the time clinical diagnosis may not be accurate because of similarity in gross appearance.⁴

Even sophisticated investigations such as computerized tomography (CT) and tumour markers may not be useful in skin tumours. In such cases histopathology alone remains a diagnostic tool.²

Melanomas arise from epidermis and these may be in situ or may be invasive.

2. Review of Literature

All major types of melanoma originate almost invariably from melanocytes at the epidermal-dermal junction and can occur in pre-existing melanocytic nevi.²

Superficial spreading melanoma²

Superficial spreading melanoma, also referred to as pagetoid melanoma is the most frequent form of melanoma (about 70% of all cases), and may therefore be regarded as the common or prototypic form of melanoma. The most frequently involved sites are the upper back, especially in men, and the lower legs, especially in women. Histologically, uniformly rounded, large melanocytes are scattered in pagetoid pattern throughout the epidermis and lie in nests in lower epidermis and singly in upper epidermis.

Lentigo maligna melanoma

Previously referred to as melanosis circumscripta preblastomatorum of Dubreuilh and also as melanotic freckle of Hutchinson. Lentigo maligna occurs on sun exposed cutaneous surfaces of elderly, commonly over the face and rarely over the forearms and lower legs accounting for 10% of melanomas.

Lentigo maligna melanoma develops from lentigo-maligna. The lesion starts as a pigmented macule that gradually extends peripherally and may attain several diameters with no induration. Invasive malignancy is characterised by thickening of the lesion with the development of elevated plaques or discrete nodules. Histologically, in the early stage,

hyperpigmentation of basal layer, with some areas showing extension to higher areas of epidermis is seen.

Acral lentiginous melanoma

Acral melanoma occurs on the hairless skin of the palms and soles and in the ungual and periungual regions, the soles being the most common site. It shows irregular, uneven pigmentation with definite borders.

Histologically, there is a radial growth phase which is characterised by a lentiginous pattern of atypical melanocytes, with some nesting.⁵The histologic picture in advanced cases is similar to that of lentigo maligna except for irregular acanthosis.²

Nodular melanoma²

Nodular melanoma by definition shows only tumorigenic vertical growth and, because of this, has a poorer prognosis. A nodular melanoma starts as an elevated, variably pigmented papule that increases in size quite rapidly to become a nodule, and often undergoes ulceration.

Histopathology

Nodular melanoma and common vertical growth phase melanoma: In a typical tumorigenic melanoma, there is contiguous proliferation of neoplastic melanocytes in the dermis forming a tumor mass that is larger than the largest nest in the overlying epidermis. The tumor mass is comprised of uniformly atypical cytologically malignant and mitotically active cells usually growing in confluent nests or in sheets. Two major types of cells are recognized, an epithelioid and a spindle-shaped cell type. Many tumors show both types of cells, but usually one type predominates.

Desmoplastic melanoma

Desmoplastic melanomas are often non-pigmented and stubbornly recurrent usually seen in the head and neck region.⁵

Breslow thickness of tumour

It is the single most important factor in predicting survival of patients. The thickness of tumour is measured from granular layer to the deepest tumour cell. Melanomas <0.76mm are thin melanomas and generally have excellent prognosis.⁵

Clark's level of invasion:^{2,5} Has a prognostic and descriptive value.

Level 1 – confined to epidermis

Level 2 – Invasion into papillary dermis

Level 3 – Invasion into papillary and reticular dermal interphase

Level 4 – Invasion into reticular dermis

Level 5 – Invasion into subcutaneous fat.

Prognostic factors

Melanoma thickness, body site, histological type of the melanoma, gender of the patient and ulceration are important indicators of patient prognosis.³ Generally, **older patients** do

less well than younger patients for the same tumour thickness, while females do better than males.⁶ **Superficial spreading** melanomas generally have a better prognosis compared with other histological subtypes, because they usually have a thin Breslow thickness.⁶

- The prognosis is best when the **mitotic rate** is zero, and worst when the rate is greater than six mitoses per square millimeter. The presence of mitoses may also be useful in identifying thin melanomas with a propensity to metastasize.⁶
- The **lymphocytic infiltrate** tends to diminish with increasing thickness of the primary melanoma, and is usually scant in deeply invasive tumors In the AJCC staging data.⁶
- **Ulceration** in stage I reduces the 5-year survival rate from 88% to 83%.
- The presence of either type of **vascular involvement** significantly reduced the survival associated with melanoma.⁶
- The presence of satellites is a significant staging attribute in the current AJCC staging system, defining a lesion as stage IV, with a poor prognosis.⁶
- Among the favorable **clinical factors** is location of the tumor on the hair-bearing portions of the limbs, in contrast to location on the trunk, neck and head, or palms and soles.
- Among the **histologic factors**: The prognosis is the same for nodular and other types of melanoma of similar thickness, and in multivariable analyses, nodular type.

Breslow's thickness: If only one attribute is known, thickness is the single strongest prognostic attribute for melanoma.⁶

Clark's levels of invasion: First described in 1967, these attributes along with Breslow's thickness measurements are the best known prognostic attributes for melanoma.⁶

3. Materials and Methods

The present study was carried out in the department of pathology in a tertiary care centre. This study included tumours of epidermis along with melanocytic tumours and adnexal tumours of skin including secondaries without restricting the study to any particular age limit. Mesenchymal tumours of skin, haematological tumours of skin, neural tumours of skin, nonneoplastic lesions of skin and all tumours arising from mucosal area of mucocutaneous junction such as glans penis and eyelid margin were excluded. The study was prospective (2years) as well as retrospective (5 years) and was done during the period of September 2004 to September 2011 i.e.7 years. Data for retrospective study was obtained from departmental records, tissue blocks and slides. Data for prospective study was obtained from clinical records, tissue specimens, tissue blocks and slides Clinical details were obtained and maintained according to the proforma.

All the biopsies and resected specimens received in the histopathology section were immediately fixed in 10% formalin for 24 hours. Gross features of the specimen were noted. Multiple sections of the specimen were taken. Then they were processed and embedded in paraffin wax. Three-

five microns thick sections were prepared and then stained with Haematoxylin & Eosin.

Detailed study of the sections was performed under the light microscope and then the final diagnosis was given.

Ethical clearance has been obtained from Ethical committee of institution.

Following Statistical methods were applied in the present study.

- 1) Number and percentage
- 2) Descriptive statistics

Malignant tumours	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
SCC	-	-	2	1	2	7	16	8	1	-	37
Verrucous Carcinoma	-	-	-	1	1	1	1	-	-	-	4
BCC	-	1	-	-	3	4	8	4	1	-	21
Malignant melanoma	-	-	-	1	1	1	4	1	-	1	9
Adnexal carcinoma	-	-	-	-	1	2	3	-	-	-	6
Secondaries	-	-	-	-	-	-	2	1	-	-	3
Total	-	1	2	3	8	15	34	14	2	1	80

4. Results

Total 133 cases presented as skin tumours of these 53 cases (39.84%) were histologically diagnosed as benign and 80 cases (60.16%) were diagnosed as malignant lesions. The ratio of benign to malignant skin tumours was 0.66:1 indicating predominance of malignant lesions.

Table 1: Distribution of benign and malignant tumours of skin

	Number and percentage of epidermal tumours	Number and percentage of adnexal tumours	Number and percentage of melanocytic tumours	Total Number and percentage
Benign	11 (20.75%)	9(54.71%)	3(24.54%)	53(39.84%)
Malignant – Primary	62(80.51%)	6 (7.81%)	9 (11.68%)	77(57.89%)
Malignant – Secondaries	3 (2.27%)	-	-	3(2.27%)
Total No of cases	6(57.14%)	35(26.32%)	2(16.54%)	133

Out of 133 skin tumours, malignant lesions accounted for 80 (60.16%) cases and benign lesion constituted 53 (39.84%) cases. Out of 80 malignant skin tumours malignant epidermal lesions were the most common lesions comprising of 62(80.51%) cases followed by malignant adnexal tumours 6(7.81%) cases, malignant melanoma 9 (11.68%) cases and 3(2.27%) cases were of metastatic lesions.

4.1 Malignant Melanoma

As shown in the above table in various studies, malignant melanoma accounted for 8.69% to 26.1% of all skin cancers. In the present study the frequency of occurrence of malignant melanoma was (11.68%) malignant neoplasms of skin which is comparable with various other studies of Chakravorthy and Dutta et al⁷ (1968) and Paymaster et al⁹ (1972). However DeoSV et al⁸ (2005) noted higher frequency of frequency of occurrence of malignant melanoma in his study.

Table 3: Comparison of frequency of occurrence of malignant melanoma in various studies

Authors	Sex	
	Male	Female
Sampat and Sirsut et al ³ (1966) (n=74)	71.8%	28.2%
Katalinic A et al ¹⁰ (2003) (n=10)	56.7%	43.3%
Talley and Harrison et al ¹¹ (1998)(n=119)	36.1%	63.9%
Present study (2011) (n=9)	33.3%	66.7%

Table 4: Comparison of sex distribution of malignant melanoma

Site	Sampat and Sirsut et al ³ (1966)	Chitkara et al ⁹ (1972)	Mukhopadhyay S et al ¹² (2008)	Present study (2011)
Head and neck	13%	20%	10%	22.3%
Trunk	5%	-	10%	33.3%
Extremities	82%	80%	80%	44.4%
Total No of cases	74	10	10	9

As shown in the table no.4 in the present study malignant melanoma was common in females which was consistent with the findings of Talley and Harrison et al⁹¹ (1998). Sampat and Sirsut et al³ (1966) and Katalinic A et al¹⁰ (2003) found higher frequency of malignant melanoma in males, as males are more exposed to sun light

Table 5: Comparison of age distribution of malignant melanoma

Age in years	Katalinic A et al ¹⁰ (2008) (n=10)	Mukhopadhyay S et al ¹² (2003) (n=10)	Present study (2011) (n=9)
0-19	1.2%	-	-
20-39	21.4%	18.2%	11.11%
40-59	31.4%	27.3%	22.22%
60-79	38.8%	45.5%	55.56%
80+	7.3%	9%	11.11%

In the present study most of cases (55.56%) occurred in the age range of 60-79 years. This observation is similar to observation to the study of Katalinic A et al¹⁰ and Mukhopadhyay S et al¹² as shown in the table no.3

The table no.3 shows frequency of cases of malignant melanoma according to site of occurrence.

Author	Melanoma	Frequency of malignant melanoma
Chakravorthy and Dutta et al ⁷ (1968) (n=10)		8.69%
DeoSV et al ⁸ (2005) (n=20)		26.1%
Paymaster et al ⁹ (1972) (n=102)		8.7%
Present study (2011) (n=80)		11.68%

In majority (44.4%) of cases the lesions were located over extremities. Sampat and Sirsut et al³ (1966), Mukhopadhyay S et al¹² (2008) and Chitkara et al⁹ (1972) also noted similar findings. In the present study there were nine cases of malignant melanoma. Out of these nine cases 4 lesions were located on the foot. Sampat and Sirsut et al³ (1966) also found foot as the most common location (in 54% cases) of malignant melanoma.

Table 7: Comparison of Clark's grading of malignant melanoma

Grade	Sampat and Sirsut ³ et al (1966) (n=66)		Present study 2011 (n=9)	
	No	%	No	%
Grade 1	2	18.2	1	11.11
Grade 2	2	18.2	2	22.22
Grade 3	4	36.4	3	33.34
Grade 4	2	18.2	2	22.22
Grade 5	1	9	1	11.11
Total No of cases	11	100	9	100

In the present study 33.34% of cases were grade 3 and 22.22% of cases were grade 2 and grade 4. In the study by Sampat and Sirsut³ et al (1966) majority of cases were grade 3 (36.4%), followed by 18.2% each of grade 1, grade 2 and grade 4 and 9% of grade 5. So our findings are comparable with Sampat and Sirsut³ et al (1966).

5. Discussion

Malignant melanomas constitute a small but significant proportion of patients with cancer. Malignant melanomas are an ideal subject for study from clinical and morphological point of view and so ubiquitous that they can affect people of all ages. A histopathological study of 9 cases of Malignant melanomas was carried out in Department of Pathology, over a period of 7 years. In the present study most of cases (55.56%) occurred in the age range of 60-79 years, 44.4% of cases the lesions were located over extremities, 55.56% occurred in the age range of 60-79 years Sampat and Sirsut et al³ (1966), Mukhopadhyay S et al¹² (2008) and Chitkara et al⁹ (1972) also noted similar findings. In the present study malignant melanoma was common in females which were consistent with the findings of Talley and Harrison et al¹¹ (1998).

Sampat and Sirsut et al³ (1966) and Katalinic A et al¹⁰ (2003) found higher frequency of malignant melanoma in males, as males are more exposed to sun light. The prognostic factors in primary skin melanoma were studied by Clark (1969) and by Breslow (1970) who observed that tumor thickness was an important indicator of behavior. As according, 33.34% of cases were grade 3, which carried somewhat intermediate prognosis.

6. Conclusion

Malignant melanomas are the most lethal cancers of the skin that occur mainly in fair-skinned people in areas exposed to sun. Malignant melanoma is notorious for the great variability of its histopathological presentation and may mimic almost any malignant tumor. The common denominator of most, although not all, tumors is the presence of melanin pigment in tumor cells. The pigment may be dispersed and finely or coarsely granular, obscuring other features of the cells. Still, the diagnosis must be based on malignant features of the cells because the presence of pigment alone may be misleading. The chief culprit is melanin pigment phagocytized by macrophages, as this may occur in a variety of skin disorders not related to malignant melanoma. Basal cell carcinomas and other lesions may occasionally shed pigment-containing cancer cells.

In the absence of pigment, the cells of amelanotic malignant melanoma may be mistaken for metastatic carcinoma or even large cell lymphoma. The prognostic factors in primary skin melanoma were studied by Clark et al (1969) and by Breslow (1970) who observed that tumor thickness was an important indicator of behavior. The present study emphasizes the various patterns of malignant melanomas in this geographic location in and around city. It is evident that early diagnosis of malignant melanoma may be of critical value to the patient. Therefore, most clinically suspicious pigmented skin lesions are excised to determine their nature and, if malignant, their stage.

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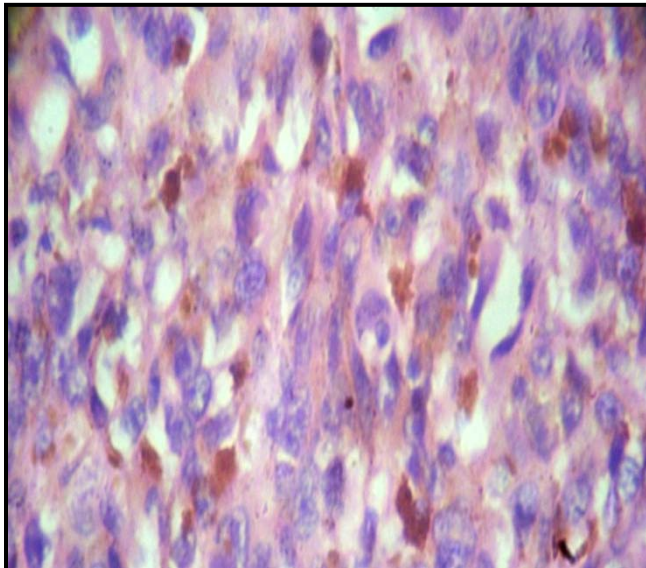


Figure 1: Malignant melanoma (400x, H&E)



Figure 2: Malignant melanoma with inguinal lymph node metastasis

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