

ORIGINAL ARTICLE

Cutaneous malignant melanoma: clinical and histopathological review of cases in a Malaysian tertiary referral centre

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Abstract

Melanoma is a lethal skin cancer that occurs predominantly among Caucasians. In Malaysia, the incidence of melanoma is low. This is a retrospective study of clinical and histopathological features of patients with cutaneous melanoma who were seen at the University Malaya Medical Centre from 1998 to 2008. Thirty-two patients with cutaneous melanoma were recorded during that period. Of these, 24 had sought treatment at the onset of disease at our centre. Chinese patients constituted the largest group (19 cases). The median age of these 24 patients at the time of presentation was 62 years. 16 patients had melanoma involving the lower limb with 12 affecting the sole of the foot. None had melanoma arising from the face. Histopathology showed nodular melanoma in 22 cases (91.6%), with superficial spreading and acral lentiginous melanoma diagnosed in 1 case each. The majority of patients (62.5%) were found to be in Stage III of the disease at the time of diagnosis.

Keywords: melanoma, cutaneous melanoma, malignant skin tumour

INTRODUCTION

The skin is the most common primary site of melanoma. Melanoma occurs more frequently in fair-skinned Caucasians, and Australia has the highest incidence in the world.¹ It is less common among Asians.^{2,3} The prevalence rate in Malaysia is about 0.5 per 100,000 for males and 0.3 per 100,000 for females.⁴

Although the incidence of cutaneous melanoma is increasing in Caucasians, the mortality has leveled off.⁵ This is attributed to the earlier diagnosis of melanoma, which can now be detected in its early stage with the use of dermatoscopy,⁶ as well as awareness of the detrimental effects of sunlight.⁷ Racial differences are noted in the incidence and predilection sites of melanoma. Acral site is the most common site in Asian patients.⁸ It has been reported that melanoma, in particular, acral lentiginous melanoma has been misdiagnosed as benign lesions.⁹ In one study, the misdiagnosis rate was 33%.¹⁰ Cutaneous melanoma is associated with high mortality and early diagnosis and treatment are important in improving the survival rates.¹¹

There are 4 major subtypes of melanoma based on the growth pattern: lentigo maligna melanoma,

superficial spreading melanoma, nodular melanoma¹² and acral lentiginous melanoma.¹³ Acral lentiginous melanoma is first introduced by Reed as a type of melanoma occurring in the palms, soles and subungual sites, with initial radial growth phase resembling lentigo maligna melanoma.¹³ The term acral melanoma is used for melanomas located on the acral sites.

The main histological prognostic parameters in melanoma include level of invasion of tumour,¹² and tumour thickness.¹⁴

The purpose of this study is to review the clinical and pathological features of cutaneous melanoma cases seen in a tertiary centre in Malaysia over a period of eleven years. This is the largest study of cutaneous melanoma from Peninsular Malaysia in the last twenty years. The previous study was also conducted in the same institution.¹⁵

MATERIALS AND METHODS

Records of cutaneous melanoma cases filed at the Department of Pathology, University Malaya Medical Centre over the 11-year period from January 1998 to December 2008 were retrieved. The histological slides were reviewed, and the

parameters studied were the types of melanoma, thickness of the tumour as recommended by Breslow¹⁴ using an ocular micrometer, level of tumour invasion according to Clark's method.¹² and presence of an ulcer. Special stains such melanin, S-100 protein and HMB45 were performed in some cases at the time of histological diagnosis. Information about clinical presentation, demographic data and treatment were obtained from the clinical records. The staging was based on TNM classification of melanoma.¹⁶

RESULTS

A total of 32 patients had histologically proven melanoma during the period of study. The Chinese constituted the largest group (19 cases), followed by Malay (10 cases) and Indian (3 cases) patients. The male to female ratio was 1:1.4.

Eight patients had initial excision of the lesion elsewhere. The primary sites of the tumours in these patients were the arm (1 case), hand (1 case), abdominal wall (1 case), buttock (1 case), thigh (2 cases), foot (1 case) and an unknown site (1 case). The treatment given to these patients was excision of the recurrent skin tumour (2 cases) and enlarged lymph nodes (4 cases). One patient had hepatic lobectomy, and another had removal of the small intestine for metastatic melanoma. One patient had melanoma of the thigh 15 years prior to the present recurrent lesion. Five patients died within 1 year and two patients were lost to follow-up. One patient with recurrent lesion is still alive at one year to date.

From 1998 to 2008, 24 patients presented for the first time to our centre for treatment of melanoma. The presenting clinical symptom was either an ulcer, or an enlarging skin lesion. The ages of these patients ranged from 22 to 88 years of age, with a median age of 62 years. The duration of symptoms was less than two years in 13 cases (54.2%), and 15 patients (62.5 %) had primary lesions as well enlarged regional nodes at the time of presentation.

Staging of patients revealed the following: Stage 0 (1 case), Stage 1 (3 cases), Stage II (5 cases) and Stage III (15 cases). The lower extremity was the most common site (16 cases) with the main location being the sole (11 of 16 cases). The acral site (Figure 1) was the most common site affected (13 cases). The other sites included plantar (11 cases), dorsum of foot (1 case) and subungual area of the thumb (1 case). The primary lesion was excised in all 24



FIG. 1: The acral site was the most common site for cutaneous melanoma

cases and in 13 cases the regional lymph nodes were also removed.

Deep X-ray therapy for recurrent lesions (2 cases) and chemotherapy for development of metastatic lesions (2 cases) was given. 5 patients died within 1 years of diagnosis and a total of 13 were dead within the first 3 years. Widespread metastases were the cause of the death in 13 cases and cardiac failure in 2 cases. A summary of the clinical features and outcome are shown in Tables 1 & 2.

TABLE 1: Clinical features of 24 cases of cutaneous melanoma

Clinical features	No of cases
Duration of symptoms (year)	
< 1	8
1-2	6
>2-3	3
>3-5	3
> 10	1
Not known	3
TOTAL	24
Site of lesion	
Lower extremity	16
i. Sole = 11	
ii. Dorsum of foot = 1	
iii. Leg = 3	
Upper extremity	6
i. Nail bed = 1	
Trunk	2
TOTAL	24

TABLE 2: Tumour stage and outcome in 24 patients with cutaneous melanoma

Outcome	Stage			
	0	I	II	III
Still alive to date (no of years from diagnosis)				
< 1		1		2
1-2				
2-3			1	
5	1			
Died (within no of years)				
< 1			1	4
1-2		1		2
2-3		1		4
Lost to follow-up			3	3
TOTAL	1	3	5	15

PATHOLOGY

The tumours were of nodular type (22 cases), superficial spreading type (1 case) and acral lentiginous type (1 case), the last involving the nail bed. In 12 cases, features of acral lentiginous melanoma (Figure 2) were found adjacent to nodular melanoma arising in the sole and dorsum of foot. The tumour had invaded the reticular dermis in 11 cases and subcutaneous fat in 6 cases. The thickness of melanoma was more than 4 mm in 14 cases (58.3%). Ulceration of the skin over the tumour was noted in 10 cases (41.6%). Melanin pigment deposition was seen (Figure 3) in the majority of cases (23 cases). In one case of amelanotic melanoma, the neoplastic cells were positive for S-100 protein and HMB 45. There was no desmoplastic melanoma in the study. The histological features are summarised in Table 3.

DISCUSSION

The present report on cutaneous melanoma is the largest study in Peninsular Malaysia for the past twenty years. Melanoma is not a common cancer in Malaysia and the National Cancer Registry data in 2003 showed that the incidence of melanoma per 100,000 population is 0.4. The incidence of non-melanoma skin cancers is 5.1.⁴ The average age of patients with cutaneous melanoma at the time of initial presentation in

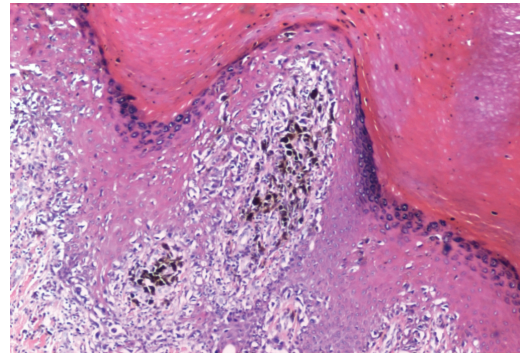


FIG. 2: Features of acral lentiginous type cutaneous melanoma showing malignant tumour cells infiltrating the epidermis (H&E, x 40)

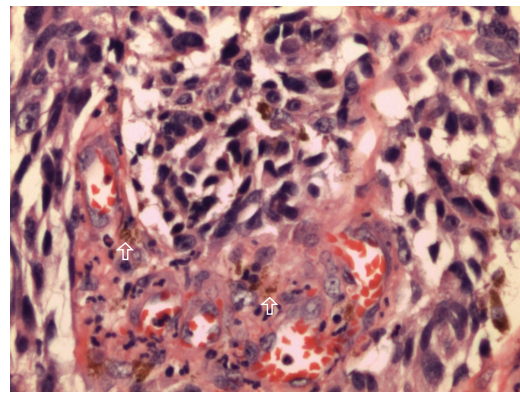


FIG. 3: Melanin pigment (↑) in tumour cells (H&E, x200)

TABLE 3: Summary of histopathological features of 24 cases of cutaneous melanoma

Features		No of cases	%
Level of tumour invasion	I	1	4.2
	II	3	12.5
	III	3	12.5
	IV	11	45.8
	V	6	25.0
Thickness of tumour (mm)	<0.75	5	20.9
	0.76-1.5	1	4.2
	1.5-4	4	16.6
	>4	14	58.3
Histological type	Superficial spreading	1	4.2
	Acral lentiginous	1	4.2
	Nodular	22	91.6
Ulcer	Present	10	42.0
	Absent	14	58.0
TOTAL		24	100.0

our study is 60.4 years, with a male to female ratio of 1: 1.4. These findings concur with other reports.^{2, 8}

In the majority of our patients, melanoma occurred in the extremities (91.6%). 13 patients had acral melanomas, involving the plantar site of foot (12 cases) and finger nail bed (1 case). The predilection sites of melanomas vary among races. The most common site is acral, especially amongst the Japanese¹⁷ and Chinese.² Similar observations were noted in our study. It is well known that melanoma occurrence is related to sun exposure. However, acral site is less exposed to sunlight, hence the aetiology is thought to be different.

A study of 275 cases of melanoma of the feet and hands by Green showed that sun exposure still played an important role in the cancer development at these sites. The patients in their study had higher mole counts in these regions, significant positive association with previous penetrative injury to the hands and feet and high exposure to agricultural chemicals.¹⁸ However, Kaskel *et al* did not observe any evidence of traumatic injury in the causation of melanoma at acral sites.¹⁹ In one study, it was noted that there was a high prevalence of diabetes mellitus with acral lentiginous melanoma (ALM).²⁰

The diagnosis of melanoma is based on the clinical features, with confirmation by histopathology. Awareness of melanoma has to be kept in mind when assessing pigmented lesions of the skin. Dermatoscopy has been regarded as a valuable tool in the clinical diagnosis of melanoma. Under dermatoscopy, the lesion can be enlarged 6 to 100 times. Thus the tumorous structures can be better visualized. This instrument can also be attached to a computer where digital pictures can be stored. Images of suspected lesions, before and post-biopsy, can be captured during follow-up with patients, and the subsequent images can be compared with the earlier ones in order to better visualize the disease's progress.²¹

Treatment of cutaneous melanoma is complete excision, with excision margins of 1 cm for melanoma with thickness of 1 mm or less, margins of 2 cm for melanoma with thickness greater than 2 mm²² and margins of 2 cm in disease in Stages I and II.²² Sentinel lymph node biopsy is recommended for tumour with thickness of 1 mm or more. It is also a predictor for melanoma recurrence.²³ Systemic chemotherapy, though not usually effective, is used in patients with advanced disease such as

Stage III or Stage IV. Dacarbazine is the more commonly used drug.²⁴ New treatment modalities being developed include targeted molecules and immunological approaches with monoclonal antibodies.²³

The prognosis of melanoma depends on the stage. The American Joint Committee on Cancer (AJCC) Staging¹⁶ of melanoma includes histological features such as thickness of the tumour, level of invasion and presence of ulcer.¹⁴ Studies from Europe,²⁵ as well as from Asian countries⁸ show that the survival rate depends upon the stage and that there is no difference between ALM and nodular melanoma. The 5-year survival rate of patients with ALM without metastases was 82% and this was similar to that of nodular melanoma.²⁵ The majority of patients in our study were in Stage III of the disease, with spread of the tumour to regional lymph nodes at the time of presentation (62%). Histology showed nodular melanoma (91%) and tumour thickness of more than 4mm (58.3%). One patient with Stage 0 disease is still alive at 5 years after treatment and 10 out of 15 patients in Stage III died within three years of diagnosis and treatment.

The findings of this review confirm that although melanoma is not common in Malaysia, the morbidity and mortality remain significant. All patients with pigmented skin lesions that are enlarging in size or show suspicious features like contact bleeding should seek early medical assessment and the clinicians should always keep melanoma in mind as a possible diagnosis.

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