

Malignant Melanoma Seen in a Tertiary Dermatological Centre, Singapore

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Abstract

Introduction: Primary malignant melanoma is an uncommon skin tumour in Singapore compared with the Western countries. The clinical characteristics of melanoma have been rarely reported in Asians. **Objectives:** Our purpose was to study the incidence, clinical characteristics and risk factors of biopsy proven malignant melanoma seen in a tertiary referral skin hospital. **Methods:** Case records of patients with histology proven malignant melanoma from January 1989 to December 1998 were retrieved. Patients were interviewed and a complete skin and systemic examination was performed. Data on demographics, histological types, clinical characteristics and risk factors were collated. **Results:** Between 1989 and 1998, 27 patients were diagnosed with histology proven malignant melanoma. There was a predominance of Chinese with a female to male ratio of 1.3:1. There was a mean lag period of 1.6 years to diagnosing melanoma and there is a general lack of knowledge among the local patients. Most of the lesions (89%) occurred on the extremities. Acral lentiginous melanoma (41%) and nodular melanoma (41%) were the two commonest histologic types. Of the nodular melanomas, 64% were observed in patients below 50 years (64%) while majority of the acral lentiginous melanomas occurred in those above 50 years (91%). In terms of risk factors, we reported a high prevalence of diabetes mellitus with acral lentiginous melanoma. **Conclusions:** This study highlighted interesting aspects in terms of clinical characteristics and risk factors in our local patients. It also served as a reminder of the need to raise awareness among the public and medical community of skin cancers or melanomas as they are potentially treatable if detected early.

Ann Acad Med Singapore 2001; 30:414-8

Key words: Diabetes mellitus, Melanoma, Sun sensitivity

Introduction

Unlike in Caucasians, primary malignant melanoma is an uncommon skin malignancy in Singapore. There have been little published data on cutaneous melanoma in Southeast Asia. We undertook this study to review the profile, clinical characteristics and outcome of 27 local patients seen over a 10-year period (1989 to 1998) in a major skin referral centre.

Material and Methods

The case records of 27 patients with histologically confirmed melanoma diagnosed between 1989 and 1998 at the National Skin Centre were retrospectively reviewed. Staging was done according to the American Joint Committee on cancer staging classification.¹ For staging, all patients underwent a complete physical examination and baseline investigations including a chest X-ray, full blood count, urea, electrolytes and liver function tests. Other investigations were ordered based on the guiding symptoms and signs.

The data were examined with regards to the epidermiology (age, sex, ethnic group) and the clinical characteristics of melanoma (body site, morphology, Breslow thickness in millimetres, staging, histogenic type and outcome). For patients who were no longer on regular follow up, a telephone interview was conducted to determine the progress, current clinical condition and knowledge of skin cancers (Table I).

Results

Demographic and Clinical Data (Table II)

There was a total of 27 patients diagnosed with primary cutaneous melanoma over a period of 10 years. Majority of the referrals were from primary health care physicians (65%). Other sources include self referrals (15%) and from other hospitals (20%). The referring doctor in 16 of the 27 referrals suspected melanoma. In the remaining cases, other diagnoses were suspected including melanocytic nevus, pyogenic granuloma, viral wart, dermatofibroma, seborrheic keratosis and squamous carcinoma.

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TABLE I: QUESTIONNAIRE TO ASSESS THE KNOWLEDGE OF SKIN CANCER

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|---|--|
| 1 | Did you suspect skin cancer before seeing the doctor?
(Answer: Yes/No) |
| 2 | Are you aware of the early signs of skin cancers?
(Answer: if yes, to name at least 1 early sign) |
| 3 | Are you aware of the risk factors of skin cancers?
(Answer: if yes, to name at least 1 risk factor) |
| 4 | Did you know how is skin cancer spread?
(Answer: Yes/No) |

There were 15 females and 12 males (female to male ratio of 1.3:1) of whom 25 were Chinese, 1 Malay and 1 Eurasian. The ages of the patients ranged from 15 to 83 years (median 53, mean 53.7).

Clinical evidence of disease was defined as the first time patient noticed a pigmented lesion and/or change in the behaviour of an existing mole. The local patients had clinical evidence of disease ranging from 1 month to 10 years (mean 1.6) prior to diagnosis. All patients were interviewed on their knowledge of skin cancers. On direct questioning, majority of the local patients (20/27) had little or no knowledge of skin cancers. We noticed that patients younger than 40 years tended to seek treatment earlier for suspicious growth compared with the elderly group. Six out of the 27 patients were asymptomatic at the time of diagnosis and were referred by their physicians for exclusion of skin cancers or cosmetic mole surgery. The commonest symptoms in decreasing order of frequency included bleeding (9/27), ulceration (8/27) (Fig. 1), increase in size (5/27), pain (5/27) and discolouration of nails (2/27) (Fig. 2).

Site, Morphology and Characteristics of the Melanoma (Table II)

The types of melanoma were (in decreasing order of frequency) nodular melanoma (41%), acral lentiginous (41%), melanoma *in situ* (11%) and superficial spreading types (7%). Acral lentiginous melanoma occurred more frequently in those older than 50 years (10/11; 91%) and the most common sites of occurrence were the upper and lower extremities (89%) for both sexes. In the lower extremities, 13 melanomas were found on the feet or toes and 3 on the legs. In the upper extremities, 9 were located on the arms/ forearms and 1 had lesion involving the hand.

Two patients (patients 1 and 31) had nodular melanoma arising from medium sized congenital melanocytic nevus (the sizes recorded at the time of diagnosis were 3 and 5 cm, respectively).

Risk Factors and Outcome of Melanoma (Table III)

Five patients gave a history of excessive sun exposure during their childhood or younger days. Out of the 5 local

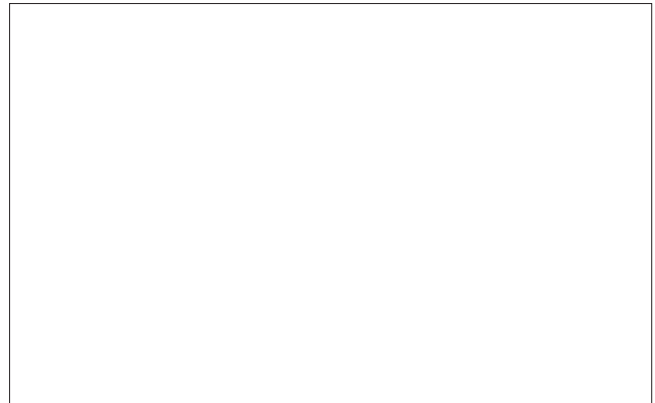


Fig. 1. Acral lentiginous melanoma presenting as a foot ulcer. Squamous cell carcinoma may have a similar appearance, but the surrounding pigmented edge indicates a pigmented tumour such as melanoma.

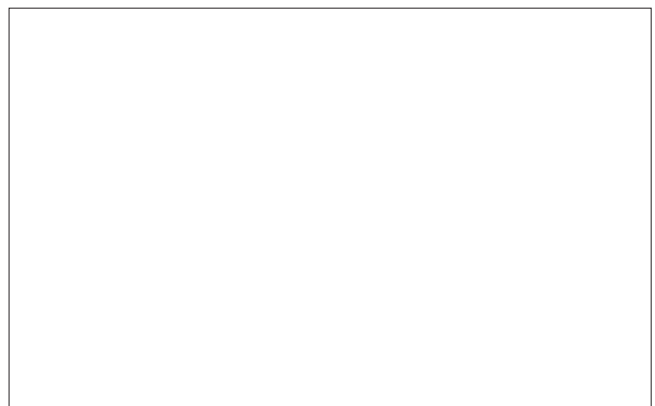


Fig. 2. Acral lentiginous melanoma with a flat, irregular pigmented patch on the adjacent skin (Hutchinson's sign).

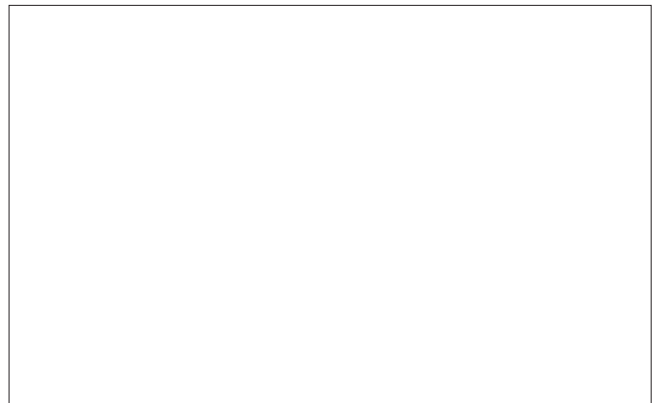


Fig. 3. Nodular melanoma arising from a congenital melanocytic nevus.

patients, 3 were mainly involved with outdoor work while the other 2 indulged in recreational outdoor activities during weekends and vacations. None of the patients regularly used sunscreen for photoprotection.

Two young patients had nodular melanomas arising from congenital melanocytic nevi on the trunk (Fig. 3). They were medium sized congenital melanocytic nevi (size ranged from 3 to 5 cm). One Chinese girl described

TABLE II: DEMOGRAPHIC AND CLINICAL DATA OF MALIGNANT MELANOMA

S/N	Age at presentation (y)	Sex	Race	Site	Duration from first clinical evidence of disease to diagnosis	Presenting symptoms	Type of malignant melanoma (MM)	Breslow thickness at initial presentation (mm)
1	15	F	C	back	5 cm since birth, gradual increase in size over 3 years	Cosmesis, gradual in size	nodular	16
2	25	F	C	L leg	1.5 y	pain	nodular	3
3	29	M	C	R arm	1 y	0	nodular	2
4	31	F	E	R arm	6 mo	increase in size	sup spreading	1.2
5	32	F	C	L arm	2 mo	0	nodular	5
6	33	M	C	back	9 mo	0	MM <i>in situ</i>	Melanoma <i>in situ</i>
7	36	M	C	R thumb	3 mo	increase in size	acral lentiginous	0.2
8	40	M	C	L arm	6 wks	0	MM <i>in situ</i>	Melanoma <i>in situ</i>
9	40	M	C	R leg	6 mo	increase in size	nodular	14
10	43	M	C	R shoulder	10 mo	increase in size	nodular	2.6
11	45	M	C	R elbow	6 mo	pain	nodular	2
12	50	F	C	L arm	2 y	0	nodular	4.8
13	52	F	C	R little toe	6 mo	0	acral lentiginous	0.825
14	53	F	C	R foot	1 y	pain, ulceration	acral lentiginous	3
15	54	F	C	R big toe	2 y	ulcer, discolouration of nailbed	acral lentiginous	2
16	58	F	C	L foot	3 mo	bleeding, ulcer	MM <i>in situ</i>	Melanoma <i>in situ</i>
17	66	F	C	L 2nd toe	2 mo	bleeding	acral lentiginous	3.8
18	68	M	C	L big toe	2 y	ulcer	acral lentiginous	4
19	69	F	C	L foot	3 mo	pain, discolouration of nailbed	acral lentiginous	6
20	70	M	Mal	R big toe	10 y	bleeding, ulcer	acral lentiginous	4.5
21	75	F	C	R arm	1 y	bleeding	nodular	3
22	75	M	C	R sole	9 mo	pain, ulcer	acral lentiginous	2
23	76	F	C	face	4 mo	bleeding	nodular	5
24	76	M	C	R big toe	2 y	bleeding, ulcer	acral lentiginous	1.8
25	76	M	C	L sole	10 y	pain, bleeding, ulcer	acral lentiginous	5
26	80	F	C	R upper arm	1 mo	bleeding	sup spreading	3.2
27	83	F	C	L foot	3 y	bleeding	nodular	3.6

C: Chinese; E: Eurasian; L: left; Mal: Malay; MM: malignant melanoma; R: right

the congenital mole as becoming more nodular and increased in size gradually over 3 years before melanoma was diagnosed. Multiple dysplastic nevi (>5) were found in 1 Eurasian patient (patient 4) and they were mainly found on the trunk and arms.

With regards to associated malignancies, 1 Chinese patient was discovered to have a solitary hepatic nodule on computed tomography (CT) scan abdomen upon diagnosis of melanoma. Liver biopsy subsequently revealed a concomitant primary hepatocellular carcinoma. There was no past history or family history of skin cancers in any patient in this series. We observed a high prevalence of diabetes mellitus associated with melanoma (44%). This was particularly seen in individuals with acral lentiginous melanoma.

All patients presented with either stage I or II disease at the time of initial diagnosis. Wide local excision was the primary treatment in all cases. Baseline chest X-ray screening and blood investigations done in all patients were normal at the time of diagnosis. Neither elective lymph node dissection nor sentinel lymph node biopsy was routinely performed in our patients. However, lymph node resection was performed when lymphadenopathy was first detected. Five patients developed metastatic disease within 12 months to 5 years of the initial diagnosis. Three patients succumbed to the disease despite chemotherapy (2 superficial spreading type; 1 nodular melanoma) while 2 patients with nodular melanoma had evidence of nodal metastases. The time to metastases varied from 12 months to 7 years following initial diagnosis. In the acral lentiginous

TABLE III: RISK FACTOR OF MALIGNANT MELANOMA PATIENTS

Risk factors	Local group	
	Patient S/N	Total no.
Excessive sun exposure	7,9,11,20,24	5
Congenital melanocytic nevus	6	1
Dysplastic nevus	4	1
Past history of skin cancers	—	0
Skin cancers in first degree relatives	—	0
Other cancers	4 (hepatocellular cancer)	1
Concomitant systemic diseases	Diabetes: 2,12,13,14,15,17,18, 19,20,22,24,27	12
	Hypertension/vascular diseases: 18,20,25	3

group, there was no evidence of metastases with a median follow-up of 3.5 years.

Discussion

The number of melanoma cases has been on the increase worldwide but its incidence in Singapore is still considerably lower compared with USA, Europe and Australia.^{2-4,6}

In Singapore, the incidence of melanoma for 1993 to 1997 was 0.4 per 100,000 per year for males and 0.5 per 100,000 per year for females (all residents).⁵

A previous study on skin cancers by Tan et al⁷ quoted 14 indigenous cutaneous melanomas (2.7% of skin cancers) seen at the National Skin Centre from 1980 to 1991. We observed a doubling in the number of new melanoma cases over the last 10 years.

As it has been well established that early recognition and diagnosis of melanoma offer a better chance for treatment, prognosis and survival,⁸⁻¹⁰ the possible reasons of delayed presentation in the local group were examined. All patients were interviewed on their knowledge of skin cancers and majority of the local patients had little or no knowledge of skin cancers. Out of the 27 patients, only 2 patients suspected skin cancer prior to diagnosis. In addition, more than 50% had minimal or no knowledge of the risk factors, mode of spread and early signs of skin cancer. Fifty-five per cent of the initial diagnoses provided by the general practitioners proved to be accurate. The differential diagnoses by the referring non-dermatologists were melanocytic nevus, pyogenic granuloma, seborrhoeic keratosis and dermatofibroma. These observations raised the concern to increase awareness of skin cancers or melanoma. Education programmes for both the public and professionals are required to improve the sensitivity to diagnosis of melanoma.

Patients and families should be taught self examination techniques^{11,12} and the public should be educated to seek early medical attention for suspicious clinical signs especially new pigmented lesions occurring on the fingers or foot and nail discolouration.

In many populations, malignant melanoma is as common in women as in men in contrast to non-melanoma skin cancers in which there is a marked male predominance.¹³ In our study, we report a slight female preponderance. Although there appears to be a higher prevalence of Chinese patients compared with the other races, it is consistent with the local racial distribution.

Cutaneous malignant melanoma can be classified into different categories on the basis of histology.¹³⁻¹⁵ The commonest category of melanoma worldwide is superficial spreading melanoma, followed by nodular melanoma, acral lentiginous melanoma and other melanoma variants.¹⁴ In our study, acral lentiginous melanoma (41%) and nodular melanoma (41%) were the two commonest histologic types and majority of the lesions occurred on the extremities (involvement of the lower limbs more than upper limbs). It is notable that the commonest clinical presentation of acral lentiginous melanoma was in the form of a non-healing, darkly pigmented ulcer while nodular melanoma tended to present with bleeding.

The most important melanoma risk factors for a given individual are as follows:^{9,16-21} a persistently changed or changing mole, irregular varieties of pigmented lesions (including dysplastic moles and lentigo maligna), a congenital mole (especially giant congenital melanocytic nevus), Caucasian race (skin type I and II), a previous or family history of cutaneous melanoma, excessive sun exposure (particularly in childhood), sun sensitivity and immunosuppression. Sun exposure did not appear to be a significant risk factor in our local group even though Singapore is located along the equator. The reason is uncertain but is possibly explained by the different skin types. A personal and family history of skin cancers were not found in our patients.

We report a relatively high frequency of diabetes mellitus in local patients (above 50 years) with acral lentiginous melanoma (44%). Majority were post-menopausal females and non-healing ulcer is the commonest clinical presentation. Out of the 12 diabetic patients with melanomas, only 4 recalled a clear history of preceding trauma to the affected sites. We are not sure whether this association between diabetes and acral melanoma occurred by chance or is there a real association between the two. However, it is well established that chronic foot ulceration has been a major cause of morbidity in patients with diabetics and there is a increased predisposition to malignant transformation such as squamous cell carcinoma occurring in

long-standing foot ulcers. Thus, we feel that while benign vascular acral ulcerations are common in diabetics, the occurrence of acral ulcers associated with dark pigmentation and discolouration of the nail may mask an underlying melanoma and must not be ignored by either the patient or health care physicians.

Superficial spreading melanoma located on the trunk was reported previously to be the commonest histologic type and site associated with a nevus.¹⁹⁻²¹ The greatly increased risk of melanoma in patients with giant congenital nevi has been known from clinical observations but the risk arising from medium or small sized congenital nevi is still contentious.¹⁹⁻²¹ Unlike other studies, 2 patients had malignant melanoma arising from medium sized congenital melanocytic nevi. The measurements of the nevi were 3 and 5 cm respectively at the time of diagnosis and both were nodular melanomas.

In conclusion, there appears to be some distinctive clinical and histogenetic features in malignant melanoma occurring in our patients. This study also highlighted the lack of skin cancer awareness in our local population and the low diagnostic accuracy of non-dermatologists. There is therefore a need to raise awareness among the public and physicians with regards to skin cancers. It is hoped that with education, the diagnosis of melanoma can be made at an earlier stage and treatment instituted earlier with improved prognosis and reduced morbidity.

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