นิพนธ์ต้นฉบับ

Cutaneous malignant melanoma : A pathologic study with clinical correlation of 35 cases.

Voranuch Punyanoravut *

Sanun Rungrunsirivorn *

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A series of 35 cutaneous malignant melanoma was studied from the year 1984 to November 1993. This tumor occurred in the age group of 18 to 82 years, and the female to male ratio was 1:1. The most common presentation was chronic ulcer and, less frequently hyperpigmented mass. The most common site was the lower extremities, and less frequently in the chest wall, head, eyelids, buttocks and abdominal wall. The pathological type revealed that acral lentiginous malignant melanoma predominated. The depth of invasion, according to the level system of Clark's was usually in level IV and V. These pathological findings and Clarkûs level are related to the poor prognosis and high mortality rate of this disease.

Key words : *Malignant melanoma*

Reprint request : Punyanoravut V,Department of Pathology, Facutly of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

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* Departmentof Pathology, Faculty of Medicine, Chulalongkorn University

วรนุช ปัญญาวรวุฒิ, สนั่น รังรักษ์ศิริ. ไฝมะเร็งผิวหนัง : การศึกษาใน 35 ราย. จุฬาลงกรณ์เวชสาร 2537 มกราคม ; 38(1) : 15-21

ได้ทำการศึกษาไฝมะเร็งผิวหนังในผู้ป่วยจำนวน 35 ราย ในช่วงปี 2527 ถึง พฤศจิกายน 2536 ไฝมะเร็ง [1] ชนิดนี้พบในช่วงอายุ 18-82 ปี ซึ่งพบอัตราส่วนของเพศหญิงต่อเพศชาย เท่ากับ 1 ต่อ 1 ลักษณะทางคลินิกที่พบมาก คือ เป็นแผลที่ผิวหนัง รองลงมาคือ ก้อนสีคล้ำ ส่วนตำแหน่งที่พบการเกิดโรคได้บ่อยที่สุดคือบริเวณขาทั้ง 2 ข้าง ตำแหน่งที่พบรองลงมา ได้แก่ บริเวณหน้าอก, ส่วนศีรษะ, หนังตา, สะโพก และหน้าท้องพบได้ประปราย ลักษณะทางพยาธิสภาพที่พบบ่อย ได้แก่ เอครัล เลนติจินัส นอกจากนี้พบว่าความลึกของการลุกลามของมะเร็ง โดยใช้ระดับความลึกของคลาคจะพบว่าอยู่ในระดับ 4 และ 5 ลักษณะพยาธิสภาพที่พบและระดับความลึกของคลาคมักจะเกี่ยวข้องกับการพยากรณ์โรคซึ่งเลว และมีอัตราการตายสูง

The cutaneous malignant melanoma derives from melanocytic cells. [2] A significantly increased incidence is concordant with high mortality. [3] The tumor either arises denovo or develops within pre-existent benign (congenital or acquired) melanocytic nevus. It also originates from junctional components, complicate dysplastic nevus and blue nevus. [3] In 1982, WHO recorded the highest incidence of malignant melanoma in white people (732 per 100,000) in Australia and New Zealand.[4] The incidence is more closely related to sporadic intensive exposure to sunlight rather than to chronic life-long exposure to ultraviolet radiation.[4] A study in Australia published in 1992 revealed that the population there had much higher levels of total sun expossure.[5] In this article present a retrospective study of 35 cases of cutaneous malignant melanoma including clinicopathologic features, morphology and correlations with the prognosis.

Materials and Methods

Data relating to thirty-five cases of cutaneous malignant melanoma were obtained from the surgical files of the Pathological Department, Faculty of Medicine, Chulalongkorn University. The data had been collected between 1984 and November 1993. All sections were reviewed by both of us.

The clinical cases were diagnoses by Hematoxylin and Eosin. Some cases required further studies on Fontana, with and without bleach, S-100 protein and HMB-45 by immunoperoxidase technique. We studied the clinical data, clinico-pathologic features, histopathology and depth of invasion according to the level system of Clark's. [6]

Results

Clinical findings

Of the 35 patients, 18 were women and 17 were men, composing a ratio of 1:1. The ages ranged from 18 to 82 years. The mean age was 56 years. The duration prior of clinical presentation varied from 2 months to 5 years with frequency between 2-6 months. The most common presentation was chronic ulcer (51%). Hyperpigmented mass and nevus were observed with decreasing frequency (43% and 6%). In females it was usually detected in the lower extremities (55%) and less frequency in the chest wall (33%). The buttocks and eyelids were effected about 6 % of the time. (Table 1) In males it was also predominant in the lower extremities (88%), scalp and abdominal wall (6% and 6%). (Table 2)

Table 1. Distribution of melanoma in females.

	Site	No.(cases)	%
Lower extremities	Foot (plantar site)	2	11
	Heel	5	28
	Phalanx	3	16
	Chest wall	6	33
	Eyelid	1	6
	Buttock	1	6
	Total	**18**	**100**

Table 2. Distribution of melanoma in males.

	Site	No. (cases)	%
Lower extremities	Foot (Plantar site)	6	35
	Heel	2	12
	Phalanx	6	35
	Thigh	1	6
	Scalp	1	6
	Abdominal wall	1	6
	Total	**17**	**100**

Pathological findings

The clinicopathological subtypes are as follows; superficial spreading malignant melanoma (8 cases, Figure 1), nodular melanoma (8 cases, Figure 2) and acral lentiginous malignant melanoma (19 cases, Figure 3A, 3B, 3C) (Table 3). The tumor size varied from 0.1 cm to 7.0 cm in greatest dimension with a mean of 2.9 cm. In the lower extremities, the pathological features were manifested as chronic ulcers (15 cases, 60%) and hyperpigmented mass (10 cases, 40%). The acral lentiginous malignant melanoma is composed of epithelioid cell (63%), spindle cell (21%) and mixed cell type (16%). The superficial spreading malignant melanoma consists of epithelioid cell (75%) and mixed cell type (25%). The nodular melanoma manifests with epithelioid cell (50%), spindle cell (13%) and mixed cell type (37%). The overall histopathological findings are epithelioid cell (63%), spindle cell (14%) and mixed cell type (23%) (Table 4). The microstaging, accordingto Clark's level of the depth of invasion was as follows : level I (3%), level II (0%), level III (14%), level IV (52%) and level V (31%), (Table 5).

Table 3. The clinicopathological type.

	No.(Cases)	%
Superficial spreading malignant melanoma	8	23
Nodular melanoma	8	23
Acral lentiginous malignant melanoma	19	54
Total	**35**	**100**

Table 4. The histologic type.

	No.(Cases)	%
Epithelioid cell	22	63
Spindle cell	5	14
Mixed cell type	8	23
Total	**35**	**100**

Table 5. Microstaging.

	No. (Cases)	%
Clarkûs level		
I	1	3
II	0	0
III	5	14
IV	8	52
V	11	31
Total	**25**	**100**

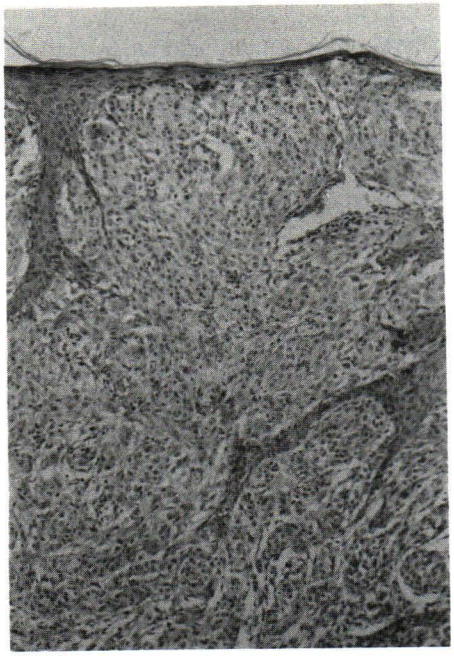


Figure 1. Superficial spreading malignant melanoma showing clusters of enlarged neoplastic cells with pale acidophilic cytoplasm and hyperchromatic nuclei infiltration of the epidermis. H & E x 200.

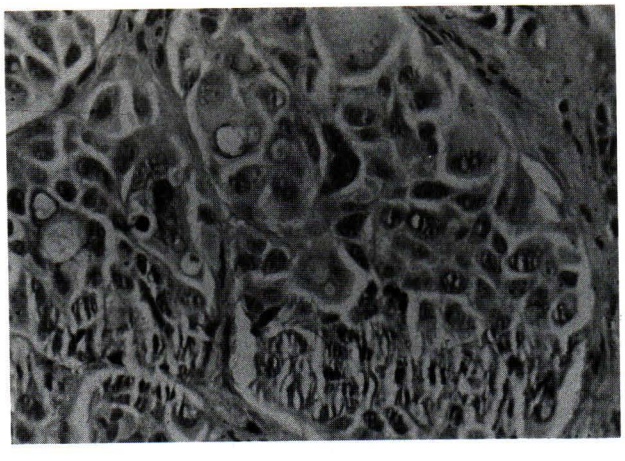
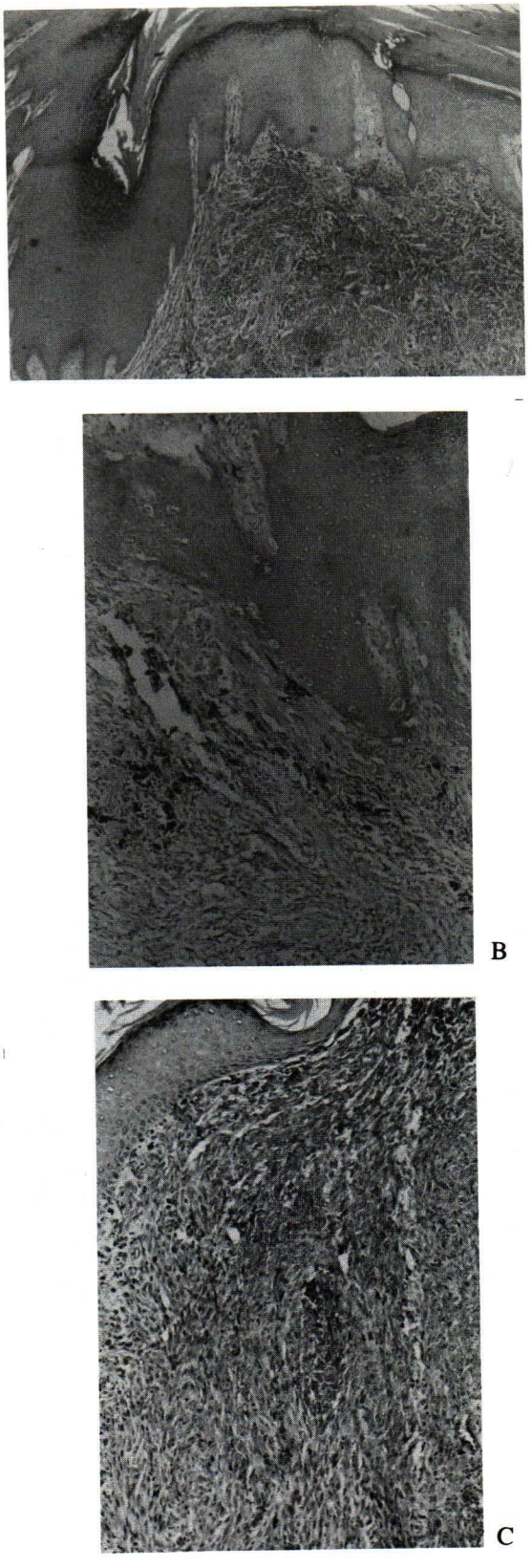


Figure 2. Nodular melanoma. Epithelioid melanoma showing alveolar arrangement. The large round tumor cells have abundant eosinophilic cytoplasm and large pleomorphic vesicular nuclei. H & E x 400.



A

B

C

Figure 3. Acral lentiginous malignant melanoma.

A. Picture showing marked hyperkeratosis, acanthosis and elongation of the epidermal ridge. H & E x 40.

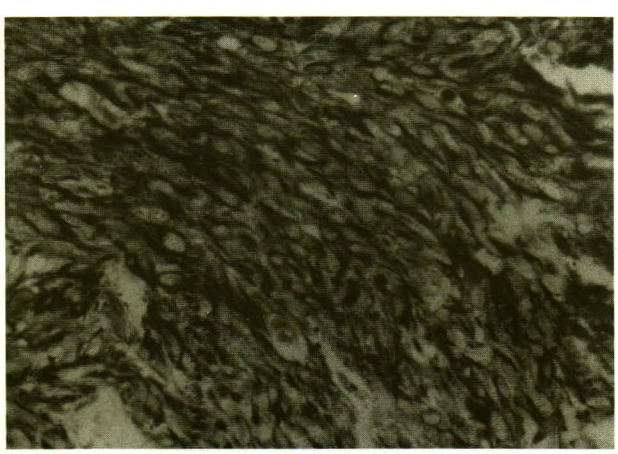
B. Spindle cells tumor showing melanin pigment in acral lentiginous malignant melanoma. H & E x 100.

C. High power of spindel cells type malignant melanoma. H & E x 200.

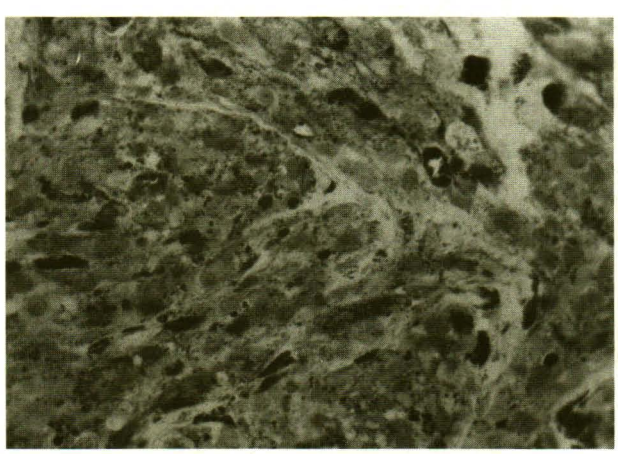
Discussion

Malignant melanoma is rare in the pre-puberty age group. The high risk age group is between 30 and 70 years.[3] In current series, the affected groups show similar range nontheless it does not affect pre-puberty patients. Although it shows a female preponderance (3:2), males have a higher mortality rate.[3] Because of the small number of cases studied, our data is not concordant with the previous report. The malignant melanoma is classified into four clinicopathological subtypes, namely, lentigo maligna melanoma, superficial spreading malignant melanoma, nodular melanoma and acral lentiginous malignant melanoma. [7] They are categorized according to onset, course, prognosis and incidence.[8] The most common types are the superficial spreading malignant melanoma and the nodular melanoma, 70% and 15%, repectively. Among cutaneous malignant melanomas, acral lentiginous melanoma accounts for only 8%, and lentigo maligna melanoma 5%.[8] In present series, the acral lentiginous malignant melanoma is the most common type because in the areas of low incidence, the tumor is most commonly seen in the lower extremities of females. [2]Thus in sporadic cases, the incidence of acral lentiginous malignant melanoma will be relatively increased.

Although the eitology is multifactorial, by far the most important predisposing factor is excessive exposure to ultraviolet light, in particular UVB (290-320 nm).[3] In Thailand, most of the population is regularly exposed to strong sunlight. However cannot evaluate the result of this exposure because of insufficient data. The tumor may arise in the pre-existing benign nevus [3] but in the current series it is very difficult to identify the pre-existing lesion because the patients are usually in an advanced stage at the time of diagnosis. From the clinical presentation we discovered that the most common clinical presentation was chronic ulcer. This must be differentiated from benign chronic ulcer or basal cell carcinoma. The second most common feature is a pigmented mass that must be differentiated from nevus, vascular tumors, seborrheic keratosis and dermatofibrosarcoma protuberans. Histologically, the tumor consists of epithelioid, spindle and bizarre cells. [6] Epithelioid melanoma may be confused with squamous cell carcinoma but the latter commonly involves the surface epithelium. Theoretically, the diagnosis of melanoma was confirmed in all of our cases by Fontana-Masson stain for melanin pigment, the immunohistochemical study for vimentin, S-100 protein (Figure 4A, 4B), cytokeratin, HMB-45 antigen, or electron microscopic examination.[9] Squamous cell carcinoma is positive for keratin but negative for vimentin, while melanoma is reactive for vimentin, S-100 protein and HMB-45.



A



B

Figure 4. Immunohistochemistry

A. Spindel cell tumor showing positive for vimentin. H & E x 400

B. The tumor stains positive for S-100 protein. H & E x 400

The spindle melanoma must be distinguished from spindle cell carcinoma and various types of sarcoma. [10] The microstaging by Clark's method reveals the majority of patients in this study in level IV and V, and less frequent, in level I and III. From the depth of invasiveness cases can be classified into low, moderate and high risk groups. Bagley, et al, classified invasiveness relationship to the mortality rate (0,23 and 37% respectively). [8] In our study, the patients were usually in the late state of the disease. Various factors, in addition to the thickness of the tumor have been cited as influencing the prognosis of clinical stage I malignant melanoma but many of them are directly related to the growth rate of the tumor and thus to the depth of penetration. Among the clinical factors that have a favorable effect are location of the tumor, sex, age, diameter of the lesion, and ulceration. The presence of ulceration reduces the 5-year average survival rate from 80 to 50%.[8] Singletary SE, et al, reported that the high number of positive nodes and presence of extranodal disease were poor prognostic factors. [11]

It was also reported that cases of primary melanoma with metastasis had spontaneous and complete regression. [12] The study was on the effect of initial biopsy procedure on prognosis in stage I and it found that the prognosis was not related to biopsy technique. However, it was recommended that all suspicious lesions be submitted to excisional rather than incisional biopsy to avoid compromising the histological assesment, given the importance of maximal tumor thickness in determining treatment and prognosis. [13]

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