A Case of Amelanotic Melanoma

Yun Seo Kang, M.D., Chun Wook Park, M.D., Cheol Heon Lee, M.D.

Department of Dermatology, Hallym University, College of Medicine, Seoul, Korea.

We report a case of amelanotic melanoma(AMM) in a 53-year-old man who presented a single, 1.5x1.5cm sized, well-demarcated, bright red nodule with erosion on the right heel for 9 months. Histopathologic findings showed irregular junctional activity in the epidermal-dermal junction and alveolar formation in the dermis. The majority of the tumor cells were seen as bizarre and giant cell of epithelioid type with atypical mitotic figure. We could not find melanin pigment in H & E stain.(Ann Dermatol 6:(2) 179-182, 1994)

Key Words: Amelanotic melanoma.

In 1806, Läenec introduced the term amelanotic melanoma(AMM) to describe little or the absence of melanin pigment of melanomas[1]. AMM constitutes only approximately 2 percent of all melanomas[2], and, in Korea, only one case has been reported by Kim et al[3].

We present a case of AMM probably associated with trauma.

REPORT OF A CASE

A 53-year-old man visited our hospital in December, 1991, with a 9 month history of a slowly growing mass on his right heel. On past medical history, he had run a nail into his right heel 10 months previously. The family history was not contributory. At first, we thought it was granuloma pyogenicum.

Physical examination revealed a single, 1.5x1.5cm sized, bright-red colored, tender nodule with erosion(Fig. 1). The rest of the physical examination was negative.

Routine laboratory studies were all within normal limits. Upper G-I series, sonogram on abdomen, and liver scan for detection of distant metastasis showed no abnormal finding. An excisional biopsy was performed.

Histopathologic findings showed erosion of the epidermis and irregular junctional activity, and alveolar formation in the dermis. The majority of the tumor cells were seen as bizarre and giant cell of epithelioid type with atypical mitotic figure(Fig. 2,3). We could not find melanin pigment in H & E stain, but the fontana stain was focally positive(Fig. 4). The lesion revealed a nodular malignant melanoma Clark level V, Breslow thickness defined as the point of maximal thickness in milimitres was 4.5mm. Immunoperoxidase studies with S-100 protein, vimentin, and factor VIII were performed. The positive reaction was noted only with S-100 protein(Fig. 5) and vimentin(Fig. 6).

Under general anesthesia a wide excision with skin graft was performed. The dissection of regional lymph nodes was not done because the patient refused to allow this.

COMMENT

Amelanotic melanoma(AMM) is characterized by little or an absence of melanin pigment of melanomas[1]. Clinically, most lesions of AMM are papular and lighter than the surrounding skin, but a few lesions manifest inconspicuous erythematous macule or plaque[4]. A few have a ring of an inflammatory reaction surrounding the lesion, but most patients have a sharp line of demarcation between the lesion and surrounding skin, suggesting a paucity of host reaction.

Received May 31, 1993.
Accepted for publication February 25, 1994.
Reprint request to: Yun Seo Kang, M.D., Department of Dermatology, Hallyn University, College of Medicine, Seoul, Korea.

Annals of Dermatology
Vol. 6, No. 2, July 1994

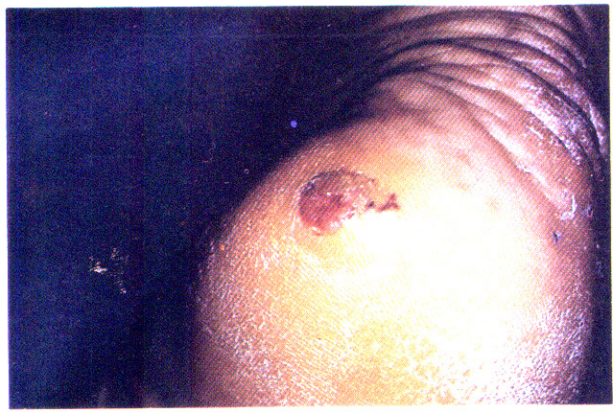

Fig. 1. 1.5 × 1.5cm sized, slightly elevating mass with erosion.

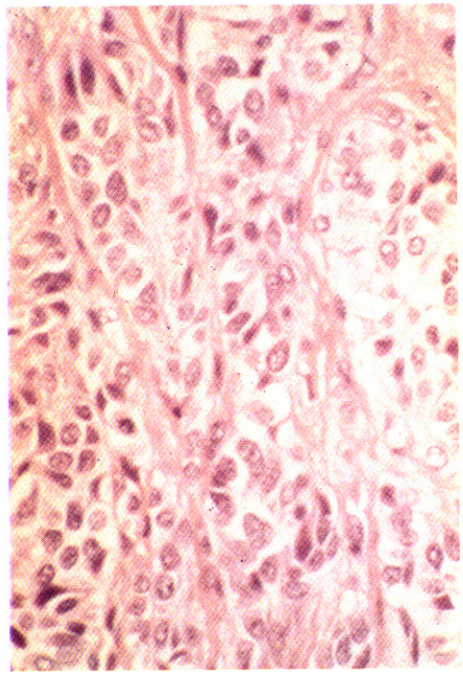

Fig. 3. High power view reveals nests of anaplastic epitheloid cells but not melanin pigment in the tumor(H & E stain, × 400).

The obvious distinction between a pigmented melanoma and an AMM is the presence or the absence of melnin pigment. However, some authors[3, 5] suggested that a few flecks of melanin pigment are usually present and can be detected after careful inspection under microscopy. Gibson[5] noted that the fontana stain is focally positive in 4 of 15

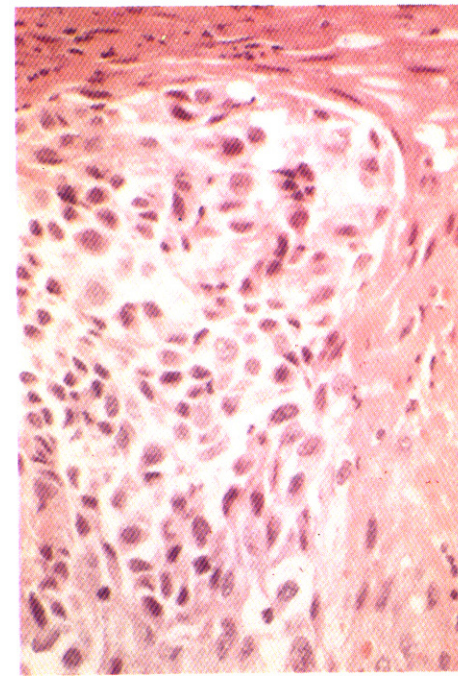

Fig. 2. Histopathologic findings showing irregular junctional activity and alveolar formation in the dermis(H & E stain, × 200).

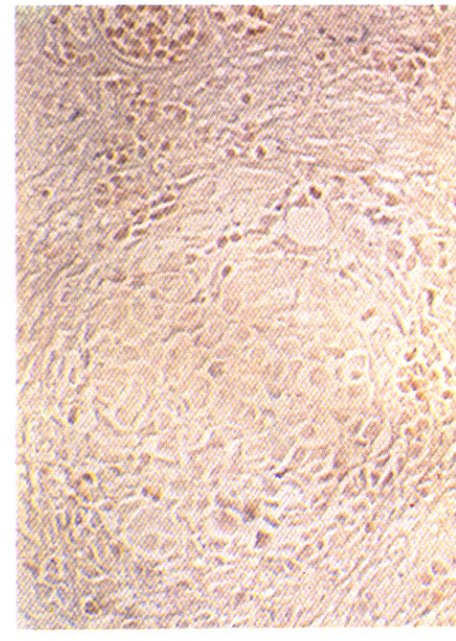

Fig. 4. A focally positive staining reaction with fontana stain is shown(Fontana stain, × 200).

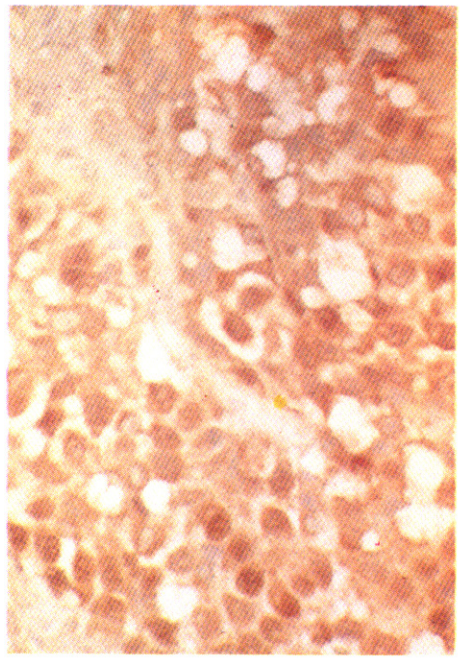

Fig. 5. Immunohistochemical staining reaction for s-100 protein is strongly positive(S-100, × 400).

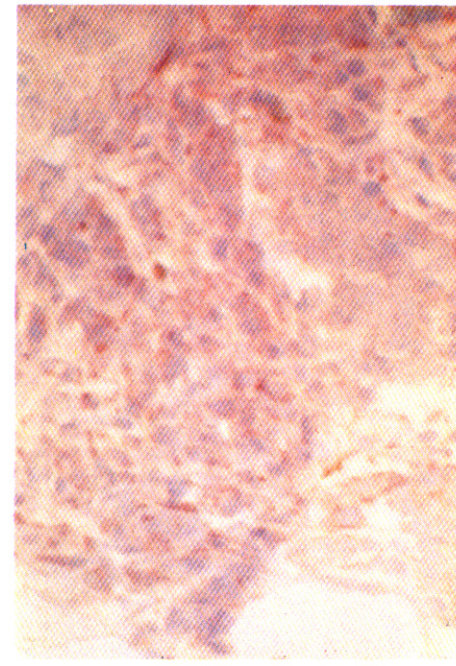

Fig. 6. Immunohistochemical staining reaction for vimentin is positive(Vimentin, × 200).

cases of AMM, and, in 2 of 4 cases, reexamination in the tumor cells. The skin lesion of the presenting case showed no melanin in H & E stain but focally positive in fontana stain. Why this difference exists in melanin production remains uncertain.

Speece et al[6] suggested that the lack of melanin pigment in an amelanotic tumor results from a deficiency in tyrosine. But Fitzpatrick[7] explained that an active tyrosinase system occurs in AMM, but that the amount of melanin produced is of such low concentration that it is impossible to detect by routine histologic tumor has the potential biochemical activity to produce melanin but that rapid cell differentiation causes the cells to lose their functioning capacity to produce and store pigment.

Electron microscopy has been used to study the structural differentiation that exists between a pigmented melanoma and an AMM. Huvos et al[8] represented that the most striking difference in tumors of human beings is a relative absence of ribosomes with their distinctive cytoplasmic pigmented granules in the amelanotic tumor as compared with numerous ribonucleoprotein particles and numerous pigment granules in the melanotic variety. The study by Gibson[5] revealed melanosomes in 13 of 15 cases of AMM. Although all stages were identified, generally the majority were immature melanosomes.

Apart from the rarity of occurrence, there are several facets of AMM, for example, incidence, presentation, and behavior, that differ from the usual pigmented melanomas. The incidence of AMM is about 2 percent of all melanomas. It affects adults of all ages, with median age in the fifth decade. Pigmented melanomas are distributed almost equally between the sexes, while females have a striking preponderance over males for AMM. Clinically most lesions have a nodular component, which varies from a somewhat papillary excrescence over the skin to a pure nodule, often with ulceration. There are also infiltrating lesion(Clark's level IV or V)[1,8]. This probably represents vertical growth. Thus we come to a conclusion that the thicker the tumor and the deeper the invasion, the poorer the prognosis[8,9]. Our case revealed a nodular pattern and infiltrating lesion(Clark leves V) as well.

AMM has a longer period of development prior to diagnosis than its pigmented counterpart, which usually causes the patient to report to a physician for definitive treatment at an earlier date. There is an

average delay of 15 months from the patient first noted lesion until therapy is instituted[8].

It is not certain whether trauma has any relation to MM, but it is interesting to note the developing of the lesion on a trauma site in our case. Although most commonly located in the lower extremeties, the primary tumors can be found in any location[3]. In an analysis of 77 patients, Ariel et al[10] showed twenty-seven patients listed as having stage I lesions, that is no metastasis to lymph node, forty-eight as having stage II lesions, metastasis to lymph node, and two patients as having stage III presenting with widespread location. The additional ten patients had AMM with metastases with no known primary location. The overall survival rate was 30 percent, patients with metastasis in stage I manifested a survival rate of 55 percent, which dropped precipitously to 17 percent for lesions in stage II.

The diagnosis of AMM is very difficult. AMM should be considered as a possibility in any progressive and indurated lesion, with or without ulceration. A prompt biopsy of the lesion is indicated. The fontana stain as well as H & E stain may be helpful. The immunohistochemical study is essential for diagnosis of MM. S-100 protein has been a valuable marker for melanocyte, normal Langerhans' cells, neuroepithelial tumors, and malignant Langerhans' cells in histiocytosis. This protein survives formalin fixation and paraffin embedding and thus can be valuable in establishing a diagnosis of spindle cell MM or amelanotic metastas is of a MM. Vimentin is found in mesenchymal cells and melanocytes and may be helpful for the diagnosis of sarcoma, lymphoma, and melanoma. If both S-100 and vimentin stain are positive, MM is indicated. Electron microscopy is considered the most definitive method of diagnosis of AMM. However it is sometimes difficult to make the distinction between primary nodular MM and metastatic melanoma, or even a Spitz's nevus, since infiltration into the epidermis of Spitz's nevus, since infiltration into the epidermis may not be present. If there is any evidence of a residual nevus, this would favor a diagnosis of primary nodular melanoma rather than metastatic melanoma. The features of Spitz's nevus that are useful for distinguishing them from metastatic melanoma are that Spitz's nevi often are associated with epidermal hyperplasia and almost always have a polarity to their organization in the dermis.

If the lesion should prove to be an AMM, a wide excision of the primary site with skin graft is the answers. Other modalities being used to treat certain malignant melanoma including AMM include cryosurgery, laser surgery, X-ray therapy, and local immunotherapy[10].

REFERENCES

1. Balch CM, Murad TM, Soong SJ et al: A multifactorial analysis of melanoma. Ann Surg 188: 732-742, 1978.
2. Guliano AE, Cochran AJ, Morton DL: Melanoma from unknown primary site and amelanotic melanoma. Semin Oncol 9: 442-447, 1982.
3. Kim JG, Chin HS, Cho CK: A case report of amelanotic melanoma. Kor J Dermatol 15: 511-514, 1977.
4. Pichler E, Fritsch P: Macular melanoma in situ. J Dermatol 177: 313-316, 1988.
5. Gibson LE, Goellner JR: Amelanotic melanoma: Cases studied by Fontana stain, S-100 immunostain, and ultrastructural examination. Mayo Clin Proc 63: 777-782, 1988.
6. Speece AJ, Chang JP, Russel Wo: A microspectrophotometric autoradiographic study of tyrosinase activity in human melanoma. in pigmented cell biology, edited by M. gorden, New York Academic Press. 1959. Cited from reference 2.
7. Fitzpatrick TB: Human melanogenesis. Arch Dermatol 65: 379-391, 1952.
8. Huvos AG, Shah JP, Goldsmith HS: A clinicopathologic study of amelanotic melanoma. Surg Gynecol Obstet 135: 917-920, 1981
9. Breslow A: Thickness, cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. Ann Surg 172; 902-908, 1970.
10. Ariel IM: Amelanotic melanoma: An analysis of 77 patients. Curr Surg 38: 151-155, 1981.
11. Arnold HL, Odon RB, James WD: Andrws' Disease of the Skin. 8th ed, WB Saunder Co, Philadelphia, 1990, pp 819-825.