

Characteristics and surgical treatment of recurrence melanoma of the foot: a case report and brief literature review

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Abstract. – **OBJECTIVE:** Despite advances in plastic and reconstructive surgery, repairing soft tissue defects of the foot remains a complex surgical challenge when conventional methods cannot cover defects. We presented a case in which a free flap was used for reconstruction and reviewed the literature.

PATIENTS AND METHODS: A 75-year-old woman with an acral melanoma history had a large exophytic mass on her right foot. Using PubMed, we found that reconstructive options in the literature include local flaps, fascial flaps, muscle flaps, and free flaps.

RESULTS: Melanoma recurred four times at the same site after complete excision of the compound nevi in the present case. Melan A, Vimentin (+), S-100 (+), and HMB-45 positivity were found in immunohistochemical staining and increased Ki-67 proliferation. The defects in soft tissue are repaired using a free anterolateral thigh perforator flap. No complications were raised in the patient.

CONCLUSIONS: Foot melanoma is difficult to be resected because it necessitates a wide excision, which can result in large defects. The free flap, in our experience, can easily be performed while preserving function and improving cosmesis. This flap is an appealing option for concealing defects in the distal extremities.

Key Words:

Melanoma, Free anterolateral femoral skin flap, Foot, Soft tissue defect.

Introduction

Melanomas appear themselves as pigmented nevus that change color, size, or shape¹. The presentation of a pigmented mole on foot can be challenging due to the long list of differential diagnoses for such a mole². The standard treat-

ment for patients with foot melanoma is wide peripheral and deep tumor resection margins or amputation, which results in a significant soft tissue defect and is frequently exposed to the calcaneus³. We present a case in which a free anterolateral femoral skin flap was used to reconstruct the lateral side of the foot after the removal of a giant malignant melanoma.

Case Report

On March 20, 2012, a 75-year-old woman went to the hospital with a brownish nodule (2.0 cm × 3.0 cm) with a 3 cm thickness above the skin on the lateral side of her right foot, which had initially been developed 20 years before. The patient had no family history of malignant melanoma. The doctor chose a surgical margin of not more than 1 cm around it to preserve the nodule. Lesions were excised entirely and repaired skin abnormalities with free flaps. A skin biopsy revealed that the lesions were compound nevi and benign tumors at that time.

Ten months later, on January 15, 2013, the patient presented with a 1.0 cm × 1.5 cm nodule at the proximal end of the skin transplantation area. Eleven months later, on December 17, 2013, the patient had a 2.0 cm × 2.5 cm nodule removed from the same lesion site, but histological examination revealed malignant melanoma.

Two nodules measuring 0.4 cm × 0.2 cm developed in the same area on October 15, 2014, ten months after the lesion was resected. A free skin flap was used to close the wound after the same physician performed significant local resection of the tumor. Histopathology revealed that the lesion was malignant melanoma. A black nodule measuring 0.5 cm × 0.5 cm was developed at the intersection of the two grafting regions on the

outside of the right foot on July 6, 2015, necessitating full-thickness skin grafting nine months later. Histopathological characterization of lesions confirmed the diagnosis of malignant melanoma once again. Neither a preoperative chest CT scan nor abdominal ultrasonography revealed metastasis during the treatment described above. The patient refused adjuvant therapy because she believed the situation was not critical. This study was approved by the Ethics Committee of China-Japan Union Hospital. Signed written informed consent was obtained from the participant before the study

Clinical Manifestation and Diagnosis

Four years later, in 2019, the patient complained of irregular brown nodal necrotic masses (7.0 cm × 5.0 cm) and two scattered black elevated nodules on the outside of her right foot that bled after being touched (Figure 1A). The main complaint and clinical observations of the patient were foul secretions, tissue loss, and ulcers. The patient had been hesitant to seek medical attention until she realized that her normal function was being jeopardized by the rapid development and extension of the foot mass. At that point, she sought medical help. The patient explained her reluctance to see a doctor due to her lack of awareness of the lump, which she believed was caused by illness. During ultrasound examination and flap acquisition, melanoma metastasis was found in the right leg, the anterior part of the ipsilateral ankle joint, the superficial inguinal lymph node, and the subcutaneous tissue of the abdomen (Figure 2), indicating that the focus was transferred from the ankle along the lymphatics. Preoperative positron emission tomography (PET-

CT) revealed glucose uptake in the right foot, compatible with the known recurrence site of the disease, and other high uptake lesions in the right groin area.

In the process of flap acquisition, Multiple metastases outside the foot were found during the process of flap acquisition, including superficial inguinal lymph node metastasis, anterior malleolus lymphatic, and other metastases.

In laboratory tests, ferritin levels were found to be high (170.1 ng/mL where the normal range is 5.0-130.0 ng/mL). At our facility, the patient underwent tumor excision in the right lateral region of the foot and resection of the ipsilateral inguinal lymph nodes. The other lymph nodes were also removed. A free anterolateral thigh flap was chosen to treat the soft tissue defects of the foot caused by tumor resection after confirming the tumor-free margin with a frozen biopsy during the procedure (Figure 1B). A biopsy of the tumor on the right foot revealed malignant melanoma. The BRAFV^{600E} mutation was not found in the genetic analysis of tumor tissue. Fortunately, the patient did not show signs of recurrence after six months of follow-up.

Histological Observation

A large malignant mass with dilated hyperplasia and dark grey skin lesions was revealed by histopathological examination. Pathological sections and staining indicated the pleomorphic nucleus of melanoma cells in the lesions, resembling birds' eyes, as well as abnormal chromatin expansion and distribution.

The diffuse cytoplasmic melanin was stained. The tendon bundle was occupied by focusing

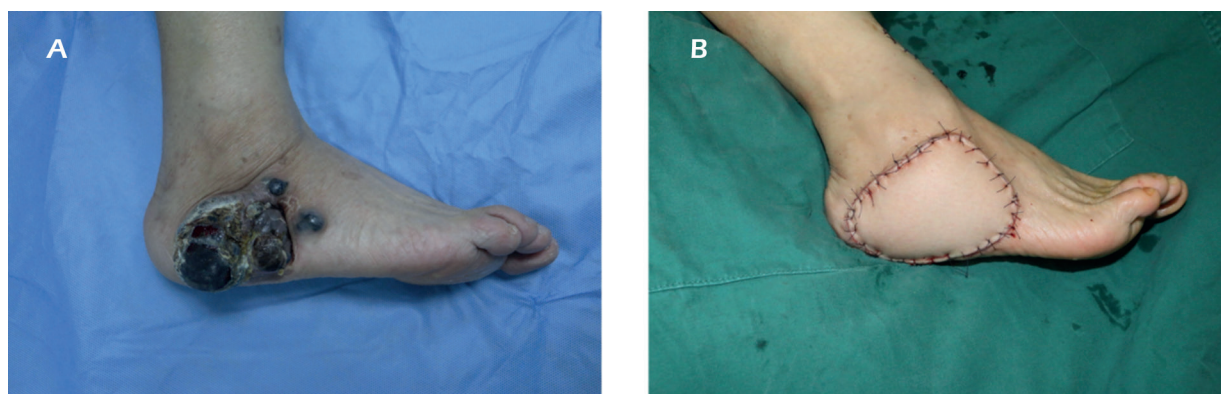


Figure 1. Acral lentiginous melanoma. Clinical presentation of large, malodorous mass obscuring lateral side of the right foot with large areas of necrosis. After tumor resection, the patient underwent defect reconstruction using a free anterolateral femoral skin flap: **A**, Preoperative image. **B**, The postoperative image demonstrates that the soft tissue defect of the foot was successfully restored.



Figure 2. Melanoma was found to metastasize along the blood vessels during operation and flap acquisition. When the flap was taken, metastasis was found: abdominal subcutaneous metastasis inguinal lymph node, anterior malleolus lymphatics, and several other sites metastasis.

melanoma, and the intrinsic structure disappeared. Some of them were nested melanoma. The tumor cells spread through the sarcolemma space and gradually invade the superficial skin and deep subcutaneous tissues (some are cancer cell nests that diffuse along the muscle fiber membrane and gradually infiltrate the superficial skin and deep subcutaneous tissue) (Figures 3 and 4).

Some lymphocytes prevent the growth of melanoma cells at the tumor edge during the invasion. Conversely, some myofibroblasts combine with melanoma cells to damage normal tissue structure and spread to the outside of the myomembrane at the site of myomembrane destruction. However, the space outside the sarcolemma is an essential pathway for tumor cell proliferation. From the lymphatic sinuses to the lymphatic vessels, the lymphatic system is another major pathway for tumor cell proliferation.

Immunohistochemical staining revealed Melan A, Vimentin (+), S-100 (+), and HMB-45 positivity, as well as increased Ki-67 (20% +) prolif-

eration but negative staining for CK-PAN, all of these were useful for diagnosis and differential diagnosis (Figure 3).

Discussion

ALM (acral lentiginous melanoma) accounts for the majority of all cutaneous melanoma subtypes in Asian populations¹⁹. ALM is expected to be a more physiologically aggressive melanoma subtype with a poor prognosis than other melanoma subtypes^{20,21}. In East Asia, melanoma is most typically found on the foot. Acral melanomas on the feet (compared to the hands) have a lower survival rate. This reason for the poor prognosis is almost certainly multifactorial²². Patients' failure to recognize their condition and clinicians' misdiagnosis of benign disease can contribute to poor survival²³.

The accuracy with which malignant melanoma is detected and managed during the initial and subsequent visits may directly impact the

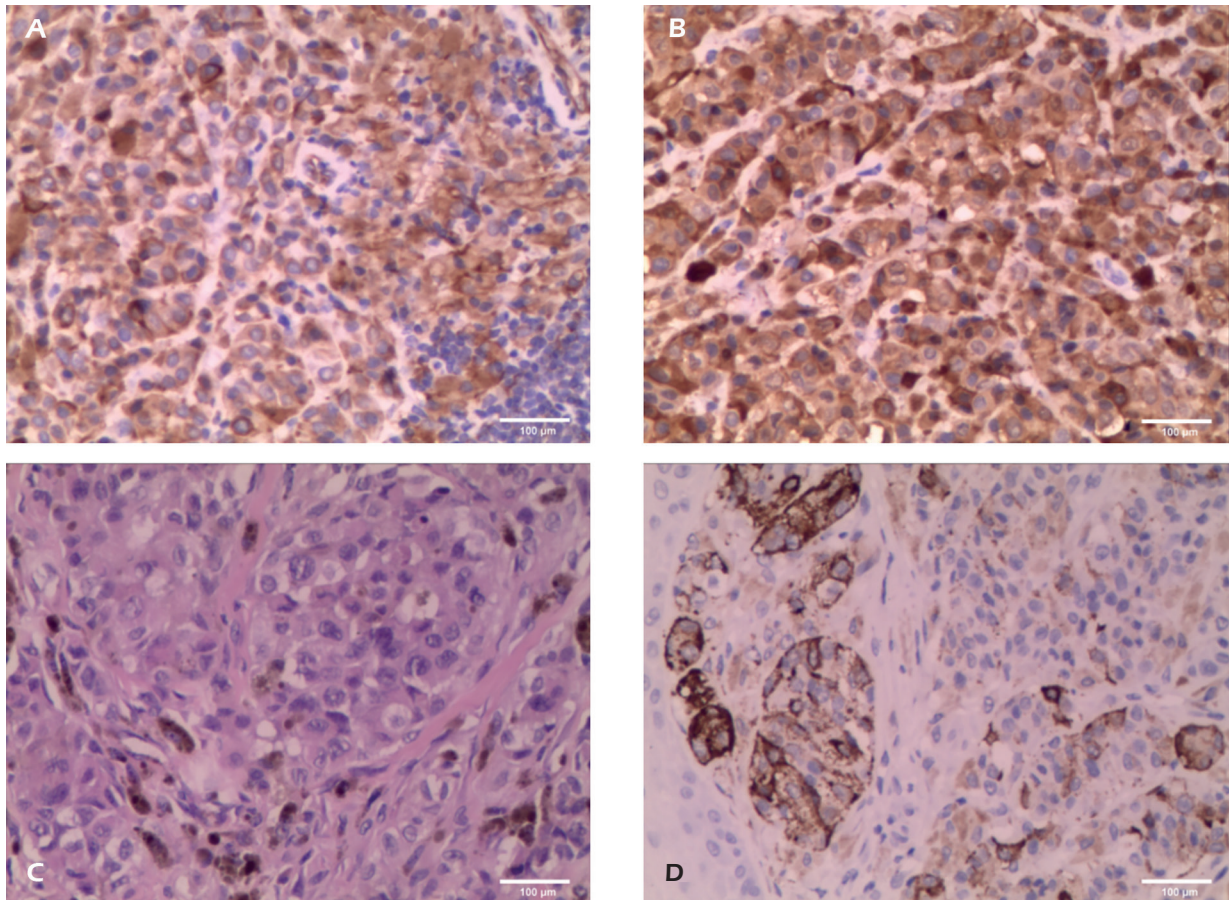


Figure 3. Characteristics of melanoma in patients (H&E 20×10): megakaryon (in the shape of bird's eye), polymorphonuclear, increased chromatin, abnormal distribution, and some cytoplasmic melanin. The tendon bundle was almost occupied by melanoma cells, showing a disordered structure, but it was surrounded by aponeurosis, which is not evident in Figure D.

prognosis of patients. Early melanomas associated with pre-existing melanocytic nevi are frequently difficult to detect, recommending dermatoscopy and pathological biopsy^{24,25}. In the present case, melanoma recurred four times at the same site following complete excision of the first compound nevi, and the lesion was diagnosed as malignant melanoma on its first recurrence. Although it is difficult to prove that compound nevi can act as a precursor to melanoma, the possibility of malignant melanoma should be considered by following the cases of compound nevi.

Depending on the location, size, and depth of invasion of the tumor, the primary treatment option for patients with ALM of the foot is wide local excision (WLE) with tumor-free margins. Several studies conducted in western countries have shown that melanoma of the foot consumes a significant amount of tissue and that surgical

resection is required due to the high rate of local and regional recurrence²⁶. Reconstructive options can be performed using local flaps, ALTP, SCIP, SGAP, PIAP, UMTP flaps, and others (Table I). Reconstruction of defects in the lower extremities remains a difficult task for a surgeon. Free flaps are a viable but time-consuming reconstructive technique²⁷.

Furthermore, the multiple recurrences, in this case, suggest that the recommended surgical margin and depth of resection may be inadequate. This case history of melanoma over two decades is unusual. Although each surgical resection was successful, the melanoma was not eliminated. The immune system may play a significant role in preventing tumor development, invasion, and metastasis.

Due to the scarcity of local soft tissue, blood circulation, and the unique nature of the foot region, it is complicated to reconstruct large soft-tissue defects in the foot following extensive

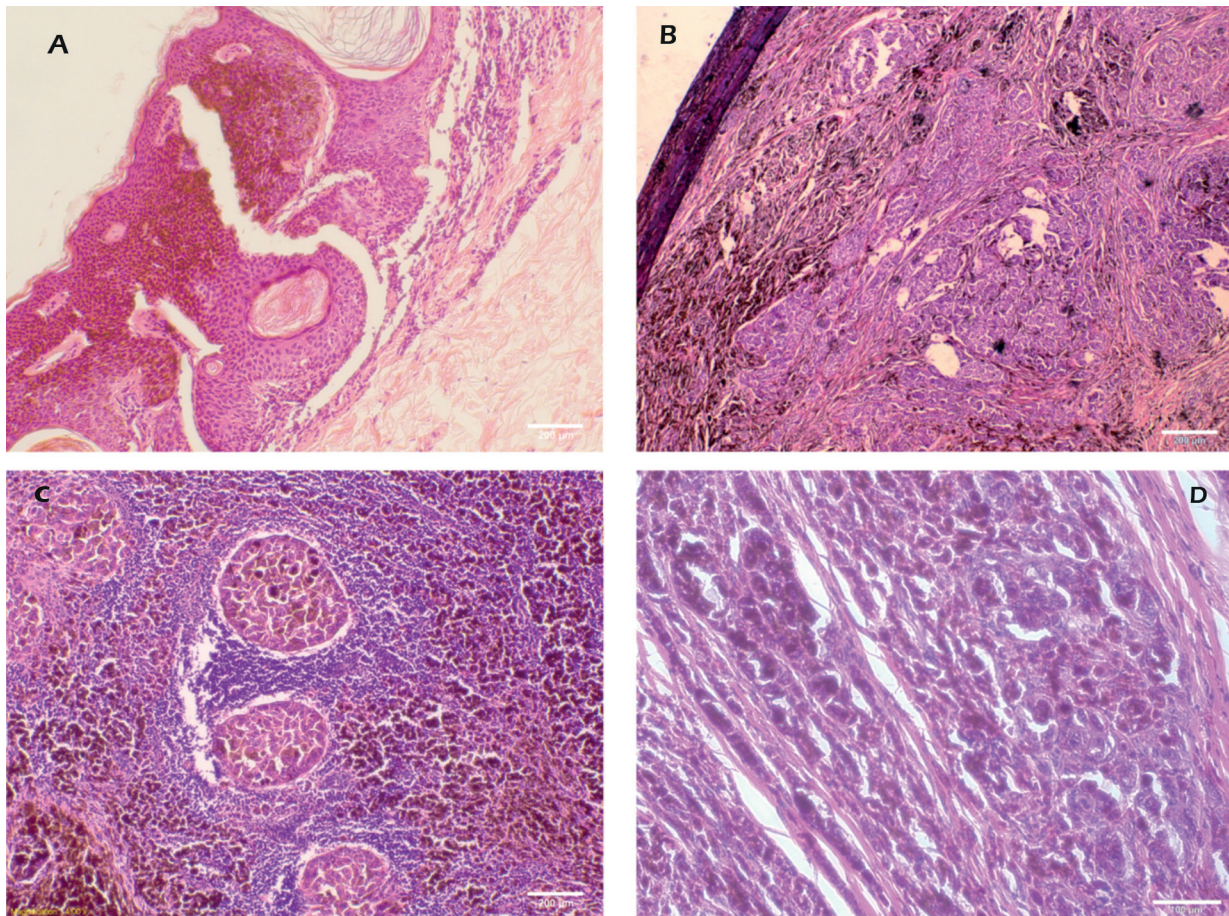


Figure 4. Typical pathological structure of cutaneous melanoma. **A**, The skin of the foot is fragile, lacking subcutaneous adipose tissue. Melanoma cells develop from the epidermis and gradually develop into deep subcutaneous tissue. There are lymphocytes at the interface of tumor focus and subcutaneous tissue to prevent its spread. **B**, Melanoma cells spread with the lymphatic space and fascia and invade the tendon tissue. Lymphocytes in the tumor mass and subcutaneous tissue interface prevent invasion. Still, once it invades the tendon, it will gradually replace the normal muscle cells with melanoma cells. The intact fascia can still wrap the tendon to maintain the basic shape because of the rapid expansion, which increases tumor tissue volume. **C**, A lot of lymphocytes are around the tumor. **D**, Finally, all of them become melanocytes due to the typical structure of melanoma. Such tendons are still surrounded by fascia, forming fascial or columnar lesions.

melanoma excision. The lateral side of the foot is frequently rebuilt with a local flap or skin graft because it is not non-weight bearing and has little impact on ambulation²⁸. However, free flaps are optimal for covering major defects because they minimize donor site morbidity. In this case, five skin tumor resections were performed. The tumor tissue was entirely removed using a negative surgical margin. However, it recurred regularly because the tumor is highly malignant with an insidious onset, invasive and rapidly growing, and has a high recurrence rate. In this case, the presence of a large and destructive tumor demonstrated the progression of advanced acral melanoma. Histopathology revealed typical ALM

characteristics that were consistent with previous cases²⁹. The characteristics and precise site distribution of foot melanoma described in this study may aid in the selection of treatment strategies and surgical techniques.

Conclusions

After a series of surgeries, subcutaneous melanoma in the front of the ankle recurred, with a 20-year survival rate. The fifth operation included flap repair, and metastases along the lymph vessels were found. There was no evidence of recurrence after a 6-month fol-

Table I. Reconstruction using a different type of flaps after malignant melanoma resection of the foot.

Author	Diagnosis	Number of cases	Defect size	Defect position	Treatment	Follow-up (months)	Outcome
Álvaro et al ⁴	Acral lentiginous melanoma	2	42.25 cm ² to 104.5 cm ²	Plantar arch, heel	Skin graft	20	None
Evans et al ⁵	Malignant melanomas	24	37 cm ² (mean defect size)	Plantar arch, heel, Plantar Forefoot	Plantar, rotation flap, Skin graft	28.6 (average)	Flap or skin graft loss, flap dehiscence
Lee et al ⁶	Malignant melanomas	63	5 cm ² to 224 cm ²	Toe, dorsum, foot plantar, heel	TDAP, SCIP, LCFP	5 to 81	Infection and flap loss
Nam et al ⁷	Acral lentiginous melanoma	52	n.r.	Heel, toe, sole, lateral/ medial side of the foot	Skin graft, local flap, free flap, sural flap	n.r.	Wound dehiscence, chronic ulceration, and gait discomfort
Moon et al ⁸	Lentiginous malignant melanoma	3	27.6 cm ² to 56 cm ²	Lateral/medial forefoot Postero-lateral heel	Reverse island medial plantar flaps	4 to 15	None
Suh et al ⁹	Acral lentiginous, Nodular, and Lentigomaligna melanoma	52	66.98 cm ² (mean defect size)	Foot dorsum, toe, sole, heel	ALTP, SCIP, SGAP, PIAP, UMTF	3.4 to 107.6	Hematoma, Seroma, Wound infection or dehiscence
Sakai et al ¹⁰	Malignant melanoma	1	15 cm ²	Toe	Flexor digitorum brevis muscle flap, skin graft	12	None
Evans ¹¹	Acral lentiginous melanoma	8	n.r.	Heel	Plantar flap, skin graft	46 (average)	Tumor recurrence (n=1), Partial flap necrosis (n=1), skin graft loss (n=2)
Tan et al ¹²	Malignant melanoma	1	180 cm ²	Sole, heel	Supercharged reverse-flow sural artery flap	4	None
Kang et al ¹³	Malignant melanoma	13	48.75 cm ² to 138 cm ²	Heel, Lateral arch of forefoot	DBSF, LSMF	6 to 48	Partial necrosis (n=4)
Kushida-Contreras et al ¹⁴	Malignant melanoma	7	25 cm ² to 54 cm ²	Foot plantar	Free ultra-thin ALT flaps.	12 to 24	Recurrent seroma (n=1), Superficial burn (n=1)
Fujioka et al ¹⁵	Malignant melanoma	1	30 cm ²	Lateral forefoot	Distally based medial plantar flap, ALTP	12	None
Gu et al ¹⁶	Malignant melanoma	7	12.4 cm ² to 19.8 cm ²	Heel	MPA island pedicle flap	8 to 35	None
Guillier et al ¹⁷	Lentiginous melanoma	1	21 cm ²	Foot plantar	Bipedicled distally based MPA flap	9	None
Larrañaga et al ¹⁸	Malignant melanoma	4	n.r.	Heel, foot dorsum	Reverse sural artery flap	60 to 86	None

Abbreviations: TDAP: Thoracodorsal artery perforator flap; SCIP: Superficial circumflex iliac artery perforator flap; LCFP: lateral circumflex femoral artery perforator flap; n.r.: not reported; ALTP: anterolateral thigh perforator flap; SGAP: superior gluteal artery perforator flap; PIAP: posterior interosseous artery perforator flap; UMTF: upper medial thigh perforator flap; DBSF: Distally based sural flap; LSMF: Lateral supramalleolar flap; MAP: distally based medial plantar artery flap.

low-up. According to histopathological examination, the lymphatics and fascial space were found to be the primary diffusion pathways for melanoma cells. After resectioning the melanoma, free flaps were used to close the wounds, preserving the maximum length and function of extremities.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Authors' Contribution

XLL and GZW conceived the review, acquired data; XLL, HL and GZW participated in the process of writing and reviewing the manuscript. All authors contributed to the conception and revision of the manuscript and approved its submission.

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