Complete spontaneous regression of a metastatic acral melanoma with associated leukoderma

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Cutaneous melanoma (CM) is the leading cause of skin cancer mortality worldwide despite constituting only 4% of skin cancers.[1] Acral melanoma (AM) is a distinct variant of CM and is generally associated with a poor prognosis. Complete spontaneous regression of CM is a rare but well described phenomenon. We present an unusual case of a complete spontaneously regressed metastatic AM with melanoma-associated leukoderma.

CASE REPORT

A 56-year-old African woman with Fitzpatrick skin phototype VI presented with a 6-month history of a progressively enlarging tumor on the medial aspect of her right thigh. She reported significant weight loss, fatigue, and right leg pain. Her medical history was unremarkable and she denied any family history of malignancy.

Upon examination, she appeared cachectic and had a 20 × 18 cm fungating tumor on the medial aspect of her right thigh with tissue sloughing and foul-smelling discharge (Fig 1, *A*). There was associated right inguinal lymphadenopathy.

Further examination revealed an isolated 5 × 5 cm grey/brown nodule on her right heel and a patch of leukoderma on the medial aspect of her right ankle (Fig 1, *B*). The patient reported no history of vitiligo or any preceding skin lesion that could have caused postinflammatory hypopigmentation in this area. The leukoderma patch had follicular repigmentation both at the periphery of the lesion and centrally. According to the patient, the heel nodule had been present for 2 years, growing rapidly at first and then stabilizing in size. She had never sought medical attention for the nodule on her heel, only presenting to her local clinic when the thigh mass was causing unmanageable morbidity because of pain and immobilization. She was an outdoor laborer, usually working barefoot. She denied a history of heel trauma.

A biopsy specimen of the right thigh tumor was obtained and revealed a malignant neoplasm with spindle cells arranged in a fascicular and storiform growth pattern, prominent necrosis, variable pleomorphism, numerous mitoses, and a pronounced lymphocytic infiltrate (Fig 2, *C* and *D*). Immunohistochemical analysis showed the spindle cells to be HMB-45 (Fig 3, *A*), Melan-A (Fig 3, *B*) and Sox-10—positive, confirming the diagnosis of a malignant melanoma.

Two 5-mm punch biopsy specimens of the right heel nodule revealed numerous melanophages admixed with extensive dermal fibrosis. Immunohistochemical staining was negative for Melan-A and Sox-10, but positive for CD163, a marker of macrophages. These findings were consistent with stage III regression of melanoma, namely complete regression with absence of neoplastic cells. These neoplastic cells have been replaced by fibrosis and inflammation or by densely packed melanophages (Fig 2, *A* and *B*).

Staging positron emission tomography—computed tomography revealed mild uptake of fluorodeoxyglucose in the right heel mass and intense heterogeneous uptake in the right thigh mass. There was also moderate uptake in multiple pathological lymph

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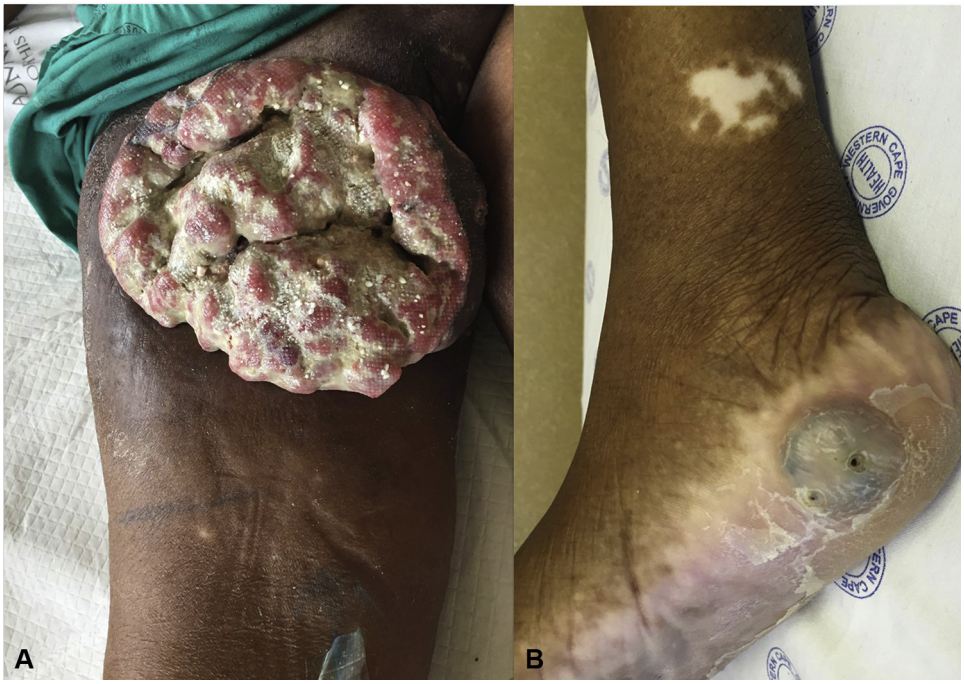

Fig 1. **A**, Clinical presentation of a fungating, ulcerative mass on the right thigh with necrosis and tissue sloughing. **B**, Regressed primary acral melanoma on the sole of the right foot with a patch of leukoderma on the medial right ankle. Note that there is a follicular repigmentation pattern at both the periphery of the lesion and centrally.

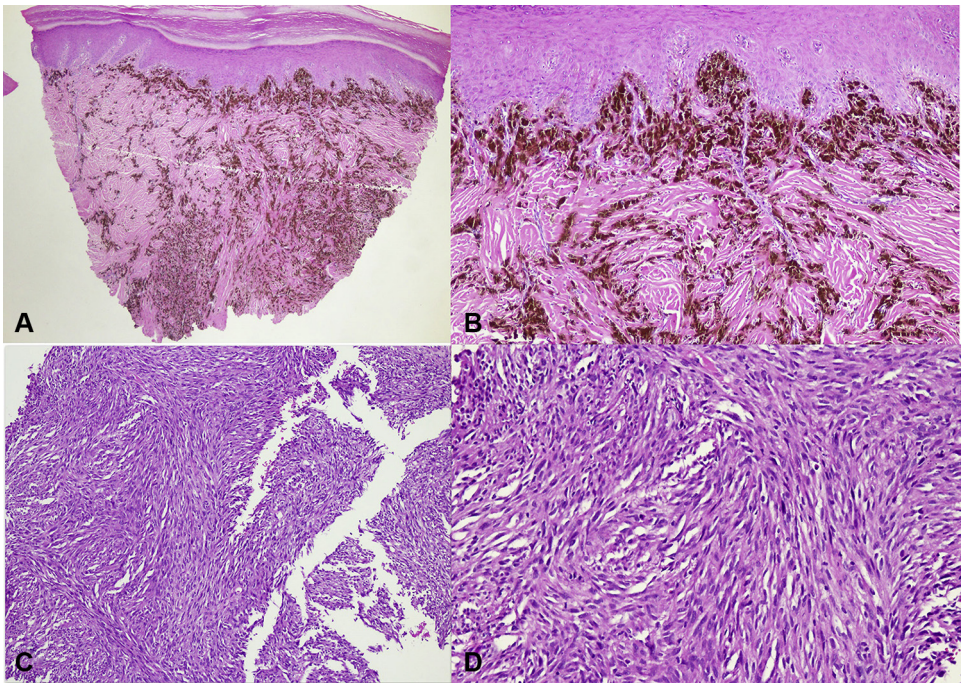

Fig 2. **A** and **B**, Histology of a 5-mm punch biopsy specimen taken from the right heel lesion reveals numerous melanophages admixed with dermal fibrosis. **B**, Higher magnification of (**A**), highlighting the extensive dermal fibrosis. **C** and **D**, Histology of spindled atypical cells arranged in a fascicular and storiform growth pattern.

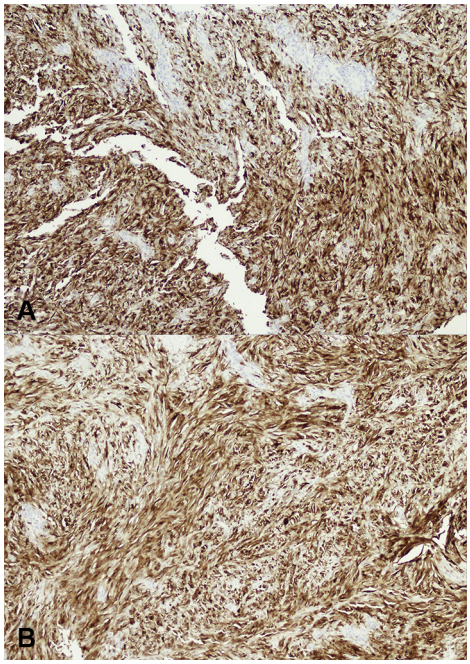

Fig 3. Immunohistochemical analysis of the biopsy specimen of the right thigh tumor showed the spindle cells to be both (**A**) HMB-45− and (**B**) Melan-A−positive.

nodes, including the right common iliac, external iliac, and inguinal nodes, representing metastases. There was no other organ involvement (Fig 4).

Wide local excision of the heel lesion was not performed in view of stage IV disease, but a repeat large incisional biopsy, clinically representative of the tumor, confirmed the absence of malignant cells and the diagnosis of complete regression.

Diagnosis was made of a completely and spontaneously regressed AM with in-transit and distant lymph node metastases plus associated leukoderma. The patient received palliative radiation therapy for the right thigh tumor. As of the time this article was written, 3 months after presentation, the patient was alive and her pain was well controlled.

DISCUSSION

AMs account for 2% to 3% of all CMs.[2] It has the same incidence in all ethnic groups, but a disproportionate representation in black, Hispanic, and Asian patients, accounting for ≥ 70% of all CM in the black population.[3] AM is thought to have unique genetic mutation sequences compared to other forms of CM. It is generally associated with a poor prognosis, with 5-year survival rates as low as 26% in a black South African population.[4] The poor prognosis is attributed to factors including, in the case of plantar lesions, the hidden location resulting in late diagnosis and a relatively high Breslow thickness at presentation, as well as a unique intrinsic aggressiveness.

Our case highlights the severe morbidity associated with late presentation. The patient did not seek medical attention because of socioeconomic factors and living in a rural setting with limited access to primary care. She was also unaware of the harmful nature of the heel lesion. This underscores the importance of patient and health care provider education about AM and improvement in screening, especially in high-risk groups.

Although the heel lesion was never fully excised, a large representative incisional biopsy specimen was obtained. Our patient fulfilled the clinical and pathological criteria for complete regression of a primary CM.[5]

Spontaneous histologically identifiable regression of primary CM occurs in 10% to 35% of cases.[6] Regression is caused by the host's immunologic response against mutated melanocytes and has been divided into 3 histologic stages by Kang et al.[7] Complete regression is a rare phenomenon, with an incidence of 0.22% to 0.27% with only 76 cases reported in English language literature since 1866.[8] Complete regression of AM seems to be exceptionally rare, and no reported cases in the literature could be found.

The clinical significance of regression is a controversial topic, with recent studies showing that histologic regression is less likely to be associated with sentinel lymph node positivity.[9] Exceptions to this include thin CM with >50% regression and primary CM that has completely regressed, where the incidence of metastatic disease is reported to be higher.[6,7,9-11]

An additional finding was the focal patch of leukoderma, representing the immunologic response that accompanies CM. This phenomenon occurs in 1.4% to 2.8% of CM cases.[12,13] Despite sharing the same pathogenic mechanism, the association of leukoderma and complete spontaneous regression of melanoma has only been reported in 1 other similar case in the literature, but not in AM specifically.[12] Melanoma-associated leukoderma is generally associated with a higher incidence of metastatic disease, but is considered an independent favorable prognostic factor in stage III and IV metastatic melanoma.[13]

This case provides an example of a complete spontaneously regressed AM with associated leukoderma and metastatic disease occurring in the same patient. Although the association between these findings and metastatic disease are yet to be

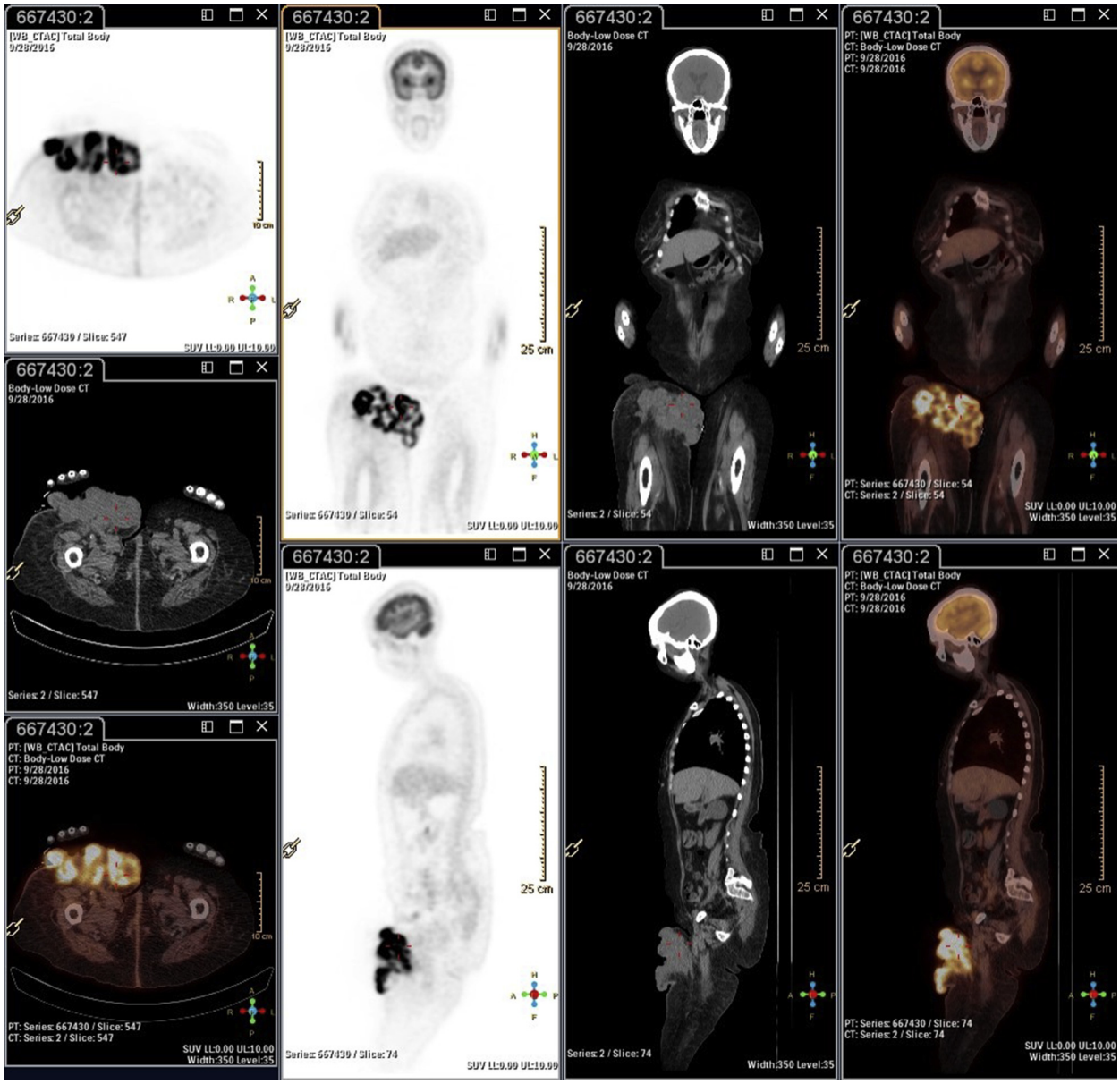

Fig 4. Staging positron emission tomography—computed tomography (left column, transaxial; top row, coronal; bottom row, sagittal) reveals mild uptake of fluorodeoxyglucose in the right heel mass and intense heterogeneous uptake of fluorodeoxyglucose in the right thigh mass. Also note the moderate uptake in multiple pathological lymph nodes.

determined, the case supports the hypothesis that it may be associated with progressive metastatic disease. This case further highlights the severe morbidity of melanoma associated with late presentation, particularly in patients with AM. Additional studies are needed to better understand the factors attributing to the poor prognosis associated with AM in the black population in Africa.

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