# Advanced acral melanoma

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In the United States, the incidence of melanoma is increasing faster than any other preventable cancer. Acral melanoma is the fourth most common type of cutaneous melanoma and is frequently diagnosed later in its course compared with melanoma in other anatomic locations. Here we describe a case of highly advanced acral melanoma.

## CASE REPORT

A 47-year-old Caucasian man presented to the dermatology department for evaluation of a mass on his left foot. Six years prior, the patient had dropped a sledgehammer on his left great toe causing significant toenail damage, nail loss, and enlarging ulceration despite meticulous wound care. Ten months before presentation, the patient noted rapid growth of the left great toe mass that began to encompass the majority of the distal aspect of his foot. As the mass grew, the patient reported foul-smelling discharge, tissue sloughing, and bleeding. Three months before presentation, a mass appeared in the patient's left groin, along with scattered firm nodules on the left calf and thigh. The patient had not sought medical care for the mass other than 1 visit to the emergency department 2 months prior, during which the patient declined oncology consultation. He attributed his reluctance to seek medical care to lack of insurance and his belief that the growth was caused by an infection.

On examination, the patient had a 30- × 17-cm fungating, irregularly shaped necrotic mass engulfing his great toe and the majority of the distal medial aspect of his foot (Fig 1). There were multiple violaceous subcutaneous nodules along the thigh and a 15-cm firm, bound-down mass in the left groin along with pronounced edema of the entire left extremity. The patient appeared pale and cachectic. A biopsy specimen of the left toe mass and a left leg nodule confirmed the diagnosis of primary melanoma and metastatic melanoma. Histology demonstrated highly atypical $S100^+$ epithelioid cells with prominent perineural invasion (Fig 2). Positron emission–computed tomography showed a mass with bony invasion causing destruction of the left hallux, enlarged inguinal, retroperitoneal, pulmonary, mediastinal, and supraclavicular lymph nodes and pulmonary nodules. Laboratory analyses showed numerous abnormalities. The patient had severe anemia with a hemoglobin of 6.3 g/dL (normal range 14.3-18.1 g/dL) and hematocrit of 22% (39.2%-50.2%). White blood cell count and platelets were elevated at 12.1 $10^9$/L (4.0-11.1 $10^9$/L) and 701 $10^9$/L (150-400 $10^9$/L), respectively. C-reactive protein and erythrocyte sedimentation rate were elevated at 15.4 mg/dL (0.0-1.0 mg/dL) and 124 mm/h (0-10 mm/h), respectively. Liver function tests showed evidence of malnutrition with an albumin of 2.3 g/dL (3.4-5.0 g/dL). Basic metabolic panel and lactate dehydrogenase were within normal limits. Genetic analysis of tumor tissue was negative for *BRAF*, *NRAS*, and *c-kit* mutations. The left foot mass was partially surgically excised by the podiatry department to improve the patient's overall quality of life. The patient was then enrolled in a blinded clinical trial of a combination of an antibody against programmed cell death protein 1 and ipilimumab, an anticytotoxic T-lymphocyte-associated protein 4 antibody versus monotherapy of both agents. He was enrolled into one of the monotherapy arms of the trial and received only

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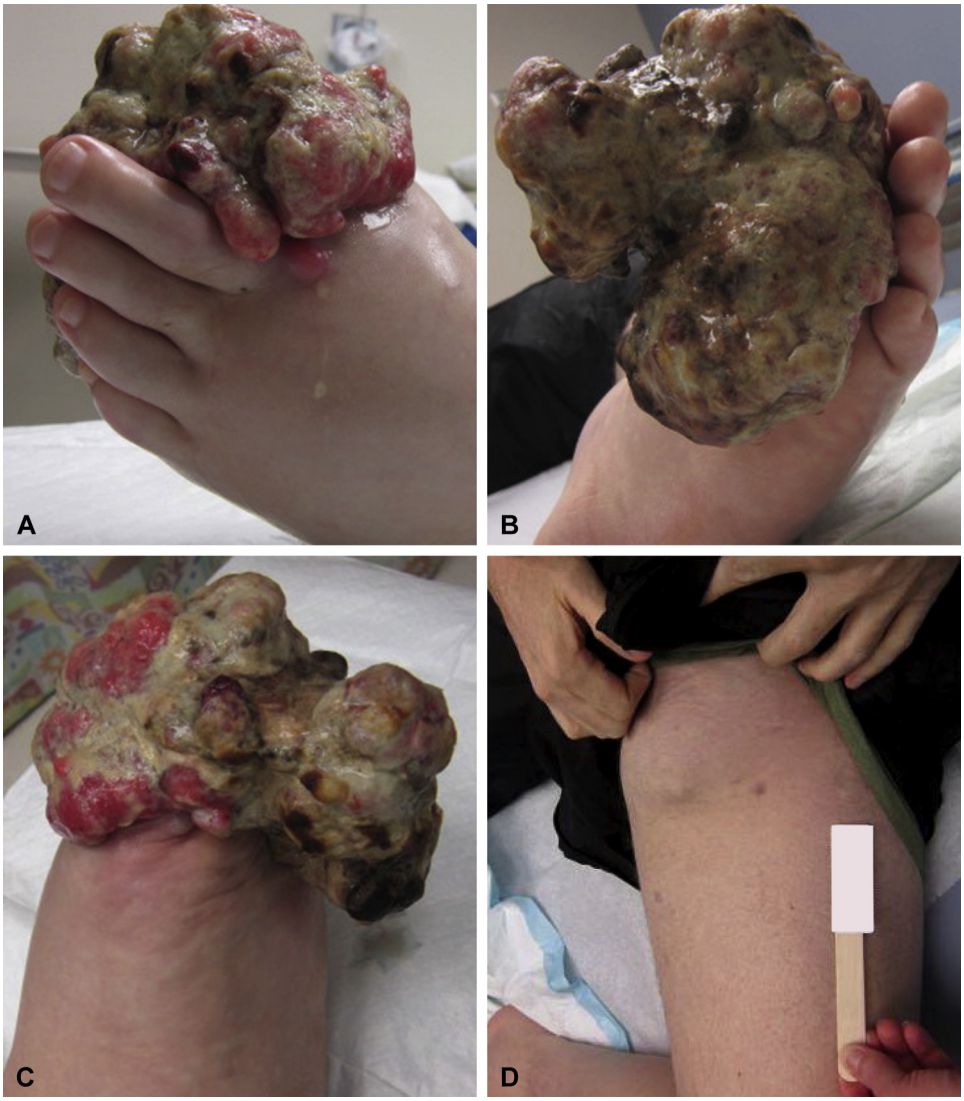


**Fig 1.** **A** to **C**, Acral melanoma. Clinical presentation of large, fungating, malodorous mass obscuring the left great toe with large areas of necrosis. **D**, Firm, lobulated mass in left groin.

ipilimumab at a dose of 3 mg/kg. Unfortunately, after just 2 doses of ipilimumab, the patient experienced severe colitis, a known immune-related adverse event, resulting in hospitalization and drug discontinuation. Once removed from the medication, the patient's colitis resolved and he elected to receive hospice care. He died of his metastatic disease 4 months after initial presentation.

## DISCUSSION

It is estimated that in 2014 more than 76,000 people were diagnosed with invasive melanoma and greater than 9000 people died of this disease.[1] Acral melanomas account for only 1% of all cutaneous melanomas, but are frequently associated with a poorer prognosis. Acral melanomas have been shown to have significantly decreased 5-year survival (52%) than matched counterparts with melanoma on the leg (85%).[2] Acral melanomas on the foot compared with those on the hand have also been associated with decreased survival.[3] This poor prognosis is likely multifactorial. Patients often attribute pedal melanomas to prior trauma and it is unclear whether or not trauma may have a causative role or simply brings attention to an existing lesion.[3] Trauma can further delay diagnosis if pigment is mistaken for subungual hemorrhage. Bob Marley, who was diagnosed with acral melanoma in 1977, was known to have a soccer injury to the same region a few months before his diagnosis.[4,5] Physicians also misdiagnose acral melanomas up to 33% of the time, with an average time to diagnosis of 13.5 months from the first recognition of the lesion.[6] Finally, it is questioned whether or not acral melanoma is an

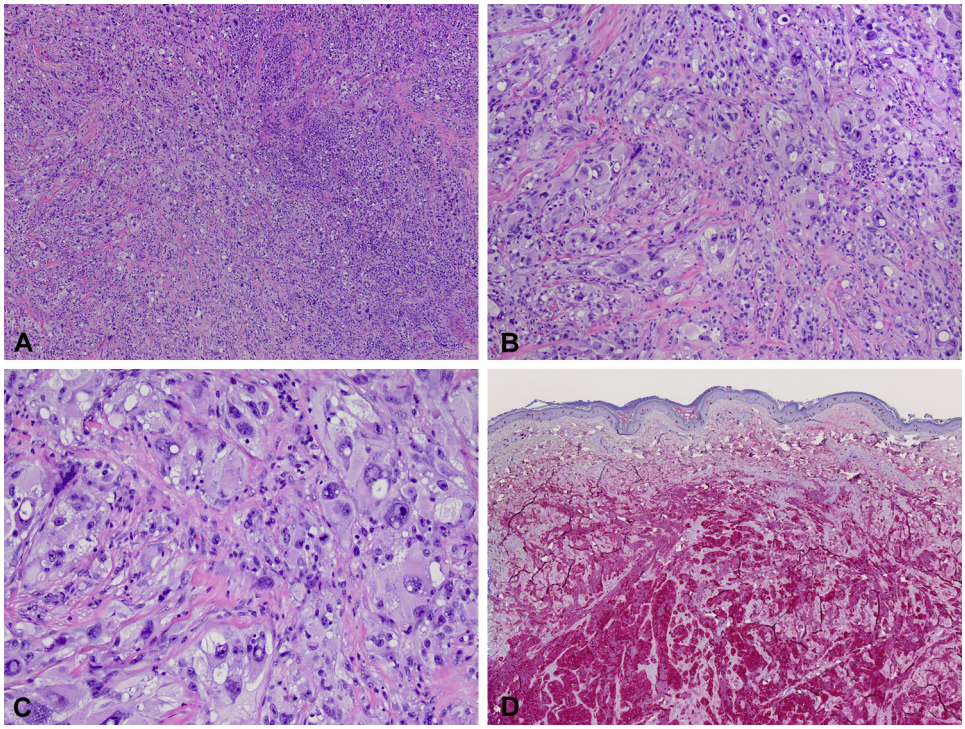


**Fig 2.** Pathology of acral melanoma. **A**, Histologically the lesion is densely cellular with minimal intervening stroma. **B** and **C**, Higher-power magnification demonstrates epithelioid tumor cells with marked cellular and nuclear atypia. **D**, An immunohistochemical study for S100 strongly and diffusely labels the tumor cells. (Original magnification: ×40.) (**A** to **C**, Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×100; **C**, ×200.)

inherently more aggressive variant of melanoma. Our patient demonstrates the natural progression of advanced acral melanoma, with a large and destructive primary tumor and diffuse metastatic disease at the time of presentation. The unfortunate combination of decreased access to health care, delayed diagnosis, neglect, and acral location led to a 6-year growth of the primary tumor and eventual death from metastatic disease.

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