

Case Report

Lower Extremity Amelanotic Nodular Melanoma

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Received: November 24, 2014; Accepted: December 24, 2014; Published: December 27, 2014

Abstract

The incidence of melanoma has increased 15-fold in the past 40 years, which is more rapid than for any other malignancy. Nodular melanoma is the second most common subtype of melanoma and is often diagnosed at more advanced stages. Nodular melanoma contributes disproportionately to the number of deaths from melanoma. We discuss the case of a patient presenting with large amelanotic nodular melanoma of the lower extremity that had progression of disease despite undergoing appropriate management. It is important for Emergency physicians to maintain a high level of suspicion for nodular melanoma given the high mortality rates associated with this malignancy.

Keywords: Nodular; Cutaneous; Melanoma

Introduction

Melanoma is the fifth most common type of cancer, representing 4.6% of all new cancer diagnoses in the United States [1]. Primary cutaneous melanoma is classified into four sub-types: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, and acral lentiginous melanoma [2]. Nodular melanoma is an aggressive tumor that exhibits early rapid growth and advanced thickness at time of diagnosis [3-4]. We describe a case of a patient with a large primary cutaneous nodular melanoma of the lower extremity with advanced metastatic disease.

Case Presentation

The patient is a 55-year-old male, with past medical history significant for hypertension, hypercholesterolemia, and diabetes mellitus. He presented to the Emergency Department with a large, fungating mass on his right lower extremity for 3 months. The mass had grown rapidly and became ulcerated with occasional bleeding and clear discharge. He denied any significant pain or neurological symptoms. The patient reported additional symptoms of fatigue and anorexia but denied any significant weight loss.

The physical examination revealed a 7 x 5 cm ulcerated, exophytic mass of the lower third anterior aspect of the right leg composed of amelanotic, beefy red tissue with yellow fibrinous granulation tissue and an 8 mm pink papule just proximal to the lesion (Figure 1). A full-body skin examination revealed large right inguinal lymphadenopathy; no left inguinal or axillary lymphadenopathy was noted.

The patient was referred to surgical oncology and underwent wide excision of the mass and core biopsy of an enlarged right inguinal lymph node. The pathology revealed ulcerated nodular melanoma with a Breslow thickness of 18mm and a mitotic rate of 8/mm². He subsequently required re-excision and wound debridement for infection, and split-thickness skin grafts to the right leg wound with excision of an adjacent 2 cm mass. Repeat pathology of the new mass confirmed the presence of nodular melanoma. He underwent computed tomography scan of the chest, abdomen, and pelvis that revealed extensive pulmonary metastatic disease and markedly enlarged right thigh, inguinal, and pelvic lymphadenopathy as well

as aortocaval lymphadenopathy (Figure 2). Given these findings, the patient was classified as having stage IV disease.

The patient was started on a single agent chemotherapy regimen with ipilimumab. At the time this report was written, the patient was in the process of completing a third cycle of chemotherapy. He was noted to have progression of disease with several small 1-2 cm in-transit lesions of the right lower extremity as well as worsening of the right groin lymphadenopathy. He elected to discontinue treatment at this time, and expired in a hospice facility.

Discussion

In the past 40 years, the incidence of melanoma has increased 15-fold, which is more rapid than for any other malignancy [5]. For the year 2014, it is estimated that there will be 76, 100 new cases of melanoma with 9, 710 deaths [6], compared to 59,000 new diagnoses in 2005 with 7,700 deaths [7]. In 2006, the lifetime risk of developing melanoma was 1 in 52 for men and 1 in 77 for women, which has increased to 1 in 34 for men and 1 in 53 for women in 2014 [6-8].

Relative risk factors for the development of cutaneous melanoma include: exposure to ultraviolet radiation, a history of severe sunburns



Figure 1: Gross appearance of primary melanoma with 8 mm in-transit lesion. Width 7 x 5 cm.



Figure 2: Large right inguinal lymphadenopathy.

experienced in childhood, chronic prolonged sun exposure, fair-skin and light hair, and a family or personal history of melanoma [9-13].

The prognosis of a patient with cutaneous melanoma depends on the staging at the time of diagnosis, which is based on a tumor-node-metastasis system. The classification takes into account tumor thickness, presence or absence of ulceration, and the mitotic rate, in addition to presence of nodal metastases and distant metastases.

In stage IV patients, the major prognostic factor is the site of distant metastasis, with visceral metastases having a poorer prognosis than metastasis to non-visceral sites [5]. Ulceration is a significant independent predictor of survival given its association with advanced depth of invasion and poor prognosis [9,14-17].

Amelanotic melanomas present a unique challenge to physicians, as they do not possess the typical brown or black hyperpigmentation often associated with malignant disease. Approximately 2 to 8% of all melanomas present as amelanotic lesions [18].

Nodular melanoma is the second most common type of cutaneous melanoma, accounting for approximately 15-30% of all melanomas [5]. It is diagnosed most frequently within the 6th decade of life and is commonly seen on the trunk, head, and neck, although it can occur anywhere on the body [5]. Grossly, nodular melanomas vary in color from blue/black to pink/red, but a significant proportion of lesions have an amelanotic appearance [18]. It can present as a symmetrical nodule with round and defined borders or as ill-defined cauliflower like lesions [5,19-21]. Nodular melanomas also tend to ulcerate, crust, and bleed [19].

Compared to other sub-types of cutaneous melanoma, nodular melanoma comprises the greatest proportion of thick melanomas [22]. This is thought to be because nodular melanoma likely develops solely from a vertical growth phase, without a pre-existing horizontal growth phase that is characteristic of other melanoma sub-types [5]. Therefore, nodular melanoma is often diagnosed at thicker, more advanced stages and is associated with poorer prognosis.

Nodular melanoma also contributes disproportionately to the number of deaths from melanoma [23-24]. A recent study showed that while nodular melanoma accounts for as low as 14% of all cases of cutaneous melanoma, it is responsible for 43% of deaths from melanoma [17]. Another study examining the diagnostic accuracy of cutaneous melanoma by sub-type noted that, compared to superficial

spreading melanoma, nodular melanomas were approximately 2 mm thicker at time of diagnosis, had a higher mitotic rate, and were more likely to be ulcerated [3]; all factors associated with poorer prognosis. Diagnosis of nodular melanoma is further complicated by atypical clinical presentation. An Australian study that surveyed patients with superficial spreading or nodular melanoma about the clinical features of their lesions noted that nodular melanoma, compared to superficial spreading melanoma, was less likely to exhibit color change, pigmentation, or asymmetry – all concerning features that usually prompt patients to seek medical care [25]. Amelanotic nodular melanoma can therefore be easily mistaken as a benign inflammatory lesion, such as folliculitis. The study did note, however, that a change in the elevation of the lesion was the most specific for nodular melanoma [25].

This case documents a patient with large, rapidly growing cutaneous amelanotic nodular melanoma with extensive metastatic disease unresponsive to chemotherapy. Early diagnosis of nodular melanoma is limited given the aggressive growth kinetics of the tumor, and it's often amelanotic appearance resembles several other benign and malignant tumors as well as some inflammatory lesions. Given the documented disproportionate number of deaths from nodular melanoma compared to other sub-types of melanoma, and the unpredictable behavior regarding disease progression and treatment responsiveness, early recognition is essential to the prevention of metastatic disease and the improvement of mortality rates from cutaneous melanoma. It is therefore critical for the emergency physician to maintain a high level of suspicion for cutaneous melanoma in patients with risk factors presenting with longstanding, rapidly growing cutaneous lesions.

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