

COMMENTARY

Acral Melanoma: A Patient's Experience and Physician's Commentary

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Received: September 3, 2018 / Published online: September 18, 2018
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ABSTRACT

This article, co-authored by a patient diagnosed with acral melanoma, discusses the patient's experience of being diagnosed with and treated with surgery for this disease. The physician discusses the epidemiology, genetics, diagnosis, treatment, and prognosis of acral melanoma. Follow-up care plans are also discussed.

Keywords: Acral melanoma; Cutaneous melanoma; Epidemiology; Prognosis; Screening; Treatment; Wide local excision

PATIENT EXPERIENCE

In April 2017, I noticed that the “bruise” on my toe was still there. I had seen it a couple of weeks prior and while it looked odd, I thought, “Maybe it will go away”. Later I tried to remove

Anonymous patient: a patient with acral melanoma who wishes to remain anonymous.

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the black line with nail polish remover. It didn't work. In my heart I knew it was melanoma.

Twenty years ago, my father had the same thing on a different toe. Biopsy confirmed it was melanoma. We thought it was not a big problem. It was “only skin cancer, after all”. Well, my father's toe was amputated, and the melanoma turned out to be stage 4. It metastasized quickly. After several courses of tough chemo and some experimental treatment, my father lost his cancer battle. He was 67 years old. I am 62.

As a result of this experience, I became very vigilant in seeing my dermatologist for yearly exams and examining myself. Being fair skinned, I am at high risk anyway. No skin cancers were ever found. As a survivor of kidney and breast cancer, certainly cancer was definitely on my radar screen. Yet, in seeing this possible melanoma, I still had initial denial and delayed making an appointment with the doctor.

A couple of weeks later, I did see my dermatologist. I had seen her only a couple of months before, so I feared this “toe thing” might be aggressive. She removed as much of this skin cancer as possible. When the results came in, they confirmed melanoma.

The next step was seeing the surgeon. There I learned that my toe would have to be amputated in order to allow proper margins around the area of the tumor. I was full of fears—fearful of pain, of difficulty in walking, and of the possibility of metastasis.

The surgeon assured me that I would be fine and walking normally in 2 weeks. I learned that while my father and I had the same type of cancer, this type does not usually run in families. This melanoma is also not caused by sun exposure.

I had the surgery and was out of the hospital the same day. The tumor was early stage and no chemotherapy was indicated. I was walking well within 2 weeks. Recovery was not as difficult as I thought it would be. I took pain medications for about 2–3 days.

Now, about a year later, I follow up with my dermatologist every 3 months, and will continue to do so for 2 years and with my surgeon every 6 months, for now. My lymph nodes are fine and I am doing well. My toes do hurt sometimes due to the absence of my fourth toe. The suggestion to tape my second and third toes together and to place a rubber wedge in the empty spot has worked well.

Honestly, I still have concerns, but 1 year later, I am less stressed. With support of family and friends, I stay focused on the positive and know I am doing all I can on my end. I make sure to use sunscreen to prevent any other kind of skin cancer and see my doctors as suggested.

PHYSICIAN'S COMMENTARY

The incidence of cutaneous melanoma has been rapidly increasing in the USA, with an estimated 91,270 new cases in 2018 [1]. Cutaneous melanoma has historically been distinguished into four main subtypes based on clinical and histologic presentation. The three most common subtypes include superficial spreading melanoma, accounting for approximately 70% of cases, followed by nodular melanoma and lentigo maligna melanoma. Acral lentiginous melanoma (ALM) is the least common subtype and accounts for 2–3% of all cutaneous melanomas [2, 3]. In the USA, for all subtypes of melanoma except ALM, non-Hispanic whites have been shown to have the highest incidence rates, as compared to Hispanic white, Black, and Asian/Pacific Islander patients. For ALM, while incidence is similarly low across all racial groups as compared to other subtypes of melanoma,

several studies have shown Hispanic whites have the highest incidence rates, followed by non-Hispanic whites [4, 5]. Given the lower incidence of all other melanoma subtypes among patients with skin of color, ALM contributes a comparatively greater proportion of all cutaneous melanomas diagnosed [5, 6].

In general, melanoma is a highly mutated cancer with a wide array of genomic alterations. In sun-exposed skin, ultraviolet light is considered to be the major contributor to mutagenesis. Mutation patterns tend to vary considerably based upon melanoma subtype and patterns of sun exposure. Overall, BRAF mutations are found in 50% of tumors and are more common in melanomas developing on intermittently sun-exposed skin (i.e., trunk). NRAS mutations are found in approximately 20% of melanomas and are more frequently found in chronically sun-exposed skin (i.e., face) [2, 7, 8]. In contrast, ALM occurs on relatively sun-protected sites, including the palms, soles, and nail apparatus, and has comparatively lower numbers of point mutations than do melanomas occurring on sun-exposed sites. Somatic mutations in *BRAF*, *NRAS*, and *KIT* have each been shown to occur in about 15% of cases of acral melanoma [9, 10]. Acral melanoma is further distinguished by its greater numbers of DNA copy number gains and losses in comparison to melanomas on sun-exposed skin [11].

Among patients with cutaneous melanoma in general, approximately 10% have a family history of melanoma [9]. Again, in contrast to other cutaneous forms of melanoma, there are currently no known familial patterns of inheritance for acral melanoma [12]. Therefore, though our patient and her father both developed acral melanoma, we are unaware of any known predisposing genetic traits that may explain this occurrence.

Interestingly, our patient detected her melanoma based on self-skin examination, as it had not been present when her total body skin exam was conducted earlier that year. A survey study by Kasparian et al. of 8178 participants showed that the highest rates of self-skin examination were reported among participants with a personal history of melanoma compared to those with a family history or no history of

melanoma. Regardless, our patient's personal experience reflects the fact that she became more vigilant regarding self-skin examination as a direct result of her father's diagnosis of acral melanoma. Consequently, our patient's melanoma was likely diagnosed at an earlier and thinner stage than it would have been had she waited for her next yearly skin examination. As there is a well-established correlation between early detection of cutaneous melanoma, tumor thickness, and improved survival, self-skin examination likely improved her prognosis [13, 14].

In general, ALM is associated with significantly worse rates of survival when compared to cutaneous melanoma overall, which may be due to the fact that it is often diagnosed at thicker and later stages than other subtypes of melanoma [5]. In a multi-institutional prospective cohort study, Madankumar et al. found that acral lesions, whether benign or malignant, were more common in patients with skin of color, although there was a low level of awareness of these lesions among the patients included in their study [6]. The authors highlighted that the worse prognosis associated with acral melanoma may not only be due to its more aggressive biological behavior, but also to possible delays in presentation and diagnosis owing to a lack of patient awareness and suspicion. Lack of physician awareness and disparities in access to care may also result in delays in diagnosis, leading to worse prognosis. Greater education of patients regarding self-monitoring behaviors, including observation of acral lesions, may help to narrow the survival gap between acral melanoma and cutaneous melanoma in general.

As with cutaneous melanoma, first-line treatment for ALM includes wide local excision with margins determined by the depth of invasion of the tumor. As in the case of our patient, wide local excision of ALM on the hands and feet may require amputation of the digits [15]. Following amputation, our patient underwent physical therapy and noted that she was able to ambulate well within 2 weeks. In the appropriate patient with cutaneous melanoma, determined by specific guidelines based predominantly on tumor thickness [16] and other

features found on pathology, sentinel lymph node biopsy can be an important prognostic indicator. A study by Ito et al. of sentinel lymph node biopsy in patients with acral melanoma specifically showed that patients with tumor-positive sentinel lymph nodes had significantly shorter melanoma-specific and disease-free survival [17]. Additionally, in cases of advanced stage melanoma, sentinel lymph node biopsy provides necessary information to determine whether a patient qualifies for potentially life-saving adjuvant therapies, including immunotherapies (e.g., the CTLA inhibitor ipilimumab and the PD-1 inhibitors nivolumab and pembrolizumab) and combination BRAF/MEK inhibitor therapy (dabrafenib and trametinib) [18–20].

Gumaste et al. analyzed recurrence patterns in acral versus non-acral melanoma and found that recurrence was significantly more common in patients with acral melanoma [21]. These authors also showed that the rate of local/regional recurrence in patients with ALM was nearly double that in patients with non-acral melanoma (39 vs. 19%). Of note, the rate of distant metastases was similar for patients with ALM and non-acral melanoma, although patients with ALM experienced worse survival outcomes overall, even after controlling for melanoma stage at diagnosis. The authors of this study suggest that widening surgical margins may improve loco-regional control and subsequently improve survival, although further studies are necessary [21].

After a patient has been diagnosed with and treated for melanoma, there is a range of practices with regards to routine patient follow-up. Patients who have developed one primary melanoma are at an increased lifetime risk of developing a secondary primary melanoma as compared to the general population, with particularly increased risk occurring within the first year after diagnosis [22]. Additionally, it is particularly important to continuously evaluate patients for evidence of local recurrence, since, as stated above, the rate of local recurrence in patients with ALM has been shown to be higher than that in patients with non-acral melanoma, and patients with ALM have also been shown to experience decreased recurrence-free survival

times [21]. Thus, as with our patient, for the first 2 years after diagnosis of melanoma, our standard practice is to see patients every 3 months for total body skin exams. We then typically continue to see patients every 6 months, indefinitely.

Interestingly, in conducting 29 qualitative interviews with Australian patients who had been treated for stage I or II melanoma, Morton et al. found that when follow-up intervals were extended (i.e., from 4 to 6 months, or 6 to 12 months), patients generally viewed this as a marker of good health. By contrast, if more frequent visits were recommended, patients viewed this as a signal that their risk of a new primary or recurrence was increased [23].

Their interviews also showed that patients perceived the benefits of long-term follow-up care to include reassurance, early detection and treatment of new skin cancers, education about melanoma, the opportunity to ask questions, and the reinforcement of sun-safe behaviors. Regarding the perceived downsides of follow-up, many study participants reported experiencing anxiety associated with the visit, citing a number of factors as the source (i.e., being told of a recurrent or new melanoma, metastatic spread of melanoma, the follow-up visit serving as a reminder of the severity of their disease, and/or prior bad experiences with initial diagnosis). Importantly, every participant noted that they felt relief once the visit was over, especially when they were told they were “melanoma-free” [23].

Our patient noted that she is less stressed 1 year after her diagnosis, owing this to her social support system, practice of sun-safe behaviors, and vigilance regarding regular skin checks. We will continue to provide our patient with compassionate care, as we monitor her carefully for any signs of local recurrence, distant metastasis, or new primary melanoma.

ACKNOWLEDGEMENTS

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures. Elizabeth Greenwald, the Anonymous Patient, David Polsky and Tracey N. Liebman have nothing to disclose.

Compliance with Ethics Guidelines. This article does not contain any studies performed by any of the authors with human participants or animals.

Peer Review. Please note, contrary to the journal’s standard double-blind peer review process, as a commentary this article underwent review by a member of the journal’s Editorial Board.

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