When the story doesn't fit

A case of acral lentiginous melanoma of the big toe

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ABSTRACT

Melanoma is an aggressive but easily preventable cancer. However, it may have a highly atypical presentation which makes early detection more difficult. This case report discusses a 25-year-old patient with a rare case of melanoma developing underneath the nail of the first toe. The case was originally diagnosed as trauma due to its rarity and epidemiological unlikelihood, however through the patient's persistence for alternative opinions the correct diagnosis was eventually made. However, this led to an amputation as well as more intense, invasive treatment.

There were several points on history (duration of the lesion, appearance of the lesion, and lack of healing progress) which when combined with the lesion's physical appearance should have made such a presentation suspicious for a more malignant cause. This case highlights the importance of early detection in the prognosis and treatment of patients with cancer, the importance of considering all aspects of a history and physical exam, and the importance of listening to and addressing a patient's concerns. As always, more common diagnoses should be first considered, but when the story does not match up with the presentation, one should move past the horses to consider the zebras.

CASE PRESENTATION

SM is a 23-year-old Chinese student who presented to his family physician with a red bruise-like discolouration under the nail of the right great toe, which he happened to notice while looking at his foot one day. It was a painless lesion roughly 5 mm by 5 mm, located in the centre of the nail, discontinuous from the nail base. SM has no family history of cancer. SM's physician concluded that the discolouration was likely caused by trauma which SM did not necessarily recall, but justified as having occurred while playing soccer.

1 month later, the discolouration had extended to the proximal edge of the nail. It became evident that the lesion was no longer contained in the nail, but rather in the nail bed and the surrounding tissue. This time, SM presented with concerns about the growth of a palpable longitudinal ridge on the nail. The family physician assured SM that despite this progression in presentation, trauma was still the most likely etiology.

1 month following this, SM presented to the physician's office with purulent discharge from the nail after the longitudinal ridge disintegrated, causing nail splitting. He was treated with cephalexin for 7 days for a suspected infection, which stopped the discharge. However, it recurred 1 month later with bleeding from the nail

bed, at which point antibiotic therapy was less effective. Over the 2 months that this occurred, the discolouration did not noticeably change in appearance. While it did not grow, it also did not show any signs of resolution.

Approximately 1 month following the second antibiotic course, SM pursued a second opinion with another primary care physician who initially corroborated the family physician's diagnosis of a trauma-induced hematoma. However, with patient persistence, SM was referred to another primary care physician with a focus in skin disorders, who expressed concern regarding the lesion. SM was provided with a referral to a dermatology clinic for a biopsy. Unfortunately, the biopsy was delayed for another month as SM traveled home over the school break. At this point approximately 5 months had passed since the initial presentation. Figure 1 shows the toe post-biopsy.

The biopsy results showed a subungual (beneath the nail) acral lentiginous melanoma with invasion extending beyond the biopsy depth. SM was urgently referred to a plastic surgeon for excision of the cancer, which resulted in an amputation of the great toe with some sparing of the distal phalanx. The sentinel lymph node from the inguinal chain was also positive for malignancy. A full body positron emission tomography scan did not detect distant metastasis. SM was then scheduled to undergo a complete inguinal node dissection.

Figure 1. Subungual melanoma on patient's toe, post-biopsy. The biopsy was taken as a core sample from the skin of the toe (ie proximal edge of the nail) inward towards the nail bed, at the site of the lesion.

DISCUSSION

Melanoma is a neoplastic disease characterised by an abnormal proliferation of melanocytes. It has a high tendency to metastasize and often has a poor prognosis if not detected early. The incidence of melanoma in Canada is 14.4 in 100 000 people. Melanoma is most prevalent in older individuals, with incidence rates peaking after age 70.^{1,2} The incidence has been increasing over the last 50 years.^{3,4} If melanoma is detected in stage III (spread to local lymph nodes), the 5-year survival is roughly 50%. Detection at stage IV (spread to distant organs/nodes) further decreases survival to 10 to 20%.⁴ Other studies have reported 5-year survival rates for stage IV melanoma to be as low as 5%.⁴ For this reason, early detection, diagnosis, and intervention is essential for successful treatment.

Acral lentiginous melanoma is a rare form of melanoma. It most often occurs on the palms, soles or in the nail unit.⁵ Although subungual melanomas are considered rare, they are the most common type of melanoma in patients of non-Caucasian descent, comprising roughly 20% of all melanomas in Asians (compared to 2 to 3% in Caucasians).⁶ This may be due to the fact that the nail blocks ultraviolet (UV) radiation, removing the association with UV exposure.⁷

Due to the location and presentation, subungual melanomas can present unique diagnostic challenges. Pigmentation within the nail unit has a broad differential diagnosis, including hematoma, infection, and various causes of melanocytic proliferation.⁸ Traditionally, the ABCDE acronym is used to represent the typical presentation of melanoma (Asymmetry, Border irregularity, Colour diversity, Diameter >6 mm, Evolution). However, this acronym has been shown to be less effective in subungual melanomas due to a wider variation in presentation.⁸ In light of this, the acronym CUBED (Coloured lesion, Uncertain etiology, Bleeding around the foot/nail, Enlargement despite treatment, Delay in healing beyond 2 months) has been purposed to improve diagnostic accuracy for unusual lesions associated with the nail unit.⁸

With regards to the current case, SM's presentation was atypical for acral lentiginous melanoma, which further complicated the diagnosis. However, some features of the history could raise the suspicion of melanoma. At the original visit, the fact that the pigmentation was discontinuous with the nail base, the colour of the lesion, and the fact that the patient was young support the diagnosis of hematoma. However, the lack of healing, lack of pain, and continued progression were inconsistent with a hematoma. The patient did not recall any trauma, which again made a hematoma diagnosis less likely.

In the 2 months following the initial presentation, the patient noticed nail changes that decreased the likelihood of a hematoma diagnosis and suggested the necessity for a wider differential diagnosis. Not only did the lesion show no signs of resolution after 2 months (meeting the CUBED criteria for delayed healing), SM's condition actually worsened with no history of re-injury or trauma. The nail developed a longitudinal ridge and then split, which presumably led to an infection. Progression of the lesion months after the original presentation should have led to uncertainty in the hematoma diagnosis, yet a second physician insisted that hematoma

with a secondary infection was the most probable diagnosis. This demonstrates how difficult it can be to accurately diagnose subungual melanomas, especially when the patient is young and has no family history to raise suspicion.

Distinguishing between a hematoma due to trauma and melanoma can be further complicated by the fact that trauma has been suggested as a risk factor for melanoma. 86% of subungual melanomas on the foot occur on the great toe, which is more likely to sustain an injury.⁶ Studies have also shown an association between recently sustained trauma and melanoma.^{6,9} This association may simply be the result of increased monitoring of the toe after injury, leading to increased detection. Conversely, it has been suggested that proliferation of melanocytes may be a response to trauma, leading to an increased risk of melanoma.⁶ In this case, no assertion can be made regarding the oncogenic role of trauma, but the fact that melanoma detection may follow injury should be reason to expand the differential diagnosis when the presentation is not typical for a traumatic hematoma. Considering melanoma more carefully may have reduced the delay in diagnosis, which could have improved the stage at which it was detected and subsequent treatment outcomes.

Treatment for melanoma varies based on stage at diagnosis. This includes a wide-margined resection if detected in-situ, resection and a biopsy of sentinel lymph node in stage I or II, or a wide-margined resection and dissection of the sentinel nodes in stage III.¹⁰ If detected in stage IV, treatment options are limited based on the ability of the primary tumor and metastases to be resected, but often includes systemic chemotherapy.¹⁰ In this case, accurate detection at the initial presentation may have resulted in an earlier stage of detection, which could have allowed treatment to be limited to excision or resection instead of amputation and inguinal lymph node removal.

CONCLUSION

This case is an unfortunate illustration of what can occur when melanoma is overlooked or misdiagnosed. The patient had an atypical presentation for subungual melanoma, which in itself is a rare disease. However, there were many aspects of the history which were inconsistent with the working diagnosis of a hematoma, and could have warranted further investigation.

Preventive medicine involves not only limiting disease occurrence through risk factor management, but restricting disease progression. Melanoma has a high mortality rate when it is not detected in the early stages, which consequently requires invasive surgical management. In this case, patient persistence ultimately resulted in a dermatology referral, but only after 4 months had already elapsed from the time of initial presentation. Many patients may not be as persistent or have the health literacy to recognize when a condition is not responding normally to treatment. For this reason, proper follow-up by the primary care practitioner is crucial to ensure that suspected injuries are resolving as expected. If not, the scope of the differential diagnosis should be reconsidered.

Melanoma can be very difficult to recognize, especially when

involving the nail unit in a patient whose demographics do not fit the usual pattern. Ultimately, some atypical presentations may be misdiagnosed in the early stages. However, as the clinical presentation evolves and symptoms become inconsistent with the current diagnosis, it is important to consider all possibilities. As is common with most secondary prevention efforts, recognizing the problem early allows for timely intervention and improves patient outcomes.

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