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Case Report

Malignant melanoma arising within tattoos as a risk factor for delayed diagnosis: a case report and systematic review

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Abstract

Malignant melanoma lesions arising in tattoo pigment pose diagnostic challenges, but current literature lacks quantitative data on delayed diagnosis. This study reports a new case involving multiple melanoma lesions in tattoo pigment, alongside a systematic review of past cases. Our objectives were to evaluate the potential for delayed diagnosis in patients with melanoma lesions in tattoo pigment and its impact on prognosis, comparing tumor characteristics with large-scale melanoma studies. A systematic review was conducted using PubMed and Ovid MEDLINE. Included studies were English-language reports of melanoma lesions in tattoo pigment, identifying new cases via case reports/series. Independent review and discussion resolved discrepancies. The review yielded 37 articles with 42 reports of melanoma lesions in tattoo pigment, totaling 43 cases. Of these, 35 were invasive, with mean and median Breslow thickness of 2.49mm and 0.9mm, respectively, which is higher than in large-scale studies. Patients also had a higher incidence of invasive lesions at diagnosis. The increased Breslow depth and risk of dermal invasion suggest a higher risk for delayed diagnosis and worse prognosis in melanoma arising in tattoo pigment. Further analysis of dermatoscopic differences is needed to improve diagnostic guidelines and avoid delayed diagnosis.

Introduction

Malignant melanoma (MM) is a tumor derived from melanocytes of the skin which is further classified histologically to inform clinical management. The term "melanoma in situ" (MIS) describes lesions limited to the

epidermis, lacking superficial or papillary dermal invasion.¹ MIS treatment guidelines are simpler and typically limited to secondary excision with reduced margins. In contrast, "invasive melanoma" lesions demonstrate dermal invasion and require a more thorough workup.² This involves assessment of vertical tumor thickness (Breslow depth) at the time of the biopsy to determine further steps in the staging process. In patients with lesions exhibiting ulceration or Breslow depth at least 0.8-1.0mm, sentinel lymph node biopsy is considered.³ Results of these studies help determine tumor stage and next steps, which may include secondary excision with larger margins, complete lymph node dissection, collaboration with medical oncology, and other adjuvant therapies when deemed appropriate.³

Because MM prognosis is largely dependent on early identification and intervention, it is essential to mitigate factors which may delay this process. There is a growing body of literature discussing the incidence of MM lesions arising in tattoo pigment. Some researchers have hypothesized that this is the result of toxic or carcinogenic effects of tattoo ink that may induce melanocyte transformation into malignant melanoma.⁴ Although current studies have yet to establish a causative relationship between tattoo ink and MM, many clinicians acknowledge the diagnostic challenges associated with such lesions.

Herein, we report a new case involving multiple MM lesions arising within an individual's tattoo pigment. Owing to the growing number of reported cases, we also conducted a systematic review of the literature to analyze prior cases. We used this data in a novel way to assess delayed diagnosis in tattoo-associated lesions relative to MM lesions not arising within tattoos. We hope this evidence promotes earlier detection of suspicious lesions within tattoo ink and improves prognosis in affected individuals.

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Figure 1. Five melanoma lesions presenting in our patient as suspicious pink-brown macules at initial presentation. **A)** Invasive melanoma lesion on the epigastric skin; Breslow depth 0.3mm. **B)** Invasive melanoma lesion on the left mid-upper back; Breslow depth 0.4mm. **C)** Melanoma in situ lesion on the right superior medial mid-back. **D)** Invasive melanoma lesion right mid-upper back; Breslow depth 0.3mm. **E)** Melanoma in situ lesion on the left proximal posterior upper arm.

Case Synopsis

A 69-year-old man with past medical history significant for malignant melanoma of the left knee presented with five suspicious pink-brown macules located on the epigastric skin (**Figure 1A**), left mid-upper back (**Figure 1B**), right superior medial mid-back (**Figure 1C**), right mid-upper back (**Figure 1D**), and left proximal posterior upper arm (**Figure 1E**).

Two of these lesions were located totally or partially within tattoo pigment (left mid-upper back and right mid-upper back), whereas the others were found in adjacent areas. Subsequent biopsies revealed invasive malignant melanoma lesions of the epigastric skin, left mid-upper back, and right mid-upper back, with Breslow thickness of 0.3mm, 0.4mm, and 0.3mm, respectively. The lesions on the right superior medial mid-back and left proximal posterior upper arm were consistent with MIS. Per treatment guidelines, the patient underwent wide local excision of the tumors with appropriate margins. He is now monitored closely for recurrence and thoroughly examined for new malignancies, with careful attention to areas of tattoo pigment.

This literature review was conducted according to Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines and was registered with PROSPERO (CRD42024560935).⁵ We searched the PubMed and Ovid MEDLINE databases with the search terms “melanoma” AND “tattoo” and included studies through July 16, 2024. The criteria for inclusion were as follows: (1) manuscripts written in English, (2) malignant melanoma lesions of the skin arising in tattoo pigment, (3) new cases identified via case report or case series (**Figure 2**).

This search yielded 197 results from PubMed and 132 results from Ovid MEDLINE. Studies classified as reviews,

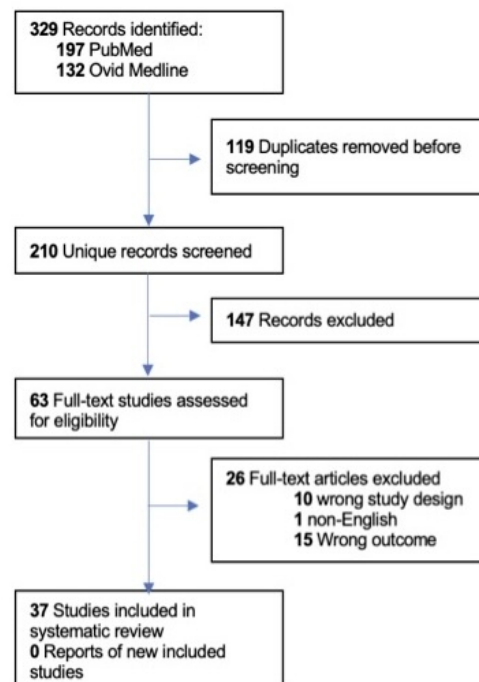


Figure 2. Selection of studies in the systematic review.

editorials, or letters were excluded, unless they also reported a new case with the appropriate outcome of interest. Manuscripts identifying tattoo pigment only in lymph nodes because of metastatic melanoma with an unknown primary were excluded, as this review is limited to cutaneous melanoma lesions arising within tattoo ink. Additional relevant manuscripts were abstracted from bibliographies. The results were reviewed independently by two authors (DS and KB), with discrepancies mediated

via discussion with a third author. This process yielded 37 manuscripts eligible for inclusion. To assess study quality, we utilized a modified version of the rating scheme from the Oxford Centre for Evidence-based Medicine.⁶ Evidence levels were based on study type, ranging from 1 (strongest evidence) to 5 (weakest evidence) as follows: (1) properly powered and conducted randomized clinical trial or systematic review with meta-analysis, (2) well-designed controlled trial without randomization or prospective comparative cohort trial, (3) case-control studies, retrospective cohort study, (4) case series with/without intervention or cross-sectional study, (5) opinion of respected authorities or case report.

Within the 37 included studies, we identified 42 cases of malignant melanoma arising within tattoo pigment, bringing the total to 43 cases including our own (Table 1). Quality assessment yielded 5 level 4 studies (case series) and 33 level 5 studies (case reports). The earliest identified case reported in 1938 describes a MM arising within a traumatic tattoo from accidental piercing with an indelible pencil.⁷ The most recent case, reported in April 2024, notes the malignant transformation of a nevus within tattoo pigment on the back of a 39-year-old man.⁸

For each study, we reported the number of new cases, tumor classification (MIS versus invasive), and Breslow depth where applicable. For cases with missing information, we reported “unknown” for both tumor classification and Breslow depth. Despite this missing data, we included these studies to accurately reflect temporal trends related to our outcome. Of the 43 cases, two were classified as MIS (4.7%), whereas 35 (81.4%) were invasive melanoma lesions with a corresponding Breslow depth reported. The remaining 6 cases (13.9%) did not include a classification other than cutaneous MM. For the invasive MM lesions in our study, the mean $\pm$ standard deviation and median Breslow thickness at diagnosis were 2.49 ± 3.64 mm and 0.9mm, respectively.

Case Discussion

When MM arises within tattoo pigment, there are obvious barriers to detection of the lesion.

Macroscopically, it is more challenging for both patients and clinicians to identify suspicious lesions when they are located within a tattoo. Further, the pigment can make dermatoscopic analysis of lesions difficult. Gall et al. highlights this in a previous study, noting how the black tattoo pigment made it virtually impossible to evaluate malignant potential using standard diagnostic criteria under dermoscopy.¹⁹ Without these criteria to guide clinical decision making, we expect an increased potential for error which may lead to delayed or even missed diagnoses.

To quantify this potential delay, we compared diagnostic characteristics of the MM lesions identified in our study to those of some large-scale melanoma studies. A study of 98,498 cases of invasive melanoma between 1989 and 2009 yielded a median Breslow depth of 0.73mm from 1989 to 1991 and 0.58mm from 2007 to

2009, compared to 0.9mm in our study.⁴³ This same study found the mean Breslow depth to be 0.77mm and 0.65mm in these respective time periods, compared to 2.49mm in our study.⁴³

Another international study used an online platform to identify and analyze 1456 melanomas between 2016 and 2020.⁴⁴ Of these MM lesions, 788 (54.1%) were classified as MIS, whereas 668 (45.9%) were classified as invasive.⁴⁴ Comparatively, only two cases in our review (4.7%) were identified as MIS; the majority were invasive lesions that required further workup and more extensive treatment. Additionally, the study reported a median Breslow depth of 0.7mm amongst invasive melanomas, which again is relatively low compared to our study.⁴⁴ Despite small sample size, our findings contradict the diagnostic norms in large-scale melanoma studies and increase our suspicion that tattoos are playing a role in the apparent delays.

Although we cannot say for sure whether the tattoo pigment is directly related to further progression of MM lesions at diagnosis, the associated macroscopic and dermatoscopic challenges, along with our quantitative findings, suggest this may be the case. If so, this may be a result of delayed suspicion on the patient end due to reduced visibility, allowing the lesion to progress further prior to seeking clinical evaluation. Contrastingly, the responsibility may fall on the physician for failing to biopsy what may otherwise have been a suspicious lesion owing to either concealment by the tattoo macroscopically or obstructed diagnostic features dermatoscopically. More than likely, our results reflect the cumulative effects of these challenges.

It is important to address these findings, as we note an increasing trend in MM lesions overlying tattoos in recent years. Over half of the cases in this study, which spans an 86-year time-period, were reported in the last 10 years. This mirrors the increase in prevalence of tattoos reported in recent years and warrants increased precaution in both patients with tattoos and dermatologists evaluating skin lesions in tattooed individuals.⁴⁵

Potential limitations in this study include data limited to published reports of cases meeting criteria for inclusion. There are likely additional unreported cases of MM arising in tattoo pigment, which may have altered our results if included. In our data extraction process, we did not have a tangible means to access large-scale clinical databases which may have allowed us to discover additional cases and mitigate publication bias. We also accounted for any discrepancies in tumor classification related to regional differences or updates in guidelines occurring within the duration of our study. For consistency, we used the most recent version of the US guidelines established by the American Joint Committee on Cancer clinical stages 0 to IIC primary cutaneous melanoma for categorization.⁴⁶ In the event where the category and Breslow depth contradict one another, we used the Breslow depth to universalize the categorization process and mitigate bias.

Table 1. Tumor Classification and Breslow Depth in Cases of Malignant Melanoma Arising Within Tattoo Pigment

Source	Cases	Tumor Classification	Breslow Depth	Level of Evidence
Sharlit, ⁷ 1938	1	Unknown	Unknown	5
Kirsch, ⁹ 1972	1	Unknown	Unknown	5
Wolfort et al, ¹⁰ 1974	1	Unknown	Unknown	5
Bartal et al, ¹¹ 1980	1	Invasive	5.8mm	5
Lee and Craig, ¹² 1984	1	Invasive	2.5mm	5
Kircik et al, ¹³ 1993	1	Invasive	1.15mm	5
Soroush V et al, ¹⁴ 1997	1	Invasive	0.75mm	5
Khan et al, ¹⁵ 1999	1	Invasive	0.9mm	5
Stinco et al, ¹⁶ 2003	1	Invasive	0.92mm	5
Paradisi et al, ¹⁷ 2006	1	Invasive	0.3mm	5
Shariff et al, ¹⁸ 2006	1	Unknown	Unknown	5
Gall N et al, ¹⁹ 2006	1	Invasive	0.95mm	5
Singh et al, ²⁰ 2007	1	Invasive	11mm	5
Kluger and Thomas, ²¹ 2008	1	Unknown	Unknown	5
Kluger et al, ²² 2008	1	Invasive	8mm	5
Jaigirdar et al, ²³ 2009	2	Invasive	1.2mm	4
		Invasive	3.9mm	
Varga et al, ²⁴ 2011	1	Invasive	0.99mm	5
Nolan et al, ²⁵ 2013	1	Invasive	0.25mm	5
Pohl et al, ²⁶ 2013	1	Invasive	0.45mm	5
Kluger et al, ²⁷ 2014	2	Invasive	0.4mm	4
		Invasive	15mm	
Kluger and Saarinen, ²⁸ 2015	1	<i>in situ</i>	N/A	5
Anthony et al, ²⁹ 2015	1	<i>in situ</i>	N/A	5
Joyce et al, ³⁰ 2015	1	Invasive	11mm	5
Caccavale et al, ³¹ 2015	1	Invasive	0.4mm	5
Tchernev Chokoeva, ³² 2015	1	Invasive	0.26mm	5
Deinlein et al, ³³ 2016	1	Invasive	1.3mm	5
Ricci F et al, ³⁴ 2018	1	Invasive	0.4mm	5
Armengot-Carbó et al, ³⁵ 2018	2	Invasive	0.35mm	4
		Invasive	0.4mm	
Cherkaoui et al, ³⁶ 2019	2	Invasive	0.7mm	4
		Invasive	0.9mm	
Veitch et al, ³⁷ 2019	1	Invasive	4.9mm	5
		Invasive	0.7mm	
Leijs et al, ³⁸ 2021	2	Invasive	6mm	4
Ricci et al, ³⁹ 2022	1	<i>in situ</i>	N/A	5
Rozen and Nahabedian (39), 2022	1	Invasive	1.05mm	5
Monfrecola et al, ⁴⁰ 2023	1	Invasive	3mm	5
Vasanthan et al, ⁴¹ 2023	1	Invasive	0.29mm	5
Zuberi et al, ⁴² 2023	1	Unknown	Unknown	5
Fidanzi et al, ⁸ 2024	1	Invasive	0.3mm	5

Our case	1	Invasive Invasive	0.4mm 0.3mm
Totals	43	Mean (± SD) = Median=	2.49 ± 3.64mm 0.9mm

SD, standard deviation

Conclusion

Our review highlights the potential for delayed diagnosis of melanoma skin cancers overlying tattoos, a finding with implications for both prognosis and management of these patients. Although a causative association remains uncertain, it is imperative that dermatologists remain vigilant when evaluating these patients, perhaps even maintaining a lower threshold to biopsy or recommending more frequent full body skin examinations in tattooed individuals. We also recommend further analysis of der-

matoscopic differences in melanomas within tattoo pigment to create better guidelines for diagnostic features within tattoos, with hopes to avoid delayed diagnosis and poorer prognosis in this growing patient population.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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