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## **Synchronous melanomas: one on tattoo and one on healthy skin**

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## **Abstract**

Tattooing is a widespread practice among the population, particularly among young people. With the increased popularity of tattoos, there have also been several reports of acute and chronic adverse events after tattooing. Malignant melanoma cases arising from tattoos have been increasingly described; however, there is no clear relationship between this practice and tumorigenesis.

We present a case of two synchronous melanomas (one located on a decorative tattoo) and update the literature.

## **Introduction**

Tattooing consists of the introduction of exogenous pigment into the dermis, in most cases for decorative purposes. We previously investigated the occurrence of melanoma on tattoos,<sup>1</sup> but no clear association between melanoma and tattoos has been demonstrated so far. Here, we report another case and update the literature by adding the recently reported cases.<sup>2-6</sup>

## **Case Report**

A 50-year-old man presented with two skin lesions clinically suspicious of malignancy. The first lesion, in the interscapular region, was located within a black tattoo. The second lesion was on the left scapula in a non-tattooed area (Figure 1a). The tattoo was done 15 years ago, and at that time, neither of the lesions was present (Figure 1b). After a dermoscopic examination (Figure 2 a-d), the lesions were surgically removed. On histological examination, both lesions were melanomas pT1a (0.4 mm Breslow thickness). There was no evidence of ulceration or mitosis. The tumor lymphocytic infiltrate was non-Brisk in the non-tattooed melanoma (Figure 2 b,c,e,f). Re-excision with 10 mm clear margins histologically showed scar tissue without evidence of residual melanoma.

## **Discussion**

A systematic bibliographic search of publications was carried out from the beginning until December 2023 using Medline (PubMed), Scopus, and Google Scholar. The following key words were used: "melanoma" and "tattoo" or "skin tattoo tumor" or "ink melanoma" to identify all reported cases of primary melanomas arising from tattoos. In total, 47 cases of melanoma on tattoo areas, including ours, are reported (38 males, 4 females, and 5 unknow). The age range was 9-82 years. In eight cases, pigmented lesions were present before tattooing. Still, in most cases (15/47), melanoma appeared after the tattoo procedure (range: 1-30 years), or the patient did not recall any previous lesions at the tattoo site (24/47). Most melanomas occurred on sun-exposed or intermittently exposed tattooed areas (24 on the arm, 8 on the back, 5 on the chest, 3 on the leg, 2 on the abdomen, and 1 on the forehead).

Interestingly, most melanomas occurred on dark blue (13/47), black (17/47), or blue tattoos (5/47), whereas most squamous cell carcinoma and keratoacanthoma occurred within red tattoos. However, this association might be incidental, as red and black inks are used frequently in tattoos. Interestingly, the tumor-infiltrating lymphocytes in this case report were found only in the non-tattooed melanoma. Various factors have been considered to assess the possibility of tattoos being carcinogenic, including local trauma from ink injection, ink composition and metabolites, ink photoreaction, and ink-induced inflammatory reactions.<sup>1</sup> Commonly, compounds used in tattoos could contain primary aromatic amines, nitrosamines, metallic pigments, and polycyclic aromatic hydrocarbons (PAHs). For example, the primary component of black ink is carbon black, which contains substantial amounts of PAHs. Fortes *et al.*<sup>7</sup> found clear evidence of an increased risk of cutaneous melanoma in workers in the petroleum, printing, and electrical and electronic industries, which can be associated with exposure to polychlorinated PAHs such as 7,12-dimethylbenz(a)anthracene, benzene, and polychlorinated biphenyls. Possible mechanisms may be due to the metabolic activation of PAHs, which could produce potentially mutagenic/carcinogenic metabolites.<sup>8</sup> Furthermore, in addition to influencing PAH metabolism within melanocytes, epoxides may elude genetic repair, creating adducts on adenine and guanine residues and leading to genomic instability.<sup>9</sup> In Europe, chemicals available on the market are defined by Regulation (EC) No. 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH), which in its consolidated version as of December 17, 2022,<sup>10</sup> sets concentration limits based on the hazardousness of substances and the requirements established by the Cosmetic Products Regulation (Regulation [EU] No. 2081/2020 amends Annex XVII of Regulation [EC] No. 1907/2006 [REACH] with entry No. 75 on tattoo and PMU ink). This restriction is applicable after 4th January 2022 and covers a large number of chemical substances (over 4000 chemical substances). It represents the first regulatory measure on a Union-wide basis on tattoo inks, after several years of fragmented legislative frameworks across EU Member States. However, the consequences of long-term skin deposition, the impurities present in actual products, and photodegradation into toxic or carcinogenic products should be considered.

## Conclusions

At present, it is not possible to support the carcinogenic role of tattoos due to the limited number of melanoma cases in tattooed individuals. The increase and prevalence of tattoos will be accompanied by a more frequent observation of melanomas arising in tattooed areas. Therefore, this possibility should be recognized by clinicians. Additionally, patients with multiple and/or atypical nevi and those



with high-risk melanoma should be informed about the risks and complications associated with pigmented lesions within tattooed areas.

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**Figure 1. a)** Physical examination showed two suspicious skin lesions: one lesion located within a black tattoo in the interscapular region and the other one on the left scapula in a non-tattooed area. **b)** The newly done tattoo, 15 years before, showed the absence of both lesions at that time.



**Figure 2.** **a)** Dermatoscopic examination of the lesion on the tattoo revealed an irregular pigmented network distorted by tattoo pigment. **b)** Histopathological analysis showed irregular junctional melanocytic nests of different sizes with variable nuclear atypia and pleomorphism. The black tattoo pigment is seen in between collagen bundles; **c)** at high magnification, contiguous proliferation of uniform moderately atypical melanocytes with upward pagetoid intraepidermal spread of atypical melanocytes (melanoma 0.4 mm Breslow [pT1a]; haematoxylin and eosin [H&E]; magnification: [b] x10, [c] x50). **d)** Dermoscopy of the non-tattooed melanoma showed an irregular pigmented network and an irregular polymorphic vascularization. **e)** Histopathological examination showed a non-ulcerated melanoma with a Breslow thickness of 0.4 mm (pT1a), and **f)** High magnification showed tumor-infiltrating lymphocytes non-Brisk ([H&E]; magnification: [e] x10, [f] x50).

