Review article

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Squamous neoplasms arising within tattoos: clinical presentation, histopathology and management

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Summary

Tattooing, which involves the placement of ink into the skin, is an ancient decorative technique that has remained popular in modern society. Tattoos have long been known to cause cutaneous reactions, which include the emergence of neoplasms such as keratoacanthoma (KA) and squamous cell carcinoma (SCC) in tattooed areas of the skin. We review the clinical presentations, histology and treatment options for squamous neoplasms, primarily KA and SCC, arising in tattoos.

Introduction

Tattooing is a well-known ancient artistic practice characterized by the intradermal placement of pigment, and it has increased in popularity over the past 20 years.[1,2] This practice may be performed for aesthetic, religious or cultural reasons.[1] In the US, the prevalence of at least one tattoo is estimated at approximately 24% in the 18–50 years age group.[2] Tattooing is also a popular practice in European countries as well, with prevalences ranging from 8.5% to 25% of the population, depending on the individual country and/or age group.[3,4]

Several types of cutaneous reactions have been observed within tattoos, including verruca, mycobacterial infections, allergic contact dermatitis, localized inflammation, sarcoidosis, foreign body granulomas, keloids, generalized inflammatory skin eruptions and malignancies.[5,6] In a survey performed in Germany in 2010, 6% of participants reported adverse reactions after tattooing.[3]

Tattoo inks and pigments are not regularly monitored by the United States Food and Drug Administration (FDA). Additionally, concerns have been raised for many years regarding tattoos and their possible association with neoplasms. A review of the literature performed in 2012 revealed 50 cases of skin malignancy occurring in tattoos, 16 of which were melanomas and 11 of which were basal cell carcinomas (BCCs).[7] Keratoacanthoma (KA) and squamous cell carcinoma (SCC) were the most commonly reported neoplasms, with 23 reported cases identified in the literature.[7] McQuarrie reported the first case of SCC arising in a tattoo in 1966.[8] Closely thereafter, Cipollaro reported a case of KA within a tattoo.[9] More recently, Barton *et al.*[10] reported a case of multiple eruptive KAs on the lips after tattoo placement.

We reviewed the literature on the clinical presentation, histopathology and treatment of squamous neoplasms, particularly KA and SCC, arising within tattoos.

Clinical presentation

In this review, we found 24 reported cases of squamous neoplasms arising within tattoos (Table 1).[5,8–21] These lesions often present as an enlarging, erythematous papule or nodule that may have associated ulceration, scale, induration, or central keratinaceous material.[1,5,8,13,15,21] Solitary nodules are most common, but multiple lesions at initial presentation or developing over time have also been described.[1,11,15,18] This phenomenon has been reported to occur in patients with ages ranging from 24 to 79 years.[9,17] The age of the

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Table 1 Clinical and histopathological characteristic of squamous neoplasms arising within tattoos.

Reference	Race	Sex	Age at initial presentation, years	Clinical presentation	Lesions, *n*	Site	Histopathological diagnosis	Age of tattoo	Duration of lesion	Ink colour of the tattoo with neoplasm	Treatment
Barton *et al.*[10]	White	F	56	Papules	Multiple (> 6)	Lip	Well-differentiated SCC with features of KA	2 months	Several weeks (multiple lesions within 8 months)	Red	PDT, PDT + PDL, shave excision
Chorny *et al.*[11]	White	M	56	Nodules with crust, size range 6–26 mm	4	Left forearm	All KA	3 weeks	Within 3 weeks	Multi-coloured	Excision
Cipollaro[9]	White	M	24	Elevated verrucous lesion, 5 mm	1	Left arm	KA	6 months	2 months	Red	Shave biopsy; electrodesiccation and curettage of the base
Fraga and Prossick[12]	Caucasian	M	54	Dome-shaped nodule, 10 mm	1	Right lower leg	Well-differentiated SCC	Not stated	4 weeks	Red and yellow	Excision
				Dome-shaped 4 mm papule	1	Right forearm	SCC, KA type	Not stated	Immediately following addition of red ink to pre-existing tattoo	Red	Excision
				Erythematous plaque, 6 mm	1	Right shin	SCC with features of KA	Not stated	Not stated	Red	Excision
				Indurated plaque, 3 mm	1	Right shin	Regressing KA	Not stated	Not stated	Red	Clinical monitoring
	Not stated	F	62	Not stated	1	Ankle	KA	Not stated	Not stated	Not stated	Not stated
	Not stated	M	66	Not stated	1	Lateral leg	KA	Not stated	Not stated	Not stated	Not stated
	Not stated	F	36	Not stated	1	Ankle	KA	Not stated	Not stated	Not stated	Not stated
	Not stated	M	53	Not stated	1	Arm	KA and SCC	Not stated	Not stated	Not stated	Not stated
	Not stated	M	52	Not stated	1	Arm	KA	Not stated	Not stated	Not stated	Not stated
	Not stated	M	50	Not stated	1	Forearm	KA	Not stated	Not stated	Not stated	Not stated
	Not stated	M	49	Not stated	1	Upper arm	KA	Not stated	Not stated	Not stated	Not stated
Goldenberg *et al.*[13]	Not stated	M	38	Hyperkeratotic, erythematous papules	4	Left forearm	Invasive SCC, KA type	1 month	1 month	Multiple colours	Excision
Goldstein[28]	Not stated	Not stated	Not stated	Not stated	1	Not stated	KA	Not stated	Not stated	Red	Not stated
	Not stated	Not stated	Not stated	Not stated	1	Not stated	KA	Not stated	Not stated	Red	Not stated

Table 1. continued

Reference	Race	Sex	Age at initial presentation, years	Clinical presentation	Lesions, *n*	Site	Histopathological diagnosis	Age of tattoo	Duration of lesion	Ink colour of the tattoo with neoplasm	Treatment
Gon *et al.*[5]	Not stated	F	60	Dome-shaped nodule with central keratinous material, 12 mm	1	Lateral right leg	KA	4 months	1 month	Red	Excision
Kleinerman *et al.*[15]	African American	F	43	Enlarging nodule	1	Right calf	KA	9 years	1 month	Red	MMS
Kluger *et al.*	Not stated	F	41	Nodule, 11 × 8 mm, rapidly growing	1	Scapula	KA	6 weeks	1 month	Red	Excision
McQuarrie[8]	Caucasian	M	40	Raised and ulcerated lesion	1	Right forearm	SCC	21 years	4 years	Red	Excision
Ortiz and Yamauchi[14]	White	F	47	Unknown appearance	1	Lip	Cystic SSC, KA-like	1–2 weeks	1–2 weeks	Red	MMS
				Dome-shaped nodule, 6 × 6 mm	1	Lip	KA-type SCC	1–2 weeks	1–2 weeks	Red	MMS
Paprottka *et al.*[16]	White	M	48	Skin alterations	1	Lower left leg	Invasive SCC	Approx. 3 weeks	4 months	Red	R0 tumour resection
Pitarch *et al.*[21]	Not stated	M	35	Ulcerated nodular lesion	1	Right arm	Well-differentiated SCC	10 years	Approx. 4 months	Black	Excision
	Not stated	F	30	Ulcerated nodular lesions	2	Not stated	Well-differentiated SCC and KA	10 months	Not stated	Black and red	Excision
Sarma *et al.*[17]	White	M	79	1 cm nodule	1	Left forearm	Poorly differentiated invasive SCC	> 50 years	Not stated	Black	Excision
Tan-Billet *et al.*[19]	White	M	51	Well-circumscribed, erythematous, verrucous 2 × 2.5 cm nodule	1	Right forearm	SCC with verrucous features	4 weeks	Not stated	Not stated	MMS
Vitiello *et al.*[18]	African American	M	39	Scaly nodules and papules on the leg	Multiple lesions	Left leg	KA	3 months	2 months	Red	Acitretin

MMS, Mohs micrographic surgery; KA, keratoacanthoma; PDL, pulsed dye laser; PDT, photodynamic therapy; SCC, squamous cell carcinoma.

tattoo at the time of presentation may vary from weeks to > 50 years after tattoo placement.[14,17] The majority of the reported cases were seen in men (15 men, 8 women, 2 sex unknown), and lesions were primarily located on the extremities.[5,8,9,11,12,15–19,21]

Eruption of KA or SCC within tattoos demonstrates a preference for those drawn in red ink, but may also be seen with black pigment and multicolour tattoos. Red pigment has long been known to be associated with tattoo reactions.[1] Mercuric sulphide, a common component of red ink, has been considered a possible cause of tattoo reactions; however, these complications have also been reported within red area of tattoos that have used alternative agents.[22] Red tattoos are the most commonly reported in association with KA and SCC, with up to 82% of cases in some series, and 64% in our previous report.[1]

Diagnosis

The differential diagnoses of KAs and SCCs arising within tattoos may include inflammation immediately following ink application, allergic contact dermatitis, hypersensitivity, foreign body reactions, pseudolymphomatous reactions, pseudoepitheliomatous hyperplasia, sarcoidosis, lichenoid reactions, bacterial, viral or fungal infeciton, malignant melanoma, BCC, dermatofibrosarcoma protuberans, and squamous neoplasms such as KA and SCC.[23]

Clinical morphology may be helpful, as a rapidly growing crateriform lesion may be suggestive of KA. Tenderness may be indicative of malignancy or infection, while pruritus may suggest a contact dermatitis or hypersensitivity. Therefore, the patient should be thoroughly interviewed for associated symptoms in order to further narrow the differential diagnosis. Histology is considered the gold standard to confirm diagnosis. Skin biopsy including punch, shave or excisional biopsy should be performed. Cultures should also be obtained when appropriate if infection is suspected.[14,17,20,23,24]

Histopathology

The histopathological similarities and differentiation of atypical squamous proliferations has been debated in the literature, making the distinction in reports more difficult. In the 24 reports in the literature, KA was the most commonly reported squamous neoplasm (15/24), while SCC made up the remaining diagnoses: three well-differentiated SCCs, one poorly differentiated SCC, five SCCs with KA features, one SCC with cystic and KA features, and one SCC with verrucous features. In two cases, both SCC and KA were reported.[1,10,13,14] This variability in diagnosis highlights the histopathological similarity of KA and SCC, and the debate about whether these lesions are separate entities or represent a spectrum of the same disease. To highlight this difficulty, Fraga and Prossick retrospectively reviewed 11 specimens from 8 patients, and reclassified four diagnoses of well-differentiated SCC as KA, and two cases of pseudoepitheliomatous hyperplasia as KA.[12]

Formation of cutaneous malignancies within tattoos is hypothesized to occur secondary to multiple inciting factors, including trauma arising from the tattooing procedure, tattoo-induced scarring, a chronic inflammatory reaction to the pigmentation, potential carcinogenesis from the pigment and potential exacerbation from ultraviolet exposure if the tattoo is in a sun-exposed site.[7,20,25] Trauma appears to be more strongly related to neoplasm development, as demonstrated by rapid development of a KA shortly after the procedure, resulting from cellular hyperplasia and localized inflammation.[18] The transepidermal elimination of tattoo pigment observed in some cases suggests a local immune response attempting to remove the pigmentation, and may suggest KA is the result of a reactive rather than neoplastic process.[18] The chronic inflammation that occurs after tattoo placement is thought to be more strongly associated with development of SCC.[25] It may be possible to differentiate the squamous proliferations based upon time of development; those that develop within a year of the tattooing procedure most likely represent KA, whereas those that develop years later secondary to chronic inflammation are most likely SCC.

Treatment

Review of the literature demonstrated that surgical excision is the most common method of treatment, with no reports of recurrence to date. Mohs micrographic surgery has also been used, notably on the calf and lip, where tissue conservation may be considered critical.[14,15,19] Vitiello *et al.*[18] reported a case of multiple eruptive KAs within a tattoo managed with acitretin; lesions were decreased in size after 4 weeks of treatment. Fraga and Prossick reported one regressing KA that appeared to be resolved post biopsy, and was therefore monitored clinically. Other approaches such as intralesional therapy with methotrexate, 5-fluorouracil (5-FU), bleomycin, interferon-alfa and systemic retinoids, have been used to treat KA with success, but no reports of these methods used for KA within tattoos are available.[26]

Conclusion

Squamous neoplasms arising in tattoos, particularly KA and SCC, are an unusual phenomenon, with few reports in the literature. Although the true incidence of such neoplasms is unclear, they should be included in the list of potential cutaneous complications related to tattooing. A direct association between tattoos and cutaneous neoplasms has not been established, but the International Agency for Research on Cancer has classified some common ingredients of tattoo ink as possibly carcinogenic (e.g. mercury, carbon black and cobalt sulphate) and carcinogenic to humans (e.g. cadmium compounds).[7] Considering the number of tattooed individuals worldwide and the small number of reported skin malignancies arising within tattoos, this phenomenon is considered by some to be coincidental. However, it is possible that cases may be underreported. Neoplasms are not included as a possible side effect of tattoo application within the online FDA consumer resources.[27] Further research is needed to determine whether there is a true association.

Learning points

- Tattooing can lead to various cutaneous complications, including the development of squamous neoplasms.
- Histopathological evaluation should be performed in all tumours arising within a tattoo.
- Commonly diagnosed squamous neoplasms within tattoos include KA and SCC.
- Based on review of the literature, red is the ink colour most commonly associated with squamous neoplasms.

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CPD questions

Learning objective

To review the clinical presentations, histology and treatments for squamous neoplasms arising in tattoos.

Question 1

Which of the following squamous neoplasms have been reported in tattoos?
(a) Squamous cell carcinoma.
(b) Keratoacanthoma.
(c) Both squamous cell carcinoma and keratoacanthoma.
(d) Melanoma.
(e) Sebaceous carcinoma.

Question 2

Which of the following is the most common ink colour associated with squamous neoplasms such as keratoacanthoma (KA) and squamous cell carcinoma (SCC)?
(a) Yellow.
(b) Red.
(c) Black.
(d) White.
(e) Purple.

Question 3

Which of the following best describes the age of a tattoo at the time of squamous neoplasm development?
(a) Several weeks to > 50 years after tattoo placement.
(b) At least 1 year after placement.
(c) More than 10 years after placement.
(d) Within 24 h of placement.
(e) Within 3 weeks of placement.

Question 4

Based on review of the literature, which of the following is the most commonly used method for treatment of a squamous neoplasm within a tattoo?
(a) Intralesional methotrexate.
(b) Complete excision or Mohs micrographic surgery.
(c) Systemic retinoid therapy.
(d) Clinical monitoring.
(e) Intralesional 5-fluorouracil.

Question 5

Which of the following best describes the clinical presentation of a squamous neoplasm arising within a tattoo?
(a) Enlarging, erythematous papule or nodule with associated ulceration, scale, induration or central keratinaceous material.
(b) Multiple keratotic nodules in a geometric distribution.
(c) Pigmented macule or patch.
(d) Erythematous macules with overlying scale.
(e) Yellow to white dome-shaped papules.

Instructions for answering questions

This learning activity is freely available online at http://www.wileyhealthlearning.com/ced

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at http://www.wileyhealthlearning.com/ced and answer the CPD questions
- Complete the required evaluation component of the activity

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