

Dermatofibrosarcoma Protuberans on Tattooed Skin: A Case Report

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ABSTRACT Dermatofibrosarcoma protuberans is an uncommon indolent fibroblastic skin tumor with a tendency for local recurrence. Its etiology is unknown, but there may be a link with vaccination sites, burn scars, and previous skin traumas. This report describes a curious case of dermatofibrosarcoma protuberans occurring secondary to a 16-year-old tattoo.

KEYWORDS: case study, dermatofibrosarcoma protuberans, DFSP, sarcoma, tattoo, tumor, wound care

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INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a low-grade sarcoma with an incidence of 4.1 per million person-years.¹ Age at diagnosis is usually between 20 and 59 years. It often localizes on the trunk, and it is slightly more common in men than in women, and among black people.^{1,2} It usually appears as a firm flesh-colored cutaneous and subcutaneous nodule with slow growth.

The neoplasm is locally aggressive and metastasizes in less than 5% of cases,³ with a 10-year relative survival of 99.1%.¹ Age at diagnosis is usually between 20 and 59 years. It often localizes on the trunk, and it is slightly more common in men than in women, and among black people.^{1,2} It usually appears as a firm flesh-colored cutaneous and subcutaneous nodule with slow growth. The neoplasm is locally aggressive and metastasizes in less than 5% of cases,³ with a 10-year relative survival of 99.1%.¹ Rare cases of fibrosarcomatous transformation have been reported.³ Histology often shows finger-like extensions that can lead to incomplete removal and relapse. For this reason, wide surgical margins or Mohs surgery is recommended.³

More than 90% of these sarcomas show a chromosomal translocation [t(17;22)(q22;q13)] with a resulting gene, the COL1A1-PDGFβ fusion protein, which behaves as an autocrine growth factor; others show different gene modifications.^{3–5} Varied treatment approaches are approved for DFSP:³ Mohs micrographic surgery, modified Mohs, complete circumferential and peripheral deep margin assessment, or wide excision with at least 2-cm margins. All of these procedures aim for clear margins, critical to avoiding relapse, because the local recurrence rate can reach up to 60%.³ Imatinib and radiation are approved for inoperable primary and metastatic tumors, but chemotherapy has not proved to be effective.^{3,4}

Extant literature includes several cases of DFSP associated with sites of previous trauma, such as burns and scars, as well as anatomic location of therapeutic irradiation or vaccinations.^{6–10} Further, about 50 cases of malignant skin and soft tissue tumors located inside tattoos have been reported in the last few decades; most reports include melanomas and basal and squamous cell carcinomas, but any association is considered coincidental.¹¹

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Tattooing deposits ink in the dermis through traumatic needle punctures; pigments and stabilizing agents are then phagocytized by macrophages to eliminate the foreign bodies that are then taken away to the lymph nodes. During this process, soft tissues react to the injury to heal the wound, and a dermal scar is created. Because the ink is trapped in the dermis, the inflammatory process continues on one side of the skin, and on the other side, the ink biokinetics and chronic UV sun exposure produce byproducts whose effects are still unclear. It has also been hypothesized that tattoo ink, by directly or indirectly altering a person's regional immunity, could induce local immunocompromise and lead, leading to carcinogenesis.¹²

This article reports a case of DFSP arising on a 16-year-old tattoo. To the best of the authors' knowledge, this is the fourth case worldwide detailing an association between DFSP and tattooing.¹³⁻¹⁵

CASE REPORT

A 29-year-old woman with a Fitzpatrick Skin Type II and no significant medical history except current smoking and class II obesity (body mass index 37.9 kg/m²) was admitted to the authors' outpatient service for evaluation of a slowly enlarging lesion on her back. The neoplasm began about 2 years before the visit and occurred within a decorative black tattoo she received 16 years earlier in Germany (Figure 1). The lesion had started growing with sudden itching at the margins, but her general practitioner thought it was "nothing to worry about" and only referred the woman to the hospital when the neoplasm was approximately 2 × 1 cm.

The lesion presented as a nontender, firm, red-violet oval nodule, with the major axis oriented along the line of the tattoo; it had a de-epithelialized area on its surface

Figure 1. DERMATOFIBROSARCOMA PROTUBERANS IN A TATTOO



Figure 2. RADICAL EXCISION OF THE SARCOMA REQUIRED WIDE MARGINS AND REMOVAL OF DEEP FASCIA



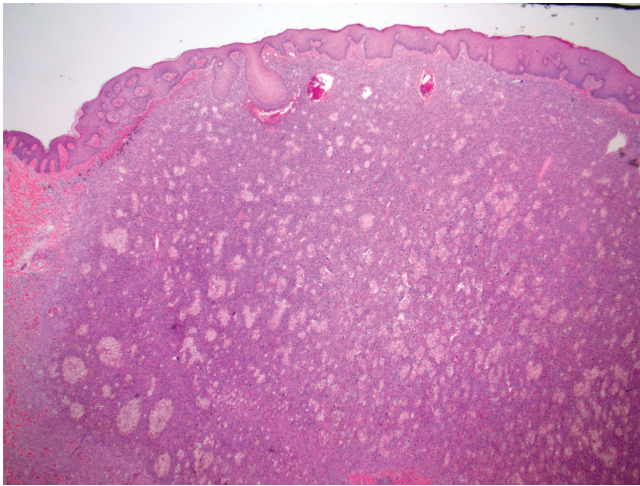
and was causing a deformation of the tattoo, which was faded in that region. The mass seemed to have a deep cleavage plane, and there was no sign of axillary or inguinal lymphadenopathy, nor were there any systemic symptoms. Differential diagnosis included benign lesions such dermatofibroma, cutaneous pseudolymphoma, and clear cell adenoma, as well as malignant neoplasms such as melanoma, Merkel cell carcinoma, and soft tissue sarcoma. Because dermatoscopy and confocal microscopy would not have definitively eliminated any of these, pathology was mandatory.

A priority elective excisional biopsy was performed with 5-mm macroscopic margins. The histologic examination confirmed the suspicion of DFSP, which appeared fully excised. The patient was called to complete

Figure 3. RESULT 3 MONTHS POSTOPERATION



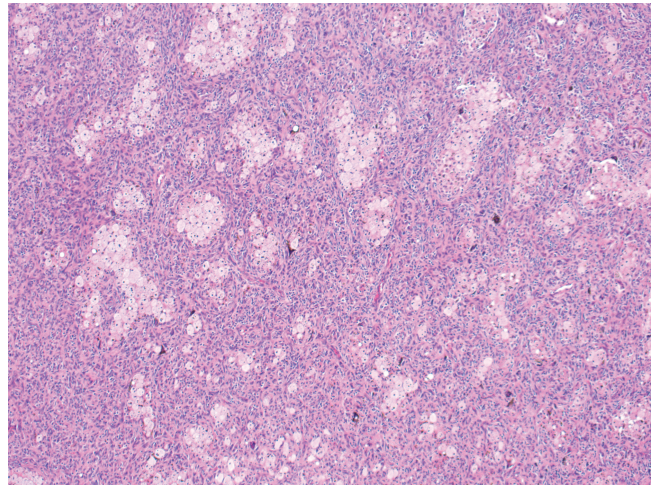
Figure 4. STAIN EXHIBITS STORIFORM PROLIFERATION OF ATYPICAL SPINDLED CELLS IN THE DERMIS AND SUBCUTANEOUS FATTY TISSUE



staging and treatment according to current guidelines.^{3,4,16} Abdominal echography and locoregional lymph node echography were negative for metastasis. These practitioners usually do not perform MRI study of patients after satisfactory clinical results in terms of outcome and survival.¹⁷

Although the lesion was completely excised during the radical excision biopsy, providers planned a surgical enlargement of margins with an immediate reconstruction; this also offered the patient the best potential cosmetic result. A 3-cm enlargement of the previous scar with an excision of the deep fascia was performed (Figure 2); reconstruction was achieved with a three-flap plasty. After

Figure 6. 10× STAIN HIGHLIGHTS TATTOO INK DISPERSAL



1 day of recovery, the patient was discharged; she was followed up for wound dressings as an outpatient. The surgical wound demonstrated good healing (Figure 3), and the postsurgical histologic examination confirmed no remnant DFSP cells in the radicalization piece. The patient was educated about regular self-examination, and she is now scheduled for clinical and instrumental follow-up every 6 months.

Pathology

The pathology of the lesion showed a 2.3 × 1.3-cm storiform proliferation of atypical spindled cells within the dermis and along the septae of the subcutaneous fatty tissue (Figure 4). Immunohistochemical staining was positive for CD34, CD68PGM1, CD68KP1, and factor

Figure 5. MICROSCOPIC ANALYSIS SHOWS FINGER-LIKE EXTENSIONS GROWING PARALLEL TO THE SKIN

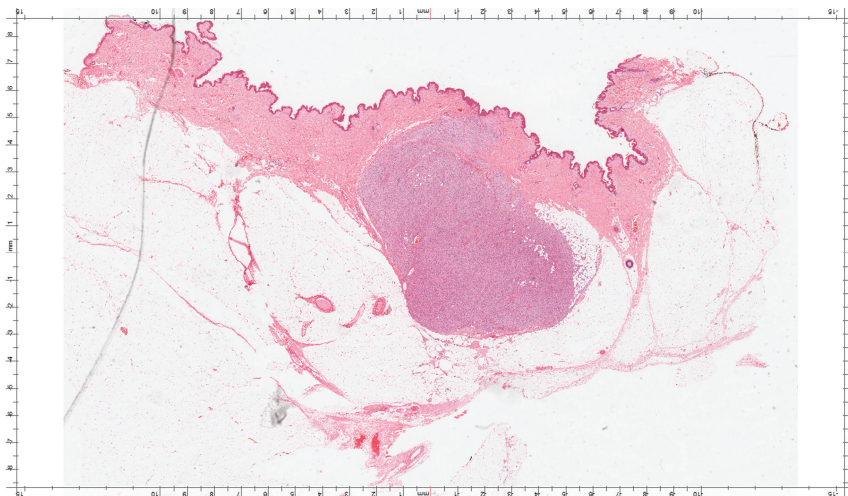
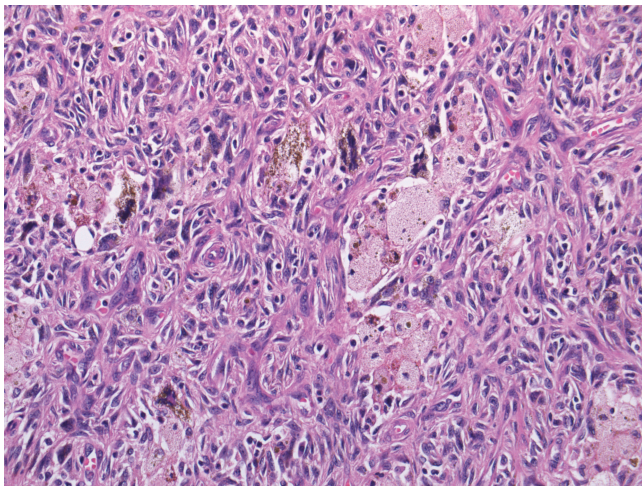


Figure 7. 40× STAIN SHOWS NEOPLASTIC AND MACROPHAGIC CELLS WITH RESIDUAL INK IN THE CYTOPLASM AND EXTRACELLULAR SPACE



XIIIa; MIB 1 was 10%. The neoplasm was diagnosed as a low-grade DFSP and was completely excised in the first excision, with no residual disease in the secondary surgical enlargement.

Interestingly, the DFSP showed the typical extensions mostly in the superficial fatty area, and it seemed to be expanding in a horizontal direction, just as the stimulating factor was superficial (Figure 5); further, tattoo ink was seen in the cytoplasm of both the neoplastic cells and the histiocytes, as well as the extracellular space (Figures 6 and 7).

The skin covering the sarcoma appeared de-epithelialized in some places, perhaps irritated by the patient's scratching in an attempt to relieve the pruritus, and granular ink pigment was found in the dermis around the lesion, in line with the tattooing history (Figure 4).

DISCUSSION

The Malignant Potential of Tattoo Ink

According to current literature, several complications can occur after tattooing, including inflammation, allergic reaction, infection, and neoplastic adverse effects, but the link with cancer has been seen as accidental until now.^{18,19} The issue of carcinogenicity in tattoos is generally unelucidated and concerns ink metabolism, solubility, and stability;²⁰ in particular, the photodecomposition of color pigments might produce other carcinogenic byproducts and enhance the cancer microenvironment.^{11,20}

No standardized international regulations exist for ink composition; thus, many different substances are included in tattoo ink. Further, the pigments, binders, solvents, and additives included have changed over time. Many metals, nanoparticles, and polycyclic aromatic hydrocarbons can be found in tattoo inks, and their single

and/or synergic effect could provoke cancer or act in the promotion and progression of preneoplastic lesions. For example, titanium dioxide nanoparticles are genotoxic; benzo(a)pyrene and cadmium compounds are carcinogenic; and benzo(a)anthracene, benzo(k)fluoranthene, benzo(b)fluoranthene, chrysene, naphthalene, mercury, and soluble cobalt salt are possibly carcinogenic to humans.²¹ All of these have been used to formulate tattoo ink. Further, the array of chemicals in tattoo ink shows different biodynamics: they may act on human cells with non-specific bonds (eg, attacking cell membranes from the extracellular space), specific interactions on biologic mechanisms (eg, inhibiting enzymes inside cytoplasm), or simple reactions to surrounding molecules (eg, modifying intercellular signaling).²⁰

A recent study indicates that tattoo inks, mostly the yellow and red inks, include some chemical impurities and azopigments that induce adaptive stress response pathways for genotoxicity.²⁰ In black ink, six polycyclic aromatic hydrocarbons and some other undetected chemical impurities with highly bioactive nanoparticles such as carbon black induce oxidative stress, p53 response, and cytotoxicity.^{21,22}

To date, interest in tattoo ink biotoxicology is increasing, and research on the related health risks is developing, with experimental models identifying many possible variables. Insofar as carcinogenesis is a multifactorial event, it will probably be some time until tattoos are linked to skin cancer as a risk factor.

Tattooing as a Stimulus for DFSP

At least 65 cases of cutaneous neoplasms on tattoos have been described, mostly arising on areas of dark ink and the extremities, with variable time intervals between tattooing and diagnosis.²³ Squamous cell carcinomas and keratoacanthomas have been most frequently identified, and they appear to be linked to red ink; melanomas also are numerous and seen more with dark inks. Basal cell carcinomas were less frequently reported but highly associated with dark inks.²³

Three cases of DFSP in tattoos have been previously reported. These cases described two males and one female, aged between 35 and 52 years. The lesions were diagnosed between 6 and 8 years after tattooing, and the evidence of skin irritation started between 1 and 5 years after tattooing. The tattoos were black in two cases and red in the other, and they were located on the back, dorsum of the forearm, and dorsum of the thigh, respectively. In contrast, the back tattoo in this case was 16 years old; the black ink had faded to a green-blue color.

Most of the previous reports on DFSPs and other neoplasms noted ink deposition in the superficial dermis; some noted this in the inflammatory cells as well. In this

case, ink was found not only in the extracellular space and histiocytes, but also in the neoplastic cells and the lesion as a whole. Because of this, the authors hypothesize that the growth of the DFSP was somehow driven and stimulated by the superficial ink deposit and that the time of the excision coincided with a phase of expansion in which cells were “eating” ink growth factor components and “making themselves felt” through pruritus. The predisposition of the patient’s fair skin to malignancies, along with adipose tissue inflammation, could have contributed to a carcinogenic microenvironment at the site of ink deposition.

The histogenesis of DFSP tumors is unknown, but many reports advocate a cause-effect association between local trauma and neoplasm growth. Radiation, immunization, accidental trauma, infected insect bites, surgical drainage scars, and burn scars^{24–26} may all cause chronic inflammation and consequent wound healing impairment; the local concentration of CD34-positive cells in tissue intended to mediate tissue repair could be overstimulated and eventually become malignant.^{14,27} Similarly, skin puncture, ink byproducts, tattoo ink components, scarring, and chronic inflammation could create local trauma leading to cell dysfunction and DFSP occurrence.

Because DFSP is so rare, it seems unlikely that all four reported cases in a tattoo are coincidental. Further, the association of basal and squamous cell carcinomas with tattoo sites²³ could suggest that tattooing can be considered a traumatic event, predisposing individuals to neoplastic evolution (squamous cell carcinoma in the epithelial subset and DFSP in the connective tissue).

CONCLUSIONS

This case reports an example of an unusual soft tissue neoplasm, DFSP, arising on a tattoo. The literature reveals many possible hypotheses concerning the carcinogenic potential of tattoo ink and many associations between skin trauma and DFSP. Because this patient’s histologic examination demonstrated that the neoplasm was growing along the outline of the tattoo and revealed black coloring inside both malignant and inflammatory cells, the authors assume that the tattoo could be implicated in the DFSP cells’ initiation.

The authors encourage general practitioners who note similar lesions on tattooed skin to do a punch skin biopsy, make quick referral to their surgical colleagues, and refer such cases to public health and community medicine. Further research is needed to illuminate the issue of tattoo ink toxicity. ●

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