Inflammatory Reactions from Organic Pigments in Red Tattoos

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Two different red pigments used for tattooing were found to give rise to inflammatory reactions in the skin. No inorganic component was found in the pigments. NMR and MS analyses elucidated the molecular structures of two different organic compounds. A bright red pigment was found to be an aromatic azo-derivative, and a red-violet pigment was found to be linear quinacridone. A strong exposure to UV-light was reported in most cases prior to the onset of the inflammation. ***Key words: Azo-dye; Inflammation.***

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Allergic reactions caused by red tattoo pigments have been known for a long time and have usually been ascribed to mercury hypersensitivity caused by cinnabar (mercury sulphide, HgS) (1, 2). Recently inflammation in red tattoos has been seen in patients who showed no sensitivity to mercury salts in epic-

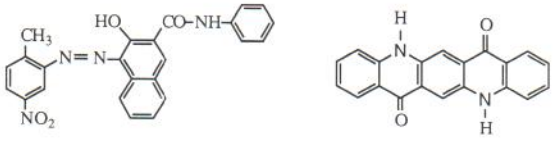
Fig. 1. Inflammatory reaction in areas of red tattoo.

utaneous tests (3, 4). However, no chemical analysis of the tattoo pigments of these patients has been performed.

In recent years we have treated several patients suffering from inflammatory reactions in red tattoos but with negative reactions to epicutaneous mercury tests. Two tattoo pigments have been found to be responsible for these cases. The strongest reactions were found for a bright red dye (Fig. 1) and a somewhat weaker reaction from a red-violet dye. Since no chemical structures of these substances could be obtained from the supplier, we performed an analysis on the two pigments responsible for the allergic reactions in the tattoos.

MATERIAL AND METHODS

Seven patients with inflammatory reactions in red tattoos and two patients with reactions in red-violet tattoos were investigated. Three of these patients had been tattooed outside Scandinavia and six in Scandinavia (Copenhagen and Lund). All 9 patients had tattoos with several other pigments, but no inflammatory reaction was seen in these colours.



1 2

Fig. 2. Molecular structure of the red pigment (1) and the red-violet pigment (2).

The immediate reaction after tattooing is exuding local skin followed by a quick-healing, crusted sore. This normal reaction without complications and with subsequent healing was reported by each patient. Itching and oedema appeared with a lag-time of one month to two years in the red and red-violet tattoos. In 6 of the 9 patients the inflammatory reaction started after a strong UV-stimulation.

The inflammatory reactions in the red areas were constant but with periods of exacerbation with ooozing resembling an acute eczema. In each of the patients all red or violet tattooed areas became swollen at the same time, followed by local severe itching or stinging. Between exacerbations the areas were less swollen with slight itching and scaling. Excision of the red parts of the tattoos was followed by total healing in all patients.

Tattoo pigments were obtained from a local tattooist.

^{1}H NMR (Nuclear Magnetic Resonance) spectra were recorded with a Varian XL 300 spectrometer (300 MHz). Mass spectra (MS) (electron impact and chemical ionization) were recorded with a Finnigan 400 and a Jeol JMS-SX 102 spectrometer. Thin Layer Chromatography (TLC) was run on silica gel with CH_2Cl_2 as mobile phase. Elemental analysis was performed by Analystjänst, Lund.

Patch testing

Patch testing was performed in standard concentrations using Al-test. All patients were tested with Cr, Ni, Co, Cd and Cu and with metallic mercury, and some of the patients also with mercury chloride (0.1% in water). Metallic mercury was tested in 0.5% conc. in vaseline. The tattoo pigments were tested as dry, pure substances. The materials were applied to the patient's back for 48 h and the tests were read after 72 h.

RESULTS

Epicutaneous tests

No delayed allergic reaction was found in any patient. Epicutaneous testing with the red and the red-violet pigment was performed on five patients. All tests were negative.

Histopathology

Examinations of punch biopsy specimens were performed for all 9 patients in the swollen red parts of the tattoos. The pigments were found both extra- and intracellularly in macrophages which often lay close to dilatated capillaries. In biopsies with red-violet pigment, both violet and red colours were found. No granulomatous reaction could be found. In inflammatory areas of the upper and middle dermis a perivascular infiltrate of lymphocytes was noticed. The infiltrates contained some histiocytes and a few plasma cells. Furthermore, in two patients a lichenoid picture was found showing distinct lymphocytic infiltrate in the dermis and some lymphocytes in the basal epidermis with liquefaction degen-

eration of the basal epithelium and some degenerative changes in the keratinocytes.

Chemical analysis

Red pigment. Punch biopsies as well as the original tattoo pigment were analysed by atomic absorption spectroscopy. No mercury, copper, nickel, cobolt, or cadmium was found. Elemental analysis showed a compound of organic origin (C 64.9%, H 4.32%, N 11.7%, O 15.9%, no sulphur was found and ashes were 4.3%).

Spectroscopic analysis. Both pigments showed very low solubilities in all lipophilic as well as hydrophilic solvents tested. ^{1}H-NMR spectra of the red pigment in $CDCl_3$ showed a complex pattern in the aromatic region, and also a methyl signal at 2.68 ppm. 2D-NMR experiments showed this methyl group to be a part of an o,p-disubstituted toluene. The mass spectrum of the red pigment showed a molecular ion at 426, corresponding to the formula $C_{24}H_{18}N_4O_4$, and the major fragments 334, 305, 290 and 234. The spectroscopic data suggested the structure 1 in Fig. 2, and this was confirmed by comparison with an authentic sample ordered from the supplier.

The trade-name of the red-violet compound was obtained from a local tattooist and the molecular structure was then confirmed by ^{1}H-NMR (in DMSO-d_6) and mass-spectroscopy, and found to be identical with 5,12-dihydro-quino(2,3-b)acridine-7,14-dione or linear quinacridone, (structure 2 in Fig. 2).

DISCUSSION

Several types of adverse reactions to tattoos have been reported (5). Granulomatous reactions to light blue tattoo pigment, probably of cobolt origin, have been described (6, 7). Discoid lupus erythematosus has been found in areas with red tattoo (8). Photosensitive reactions in red parts of tattoos were correlated to the mercury sulphide content (9). To our knowledge no reaction to tattoo pigments of pure organic compounds of known molecular structure has been reported. The bright red pigment causing allergic reactions in our patients was found, by spectroscopic analysis, to be an aromatic azo-compound. This compound is marketed as Pigment Red 22 or Devil's Red.

The red-violet compound was identified by NMR and mass spectroscopy to be linear quinacridone, also known as Pigment Violet 19 or Dark Violet. This compound is known to exist in three different phases; two bluish red and one violet. It has been shown by chemical studies that the pH and the solvent used determine the proportions of these three different phases (10).

Most patients who reacted to the red pigment stated that the reaction started after exposure to strong UV-stimulation. Photoallergic reactions to yellow cadmium sulphide pigment in tattoos have been reported (11). Aromatic azo-compounds such as Devil's Red are known to react photochemically giving the more unstable cis-isomer as product. Aromatic azo-compounds are also known to evoke contact dermatitis (12). Whether the reactions in the red areas are of photoallergic or pure allergic nature has not yet been evaluated.

No patient showed positive reaction to the tattoo pigments on epicutaneous testing. Both tattoo pigments are extremely insoluble in all solvents tested, and thus no penetration through the epidermis is expected. However, when administered into the dermis as in the tattooing process, allergic reactions can occur.

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