Allergic reaction to a green tattoo with nickel as a possible allergen

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CASE REPORT

A 40-year-old woman visited the allergology department because of a 10-year-old tattoo on her right lower leg that had been itching for 4 years, specifically in the green part. The other tattoo areas, that is, red and black, were asymptomatic. There were no triggering factors, and the patient had no further relevant medical history. On physical examination, we observed excoriations on the lower right leg, mainly in the green tattooed area (Figure 1). Skin biopsy showed a lymphohistiocytic inflammation with green pigment agglomerations. Patch testing on the back was carried out with the European baseline series, Dutch supplements, and a metal series. The original green tattoo ink could not be retrieved for testing. Remarkably, during patch testing, the patient's dermatitis worsened. The results included ++ reactions to nickel sulfate 5% pet. and methyldibromo glutaronitrile 0.3% pet. on day (D) 3. Furthermore, a +++ reaction to sodium tetrachloropalladate 3% pet. and a + reaction to cadmium chloride 1% pet. were observed on D3.

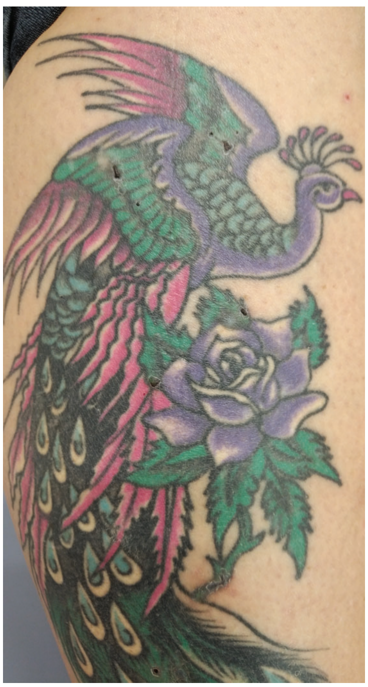

FIGURE 1 Picture of the patient showing excoriations in the green part of a tattoo on the right lower leg

In order to identify chemical elements present in the pigment region, chemical analysis of the skin tissue was carried out. A 3-μm-thick formalin-fixed paraffin-embedded section was analysed after paraffin removal by use of chemical imaging techniques, namely, micro-X-ray fluorescence analysis (μ-XRF) and laser ablation-inductively coupled plasma-mass spectrometry (LA-ICP-MS). Because, with these techniques, no extraction of the pigments had to be performed before analysis, elemental distribution patterns within the tissue could be recorded, and by using these distributions we were able to distinguish between endogenous elements coming from the skin tissue itself and exogenous elements from the tattoo ink. The quantification of the present elements was performed with LA-ICP-MS by use of an external calibration with matrix-matched standards made from gelatin. These standards, which contained defined element concentrations, were sectioned to the same thickness as the tissue thin section, and analysed with identical laser ablation and mass spectrometric parameters. The elemental concentrations in the gelatin standards were determined with LA-ICP-MS after acidic digestion. Detailed method descriptions and parameters are shown in Supporting Information File S1.

By using μ-XRF and LA-ICP-MS, we showed that chlorine, titanium, chromium, iron, nickel, copper, zirconium and niobium were present in the pigment region. As one example, the results for nickel are shown in Figure 2. The microscopic image of the investigated thin section shows green pigment agglomerations beneath the epidermis in the dermis (Figure 2A). Figure 2B shows the obtained distribution patterns for nickel (magenta) and phosphorus (blue) as an overlay image. Phosphorus as an endogenous element was used here to visualize the tissue structure of the skin. Because there is a higher phosphorus content in the epidermis than in the dermis, these two skin layers can be distinguished, and the tissue can therefore visualized. From this phosphorus distribution in the overlay image with the nickel distribution, we can clearly see that the nickel signals were mainly located beneath the epidermis in the dermis of the skin, as we expect in a tattoo, and as is

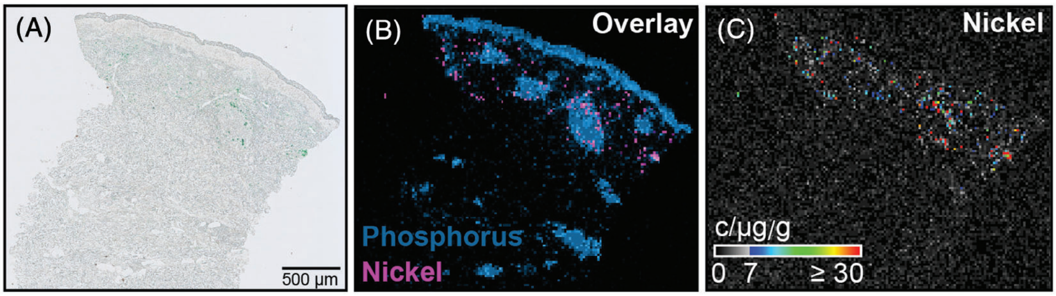

FIGURE 2 Elemental analysis by means of laser ablation-inductively coupled plasma-mass spectrometry. (**A**), Microscopic image of the investigated thin section. (**B**), Overlay image of phosphorus (eg, from nucleic acids for visualization of the tissue structure) and nickel. The overlay image facilitates the allocation of the nickel signals within the tissue structure. (**C**), Quantitative distribution of nickel. Signals below the limit of quantification (7 μg/g) are illustrated in grey

also visible in the microscopic image. Comparison of the overlay image with the microscopic image shows good concordance of both. Figure 2C shows the detected nickel concentrations as a concentration heat map in a colour scale from blue to red (assigned to 7 μg of nickel per gram of tissue and >30 μg of nickel per gram of tissue). Concentrations below the limit of quantification (7 μg/g), and that could therefore not be determined, are shown in grey. Within the concentration heat map, all red hotspots show nickel concentrations of ≥30 μg per gram of tissue. For some areas, lower concentrations (shown in blue, green, and yellow) were also detected. In general, the concentration heat map shows that the concentration of nickel varied widely within the dermis, which can be explained by local pigment agglomerations.

All other detected elements were distributed in the pigment regions as well (Supporting Information Figure S1). Furthermore, quantification was performed for copper, titanium, and chromium (Supporting Information Figure S2). Very high local concentrations of copper (≥1 mg/g) and titanium (≥3 mg/g) were observed (Supporting Information Figure S2f,c). The local concentrations of chromium were ≥50 μg/g (Supporting Information Figure S2d). The other elements were determined qualitatively. Palladium and cadmium were not detected in the pigment region. On the basis of the clinical, histological and allergological findings and the chemical analysis, we conclude that nickel is the most likely allergen causing the symptoms in this patient.

DISCUSSION

Tattooing is a popular trend in body art, with a prevalence in Europe of 12% having been reported.[1] However, complications can occur, such as infections, allergic reactions, foreign body reactions, and autoimmune diseases.[2] Allergic reactions appear weeks, months or years after tattooing. Therefore, it is difficult to trace the used ink and its components, and the possible allergens. In addition, false information about ink components has been reported.[3] Moreover, impurities such as heavy metals can be found in inks, even though they are not listed.[4] This lack of information makes the identification of possible allergens challenging. Therefore, the ink components were identified by chemical analysis of the tattooed skin tissue directly. As critical components, we identified nickel (Figure 2) and chromium (Supporting Information Figure S1c), which were still present in the tattoo years after tattooing. The chromium and nickel concentrations that we found are significantly higher than in the surrounding tissue, but not as high as, for example, those of the detected copper and titanium. Whereas copper most likely originates from copper-containing phthalocyanine pigments and titanium from TiO_2 pigments, we assume that chromium and nickel were present as impurities in the used ink. The relevance of the presence of nickel and chromium strongly depends on their chemical binding forms with respect to solubility and thus bioavailability. The chemical species cannot be evaluated with the techniques that we used, so it is difficult to make statements about solubility and bioavailability. However, in the review of Laux et al, it was argued that, because deposited pigments and other components are present lifelong in the human body, even slow metabolic processes are important.[5]

In allergic reactions to tattoos, the role of nickel is still unclear. Nickel has been suggested before as a possible allergen in a red tattoo reaction.[6] However, Serup et al assume that nickel is unlikely to be the culprit allergen in red tattoo reactions, because the percentage of nickel sensitization in these patients was not significantly higher than in the European surveillance report.[7] Furthermore, it was mentioned that sensitization also occurred prior to tattoo placement. Green tattoo reactions are less frequently reported than red tattoo reactions. The reported allergen in these cases was mainly chromium.[8-10] In our patient, testing for hexavalent chromium (Cr[VI]) by the use of potassium dichromate gave negative results. However, because chromium was detected in the pigment region, and the chromium species in the pigment region could not be determined, chromium cannot be totally excluded as a possible allergen. For example, trivalent chromium (Cr[III]) is capable of eliciting dermatitis. Nevertheless, we assume that nickel played a significant role in allergen formation, as it was the only element both patch tested positive and identified by the chemical analysis of the skin tissue. Furthermore, the worsening of the symptoms during patch testing supports the idea that the culprit allergen was tested. In conclusion, we report a patient with an itching green tattoo with nickel as the most likely culprit allergen. The role of nickel in chronic tattoo reactions remains unclear.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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