

Consumer leather exposure: an unrecognized cause of cobalt sensitization

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Summary

Background. A patient who had suffered from persistent generalized dermatitis for 7 years was diagnosed with cobalt sensitization, and his leather couch was suspected as the culprit, owing to the clinical presentation mimicking allergic chromium dermatitis resulting from leather furniture exposure.

Materials and methods. The cobalt spot test, X-ray fluorescence, inductively coupled plasma mass spectrometry and scanning electron microscopy were used to determine cobalt content and release from the leather couch that caused the dermatitis and from 14 randomly collected samples of furniture leather.

Results. The sample from the patient's leather couch, but none of the 14 random leather samples, released cobalt in high concentrations. Dermatitis cleared when the patient stopped using his couch.

Conclusions. Cobalt is used in the so-called pre-metallized dyeing of leather products. Repeated studies have found high levels of cobalt sensitization, but not nickel sensitization, in patients with foot dermatitis. We raise the possibility that cobalt may be widely released from leather items, and advise dermatologists to consider this in patients with positive cobalt patch test reactions.

Key words: cobalt; dermatitis; leather; patch test reactivity; sensitization; spot test.

Cobalt is a strong skin sensitizer (grade 5 of 5 in the guinea-pig maximization test) (1), and penetrates the skin and causes contact sensitization and allergic contact dermatitis (2–4). Cobalt chloride is included in baseline patch test series all around the world, and is one of the most frequent allergens to elicit reactions on patch testing (5, 6). Although traditional sources of cobalt exposure

have been claimed to include metallic consumer items, we have so far only identified low proportions that release cobalt in amounts that may cause dermatitis (e.g. when examining jewellery, belts, mobile phones, laptops, and non-professional work tools) (7, 8). On the other hand, we have identified cobalt release from a high proportion of dental and orthopaedic implants, and wondered whether such exposure could explain the high prevalence of cobalt sensitization in patch test populations. We acknowledge that cobalt exposure is relatively common among workers in some occupations, e.g. metal workers, who are exposed to hard metal alloys (9), construction workers, who are exposed to cement, and pottery workers, who are exposed to clay and glaze. However, as most patients in our clinic are not occupationally exposed to cobalt, and as it is often difficult to identify the source of cobalt exposure, the clinical relevance of a positive patch test reaction to cobalt

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Conflicts of interests: Jacob P. Thyssen, Per Møller and Morten Jellesen sold the cobalt spot test to SmartHealth (Phoenix, AZ, USA) after its development, and will receive royalty fees for annual net sales of the spot test.

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is identified in only ~ 25% of patients (7). Here, we present an unrecognized source of cobalt exposure causing severe chronic dermatitis in a male patient. Various analyses of leather samples were conducted to determine cobalt content and release, and a discussion on cobalt in leather is provided.

Materials and Methods

Medical history

A 66-year-old non-atopic male accountant without any kind of previous industrial work was referred with a 7-year history of generalized dermatitis. Disease onset began with a burning sensation at the site of papules on the forearms. The dermatitis soon spread to the entire body, and was accompanied by chronic vesicle formation on the palms and soles. Following topical corticosteroid therapy, the patient was treated by the local dermatologist with ciclosporin (dose and duration unknown) and prednisolone (dose 10–25 mg, duration unknown). He experienced some, but not complete, resolution of dermatitis during this treatment. Whereas ciclosporin therapy was interrupted because of mild nephrotoxicity, prednisolone treatment was continued. The patient was referred to a tertiary dermatological department, and treated with acitretin (dose and duration unknown), and then with a 3-year course of alitretinoin at a dose of 60 mg/day combined with prednisolone 10–15 mg/day. He was then patch tested for the first time, and had a positive test reaction to cobalt chloride only (grading unknown). He was subsequently referred to the department of Dermato-Allergology at Gentofte Hospital. He still suffered from generalized and very xerotic dermatitis. As xerosis was suspected to be an adverse effect of the high dosage of alitretinoin, systemic treatment was paused, and he was treated with topical mometasone ointment once daily. After the change in treatment, the morphology of dermatitis became vesicular in the hands and feet, and papular on the body and extremities. Patch testing with the European baseline series, a supplementary treatment series and a special fragrance series confirmed a positive test reaction (1+) to cobalt chloride 1% in petrolatum after 72 hr, in spite of treatment with 5 mg of prednisolone daily. Several punch biopsies confirmed the diagnosis of dermatitis. The patient was then treated with systemic azathioprine, but therapy was stopped because of elevated hepatic enzymes in the serum. Repeated secondary infections with *Staphylococcus aureus* were treated with appropriate antibiotics. However, it was remarkable that each time the patient was hospitalized for 1 week the dermatitis rapidly

improved, and that the skin flared when he returned to his home.

Identifying the cobalt source and work-up

On first consultation, we considered potential sources of cobalt exposure, as the referral letter indicated cobalt sensitization. The patient had a dental implant in his upper mouth inserted 15 years previously. The chemical composition as given in the data sheet from the material supplier indicated that there was no cobalt in the dental implant. On re-inspection of the patient's back, there was an impression that the dermatitis mimicked typical chromium dermatitis as seen in patients spending long amounts of time on their leather couches. When the patient was directly questioned about his use of leather furniture, he informed us that he purchased a leather couch 9 years ago, that is, 2 years before dermatitis onset, and that he used it on a daily basis. The couch had been produced in northern Italy, and had a yellow–brown colour.

Leather samples from the patient's couch were collected and analysed. First, the brown leather piece was placed on a napkin, and a yellow cobalt test solution containing nitroso R salt was then poured over it (10). Instantly, an orange–red halo was noted around the leather (Fig. 1), indicating that cobalt ions were released in amounts that may result in allergic cobalt dermatitis. The contents of nickel, cobalt and chromium in the leather sample were then determined with inductively coupled plasma mass spectrometry (ICP-MS). The sample was dried at 65°C overnight (dry matter content 94.4% wt/wt), and then cut into small pieces with a titanium knife. Two subsamples of 0.3 g were weighed into quartz vessels, and 4 ml of concentrated nitric acid and 1 ml of concentrated hydrochloric acid were then added (both Plasmapur grade from SCP Science, Clark Graham Baie D'Urfé, Quebec, Canada); this was followed by microwave-assisted digestion (Multiwave 3000; Anton Paar, Graz, Austria) at a temperature up to ~ 200°C (40 min). The sample digests were subsequently diluted with 2% nitric acid, and the contents of cobalt (isotope: ⁵⁹Co), chromium (isotope: ⁵³Cr) and nickel (isotope: ⁶⁰Ni) were determined by ICP-MS (Agilent 7500ce; Agilent Technologies, Waldbronn, Germany) in the CRC mode, with helium as the cell gas. Quantification was performed by external calibration with internal standardization (isotope: ⁶⁹Ga). Certified stock standards were used for all elements (CPI International, Amsterdam, The Netherlands). The following concentrations were obtained, with an estimated measurement uncertainty of 10% (estimated from duplicate determinations): cobalt, 800 mg/kg; chromium, 36 000 mg/kg; and nickel, < 1 mg/kg (mean of duplicate



Fig. 1. Orange–red discolouration of a tissue on which the cobalt spot test solution has been poured. A cobalt-containing alloy, releasing cobalt, was also applied as a control.

determinations). Chemical analysis were then performed on the surface of the leather with scanning electron microscopy (JEOL 5900; JEOL Ltd, Tokyo, Japan) in combination with energy dispersive spectroscopy (Oxford Link ISIS analyser; Oxford Instruments, Oxford, UK), with INCA Energy EDS software. The leather was carbon-sputtered before analysis, and carbon was thus subtracted in the final result: Co, 0.8 wt%; Cr, 7.8 wt%; O, 43.9 wt%; P, 31.9 wt%; Na, 5.1 wt%; S, 4.5 wt%; Cl, 2.1 wt%; and K, 3.9 wt%. Finally, X-ray fluorescence (XRF) (Oxford Instruments Industrial Analysis, X-MET 7500; Oxford Instruments Analytical, Oy, Finland) analysis confirmed cobalt in the leather sample. The patient was then instructed not to use the couch, owing to cobalt release, and underwent topical coal tar and corticosteroid therapy for 3 weeks. Despite prednisolone being stopped, the dermatitis rapidly improved. Although the patient still had mild generalized dermatitis at last follow-up, the vesicular aspects of the hand eczema had cleared, leaving behind keratotic changes, and the patient reports continued improvement.

Analysis of Leather Samples from a Furniture Store

We contacted a Danish furniture store and asked for samples of leather used in their furniture. In total, we received 14 random samples in different colours, which were cut and analysed. First, XRF analysis showed traces of cobalt in only one sample (brown colour), whereas chromium was found in all of them in high concentrations. When the cobalt spot test solution was poured over the 14 leather samples, no positive test reactions were found.

Discussion

Numerous sources of cobalt exposure exist, as reviewed recently (7). Nonetheless, it is often difficult to determine the clinical relevance of positive patch test reactions to cobalt chloride, and especially in consumer cases, as the source of cobalt is often not evident. Although the recently developed cobalt spot test has proved to be useful for screening purposes (10), surprisingly few jewellery, hair clasps, mobile phones and work tools release cobalt in significant amounts in market surveys (11–13). Hence, there seems to be a hitherto overlooked source of cobalt causing the high prevalence of positive test reactions to cobalt in patch test populations. As a large-scale investigation of cobalt in leather has not yet been conducted, we do not know whether this is a single case of cobalt dermatitis resulting from leather exposure, or whether this is a quantitative problem. As the 14 leather samples showed no cobalt content, it is possible that cobalt in leather causes cobalt sensitization and dermatitis in only a few individuals. Market surveys are clearly warranted.

There are essentially three stages in leather manufacture: (i) animal husbandry and slaughter; (ii) tanning; and (iii) product manufacture. Tanning is the stage in which leather is processed to avoid degradation. Unwanted substances are removed from the leather, which is also trimmed and soaked in a chrome bath. Chromium complexes replace some of the collagen, and stabilize the leather. Vegetable tanning is also sometimes used. Subsequently, depending on the quality and purpose, the leather is dyed, shaved, and finished. Whereas some leather is dyed without the addition of pigments (so-called aniline-dyed leather), most leather is dyed with pigments. This typically involves fixing a variety of compounds onto the very reactive chromium (<http://nzic.org.nz/ChemProcesses/animal/5C.pdf>). As previously stated, little is known about the tanning agents and dyes used, and much information is unknown or kept secret by manufacturers (14). However, a recent article listed potential contact sensitizers in Indonesian leather workers (15); the dyeing agents included Disperse Orange 3, Acid Yellow, *N*-isopropyl-*N*-phenyl-4-phenylenediamine, hydrogen peroxide, and benzidine, but not cobalt. However, apparently, consumer requirements for both wash and light fastness in leather goods has recently led to a shift away from direct dyeing and acid dyes to the faster pre-metallized and reactive dyes (<http://nzic.org.nz/ChemProcesses/animal/5C.pdf>). There are two classes of pre-metallized acid dye, 1:1 and 1:2 metal complexes, in which, respectively, one or two dye molecules are complexed with one metal atom (16). The dye molecules form strong coordination

complexes with the metal ion, which is mostly chromium or cobalt, although copper, iron and nickel can also be used. Although the metal dye complexes are established prior to the dye application process in pre-metallized acid dyes, these complexes are first applied when a solution containing the metal is applied to a suitably dyed fibre with a mordant dye (16). The colours of pre-metallized dyes tend to be slightly brighter than those of mordant dyes. When 21 shoes purchased from different countries were examined for their metal content in Sweden by the 'Naturskyddsforeningen', cobalt was found in all of them (range, < 0.3–16 ppm), although the concentrations of cobalt were much lower than that of, for example, trivalent chromium (<http://inspirationgreen.com/toxins-in-leather-shoes.html>). Also, cobalt reactivity was very common when published studies on shoe dermatitis were pooled, as cobalt sensitization affected 13%, whereas nickel sensitization only affected 8% (17). Moreover, cobalt sensitization was significantly associated with textile and leather work [odds ratio (OR) 1.52; 95% confidence interval (CI) 1.09–2.12] in an Italian study on occupational contact dermatitis (18). In a later study by the same group, this finding was confirmed, as cobalt

monosensitization (OR 1.85; 95% CI 1.10–3.09) and concomitant cobalt, nickel and chromium sensitization (OR 2.19; 95% CI 1.10–4.33) were significantly associated with textile and leather work (19).

Taking these findings together, there are strong indications that cobalt can be found in leather and textiles, and that exposure can cause cobalt sensitization and dermatitis. Studies are required to clarify whether cobalt is present in all leather product categories (e.g. gloves, shoes, trousers, coats, bags, watch straps, wallets, leather seats and steering wheels in cars, and furniture) and whether certain colours of leather should be particularly suspected. Also, investigations should be undertaken to clarify whether nylon and other synthetic polyamide fibres, wool and silk also contain and release cobalt, as pre-metallized dyes can also be used for dyeing such clothing (16). In the meantime, patch testers should at least consider leather as a potential source of cobalt exposure in patients with cobalt patch test reactivity. This could be of particular relevance in patients with chromium and cobalt sensitization and foot dermatitis, where chromium-free footwear is used but the patients still suffer from dermatitis.

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