

A positive cobalt spot test falsely indicating an occupational allergic contact dermatitis caused by cobalt

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Summary

Background. For investigation of chemical exposure in allergic individuals, spot tests are invaluable. A reagent may react with a specific compound to give a specific typical colour, and thus indicate the presence of the specific substance. Spot tests can give both false-negative and false-positive reactions. To confirm the presence of the substance and quantify it, more sophisticated methods are required. On the basis of a positive cobalt spot test result, a woman was initially diagnosed with an occupational allergic contact dermatitis caused by cobalt.

Objectives. To investigate cobalt release from three different metal weaves to which our patient was occupationally exposed.

Methods. The cobalt gel test and atomic absorption spectroscopy (AAS) were used to investigate the metal weaves. Two types of extract based on artificial sweat and nitric acid, respectively, were investigated with AAS.

Results. No cobalt release was demonstrated with AAS.

Conclusions. When a diagnosis of allergic contact dermatitis caused by a sensitizer based on a positive spot test result will have far-reaching consequences, such as change of work, retraining, and claim on and payment of worker's compensation, conformational analysis must be performed.

Key words: AAS; alloys; cobalt; contact allergy; false positive.

In patients with long-lasting dermatitis, and particularly hand dermatitis, patch testing is mandatory. When contact allergy to a sensitizer has been established, the reading dermatologist has to investigate whether this contact allergy has any present clinical relevance. Arriving at a diagnosis of allergic contact dermatitis in an individual with contact allergy requires (i) the demonstration of present exposure to the sensitizer and possibly cross-reacting substances, and also (ii) assessment of whether the exposure to the sensitizer

suffices to explain the dermatitis under investigation with regard to its localization and course on the one hand, and the type and magnitude of the exposure as well as the degree of patch test reactivity on the other (1, 2).

When chemical exposure is investigated in hypersensitive individuals, spot tests are invaluable. Spot tests can be used to detect both inorganic and organic substances (3, 4). A reagent may react with a specific compound to give a specific typical colour, and thus indicate the presence of the specific substance. To confirm its presence and quantify the substance, more sophisticated methods are required (5). The need for conformational tests is illustrated by the following case report.

Case Report

A 54-year-old woman worked for a company manufacturing flexible cable and pipe seals based on the elastomer

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ethylene propylene diene monomer (EPDM). The seals are used for electric cables passing through constructions that are required to be water-tight and fire-safe. The EPDM rubber is purchased as 'endless rubber belts' that are extruded into different layers that are later vulcanized. These layers are later pressed together to form the seals, except for the outer layer, which is glued with a cyanoacrylate-based adhesive. This makes the cable and pipe seals adjustable to the desired sizes. The patient's job was to mount the seals together with an arming metal weave in the middle, using cyanoacrylate-based adhesive. She had no history of atopic dermatitis.

She was referred to the department of dermatology in Karlshamn because of dermatitis localized to the forehead and scalp. The dermatitis appeared during the summer, when the temperature at the workplace was substantially elevated. The dermatitis improved during weekends when the patient was not working. At examination, an erythematous dermatitis was present on the forehead, and there was some fine scaling on the scalp.

An occupational allergic contact dermatitis was suspected that, either alone or in combination with irritant factors and/or an endogenous dermatitis, could explain the skin manifestations (6). Because of the suspected occupational background, the patient was referred to the Malmö clinic of occupational and environmental dermatology within the dermatology department in Karlshamn. Patch testing was performed with the European baseline series, a plastics and glue series, and 29 test preparations representing her work environment, including various qualities of rubber and tapes tested as they were and as ultrasonic bath extracts (7), marking dye, various greases, and the cyanoacrylate-based adhesive. The IQ Chambers® (Chemotechnique Diagnostics, Vellinge, Sweden) technique was used, with the chambers applied on the back and secured with Medipore™ surgical tape (3M, Neuss, Germany) under occlusion for 48 hr. The tests were read twice, after 4 and 7 days. Strong vesicular reactions to nickel and cobalt were seen. The patient had pierced earlobes and a long history of metal intolerance. During her work, she handled the metal weave throughout the working day; release of nickel and/or cobalt seemed likely, with contamination of the hands and subsequent transfer of the sensitizers to the head. She wiped her face with her bare hands, as she was sweating a lot in the elevated temperature at work. However, the dimethylglyoxime test for nickel on the metal weave gave a negative result. The weave was brought to the Malmö department for cobalt analysis, and a worksite visit was planned.

The worksite visit during the summer did not show, except for the exposure to the metal weave, any

significant metal exposure or any other hazardous exposure that could be suspected to contribute to the patient's dermatitis. On the other hand, it was obvious that, in the hot working environment, she handled the metal weave with her hands and that she wiped her sweating face with her hands.

Chemical analysis

Samples

The metal weave handled by the patient was investigated with the cobalt gel test (8) and atomic absorption spectrometry (AAS). In a second round, two additional metal weaves from the company were investigated in the same way. The tested metal weaves were from the same producer, but had different sizes and shapes.

Cobalt gel test

The cobalt gel test reagent mixture was prepared by dissolving 0.1% (wt/wt) oxalic acid, 0.02% (wt/wt) disodium-1-nitroso-2-naphthol-3,6-disulfonate (nitroso R salt) (both from Sigma-Aldrich Chemie, Steinheim, Germany) and 5.0% (wt/wt) sodium acetate (J. T. Baker, Mallinckrodt Baker, Denventer, The Netherlands) in demineralized water.

To prepare the cobalt test gel, 3 g of agar powder (Sigma-Aldrich) was dissolved in 100 ml of deionized water. The mixture was stirred slowly on a heated plate until the agar was dissolved and the mixture reached 80°C. Fifteen millilitres of the reagent mixture was added to agar solution (8). The metal weave was placed in a Petri dish, and covered with the cobalt gel test reagent mixture.

Atomic absorption spectroscopy

After performance of the cobalt gel test, the metal weave was extracted in 5 ml of artificial sweat, consisting of deionized water, 0.5% (vol/vol) sodium chloride (Acros Organics, Morris Plains, NJ, USA), 0.1% (vol/vol) lactic acid (Sigma Chemical Co., St Louis, MO, USA), and 0.1% (vol/vol) urea (Sigma Chemical Co.), prepared as described in (9). The pH was adjusted with ammonia (Scharlau Chemie, Barcelona, Spain) to 6.4. The metal weave was put in artificial sweat in a tube for 1 week at room temperature on a Boule mixer 440 (Boule Medical AB, Stockholm, Sweden), with slow and gentle rocking. The cobalt concentration in the extract was later determined with an AAnalyst 800 Atomic Absorption Spectrometer (Perkin Elmer Instruments, Norwalk, CA, USA) equipped with Zeeman background correction and a graphite furnace. Additional tests were also performed

with extraction in nitric acid. The metal weave was extracted in 5 ml of 0.2% nitric acid for 3 days and 1 week. The instrumental detection limit for cobalt was $\sim 0.001 \mu\text{g/l}$.

Results and Discussion

When the metal weave handled by the patient was subjected to the cobalt gel test, a colour change was observed and interpreted as a positive spot test result (8). Our department has its own chemical laboratory with experienced chemists and technicians. When the cobalt gel test was studied (8), various cobalt-releasing objects, including a necklace for which cobalt release had been demonstrated with AAS (10), were investigated. The colour change for the metal weave was identical to the colour change obtained for the cobalt-releasing necklace.

The cobalt release seemed to explain the dermatitis under investigation, but, as this finding would most likely have consequences for the patient and the employer, additional analyses with AAS were initiated. Surprisingly, not only the extract in artificial sweat but also the extracts made in nitric acid were negative. Because of this, we wanted to investigate another metal weave of exactly the same type. Unfortunately, this type of metal weave was not available at the company any more, but we obtained two similar weaves that, according to the production manager, were identical in composition but differently shaped to the one that we had investigated. According to the manager, all three metal weaves were made of tin-plated copper. Given this information, the results of the analysis of the other weaves, with no cobalt release detected for either the spot test or for the AAS tests after extraction with artificial sweat or nitric acid, were not surprising. Obviously, the patient did not suffer from an occupational allergic contact dermatitis caused by cobalt release from the metal weave. Additional patch testing with copper sulfate at 2% in petrolatum and tin at 50% in pet. resulted in negative reactions when read on D3 and D7.

Spot tests are invaluable for the investigation of chemical exposure to some sensitizers, particularly metals and formaldehyde (5). It is in the nature of spot tests that they can give false-negative results, as they

have lower sensitivity than other, more sophisticated, chemical methods. It is also well known that they have lower specificity, which may result in false-positive reactions. For the nitroso R salt, several possible causes of interference have been described, as the reagent may form complexes with other metals, such as copper and tin. Some of these metal complexes have a similar colour to the cobalt complex, indicating a positive cobalt spot test result (11). This knowledge about spot tests is the basis for the following recommendation when a spot test has indicated the occurrence of a specific substance: 'to confirm its presence and quantify the substance more sophisticated methods are required' (5). Should, then, spot tests be used at all, given that there is a risk of both false-negative and false-positive results? The answer is an unconditional yes, but one has to be aware of the limitations of the spot test. Unless there is a need for confirmation or rejection of very low degrees of exposure, for example in someone with a high degree of reactivity (1, 2), and, at the same time, pronounced exposure to a metal object possibly containing the metal under consideration, a negative spot test result can be considered to be a demonstration of no exposure to the sensitizer. The situation is more complicated with a positive spot test result. For practical reasons, it is only reasonable to carry out confirmatory analysis when the possible consequences include not only the individual who is the reason for the spot test, but also others, such as the employer and the society. When, for example, a cobalt spot test gives a positive result with cheap jewellery, there is no need to confirm the occurrence of cobalt release, as the cobalt-hypersensitive individual can stop wearing the jewellery. On the other hand, in the reported case, a diagnosis of occupational allergic contact dermatitis caused by cobalt might have had far-reaching consequences, such as change of work, retraining, and claim on and payment of worker's compensation.

In conclusion, spot tests are invaluable tools for the assessment of clinical relevance to show exposure to some sensitizers, but one has to be aware of their limitations, so conformational analysis can be performed when indicated, as in the reported case.

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