

Chromate or titanium allergy – the role of impurities?

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The prevalence of metal allergy is substantial in the general population, and is rising steadily within the ageing population requiring medical devices (1). Nickel, cobalt and chromium are the classic contact allergens both in adults and in children (1, 2), and titanium is recommended as an alternative because of its excellent biocompatibility, high corrosion resistance, and inert character in the human body. Allergic contact dermatitis caused by titanium has only ever been very rarely documented. We report a case of a positive patch test reaction to titanium nitride in an 8-year-old girl suffering from shoe dermatitis. Even if the sensitization route remains unclear, it could be related to impurities, such as chromium contained in the commercial allergen.

Case Report

An atopic 8-year-old girl who needed a dental brace was referred for additional patch testing in order to exclude contact allergy to metals used in dental materials. She had a history of palmoplantar dyshidrosis resulting from contact dermatitis caused by chromium in shoes.

Patch tests were performed with the European baseline series (Chemotechnique, Vellinge, Sweden; Trolab, Almirall Hermal, Reinbek, Germany) (with paraphenylenediamine diluted 1:100), an acrylate dental series (Chemotechnique; Trolab, Almirall Hermal), and a selected metal series [mercury 0.5% pet., mercury chloride 0.1% pet., mercuric ammonium chloride 1% pet., palladium chloride 2% pet., gold sodium thiosulfate 2% pet., titanium nitride 5% pet., titanium dioxide 10% pet., titanium oxalate 5% pet., calcium titanate 10% pet., titanium



Fig. 1. Positive patch test reactions to titanium nitride (+) and titanium oxalate (+).

10% pet., vanadium 5% pet., molybdenum 5% pet., vanadium(III) chloride 1% pet., potassium dicyanoaurate 0.1% aqua, ammonium hexachloroplatinate 0.1% aqua, and ammonium tetrachloroplatinate 0.25% aqua; all from Chemotechnique]. The patch test materials used were IQ Ultra[®] (Chemotechnique), covered on the upper back with Mefix[®] (Mölnlycke Healthcare, Mölnlycke, Sweden).

The patch tests read at D2 and D4 were positive for wool alcohols (D2, +; D4, +), chromium 0.5% pet. (D2, +; D4, ++), titanium nitride (CAS 25583-20-4) (D2, +;

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Fig. 2. Positive patch test reactions to titanium nitride (+) and titanium oxalate (+).

D4, +), and titanium oxalate (CAS 14677-00-0) (D2, +; D4, +), confirmed twice (Figs. 1 and 2). Patch tests with titanium nitride and titanium oxalate were performed in 30 control subjects to exclude irritancy. These tests gave negative results, including in atotics.

Discussion

Titanium is a strong, light, metallic element (symbol Ti; atomic number 22) used mainly for its mechanical benefits in osteosynthesis, arthroplasty, pacemaker encasing, and orthodontic wires. Indeed, titanium and its alloys are known for their excellent biocompatibility, their high resistance to corrosion, the absence of any carcinogenic risk, and their lack of sensitization, which make them recommended alternatives for patients with nickel, cobalt or chromium allergies (3). Titanium salts are also used in cosmetics such as sunscreen products (titanium dioxide) and antiperspirants (4, 5).

Although titanium alloys have often been considered to be inert materials within the body, it was recently reported that their use might induce a toxic or allergic reaction in certain circumstances (3, 6). The rare cases of delayed allergy to this metal reported so far have involved pacemakers, osteosynthesis plates, and dental implants (4, 6). There is also a description of an occupational case secondary to welding (5).

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Table 1. Results of inductively coupled plasma mass spectrometry on mineralized samples of different commercialized titanium allergens

Materials	Chromium concentration (µg/g or ppm)
Titanium dioxide (CAS 13463-67-7)	1.53
Titanium oxalate (CAS 14677-00-0)	0.21
Titanium (CAS 7440-32-6)	5.22
Titanium nitride (CAS 25583-20-4)	10.82
Calcium titanate (CAS12049-50-2)	0.24

Materials from Chemotechnique, Vellinge, Sweden.

The titanium alloys are made of pure titanium or associated with aluminum (6%), vanadium (4%), or niobium (standard titanium alloys TiAl6Nb7 and TiAl6V4) (1, 4). One explanation for the increasing number of reactions to titanium materials may be the presence of impurities as a result of the production process (Al, Be, Ni, Cd, Co, Cr, Cu, Fe, Hf, Mn, Mo, Pd, and V). These small amounts are considered to be insignificant from a metallurgical perspective, but may be sufficient to trigger allergic reactions in patients sensitized to the corresponding allergens (3, 4). In our case, inductively coupled plasma mass spectrometry on mineralized samples was performed to detect impurities possibly present in the commercialized allergens (titanium, titanium nitride, titanium oxalate, titanium dioxide, and calcium titanate). Not only did the results show the presence of many impurities in the commercialized titanium samples analysed, but, above all, these samples contained traceable amounts of chromium, up to 0.001% (10.82 mg/g) in the titanium nitride one (Table 1). However, there is no proof that the level of impurities in the patch test titanium salts is sufficient to cause elicitation.

Indeed, chromium is tested in the European baseline series at 0.5% pet. A patch test and a repeated open application test (two applications per day for 15 days) with titanium nitride in a highly chromium-sensitized patient remained negative.

Therefore, in our case, the relevance of the positive patch test reactions remained unclear.