Titanium Allergy in Dentistry: A New Allergen in Rapidly Evolving Implant Dentistry

Abstract
Although titanium is considered as the biocompatible material and widely used in medical and dental fields, the clinical application of this material is still a critical issue due to the possible adverse host response. Very few case reports related with titanium-based hypersensitivity reactions with dental implants proved the existence of titanium allergy. The present case report describes 56-year-old male showing allergic symptoms after 1 week of dental implant placement with no perioral or facial signs, but eczema was shown on the distant body parts, and the complete remission was attained after removing the dental implant.

Keywords: Dental implants, titanium, hypersensitivity, immunology

Introduction
Titanium is generally not considered to provoke sensitivity reaction due to its biocompatible property. Although in light of very few relevant published clinical reports regarding contact dermatitis (CD) or granulomatous reactions to titanium upon its use in dental implants, pacemakers,[1-4] hip prostheses,[5-7] surgical clips, and osteosynthesis, the titanium allergy is still an ongoing debate. The titanium sensitivity is characterized by the localized accumulated macrophages and T-lymphocytes and the absenteeism of B-lymphocytes, thus pointing toward Type 4 hypersensitivity. The documented occurrence of hypersensitivities in few patients raises the query that metal sensitivity may arise after the exposure to titanium for some patients in certain circumstances. The amount of titanium use in the current scenarios has increased due to developments in smelting technology, and hence, providing extra opportunities for humans to be sensitized to this metal. This case report demonstrates the emergence of allergic symptoms after 1 week of dental implants placement. Although the dental implant after placement was having no perioral or facial signs, however the signs of eczema were observed on the distant body parts including the hands, skin, and back. The removal of the dental implant resulted in complete remission of the lesions.

Case Report
A 56-year-old male with no history of allergic symptoms reported to the department of periodontology for the removal of a well-placed implant with prosthesis in relation to upper left central incisor. The patient’s history revealed implant placement in the left upper central incisor region 6 months back by private practitioner after which the patient noticed generalized eruptions involving almost all the surfaces of the body including axilla, groin, chest, shoulder, forearms, hands, within a week of dental implant placement [Figure 1] with no obvious peri-oral signs and symptoms. Following this he first consulted a dermatologist after 10 days of implant placement, who considered this a skin problem and diagnosed it as generalized pruritus. Raised eosinophilic count was present in hematological reports after 2 weeks of implant placement. He was prescribed antihistaminic (H1 antagonists) as an anti-allergic, but the eczema did not resolve. Skin biopsy was advised to rule out dermatitis herpetiformis and gliadin antibody (IgG, IgA) along with tissue transglutaminase (Ttg) test after 2 months to rule out celiac disease after

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observing continuous eruptions without much relief with anti-allergic as well. All tests reported negative. There were no significant pathologic findings observed around the implants [Figure 2], and radiographically, the surrounding bone appeared normal. The patient was systemically healthy, with no history of medications or other suggestive medical treatment. The patient went to numerous skin clinics and hospitals and had taken anti-allergic medication, local and systemic steroids, and obtained only symptomatic relief but complained of the eruptions again after stopping the medications. The patient had also reported back to the private clinic after 4 months and requested for implant removal for which dentist convince him not to get it removed considering no perioral signs and symptoms and placed the crown as well. With regular medications and consulting dentist and dermatologists, he finally visited to the department of periodontology for the removal of implant. Considering the clinical symptoms, laboratory investigations and opinions from the departments of dermatology and medicine, a diagnosis of titanium implant allergy was made, and the patient was advised to go for the patch test before the removal of implant. The informed consent was obtained for the retrieval of the implant and for displaying the clinical images of the patient. After denial of the consent for the patch test by the patient, the implant removal was done atraumatically. The anti-allergic medications were stopped after 1 week as there was considerable relief in symptoms. The patient was rehabilitated with removable partial denture for the esthetic reasons. At 6-month follow-up, the lesions on all the body surfaces disappeared completely, and there were no signs of itching or pain [Figure 3]. The patient exhibited remarkable progress with complete remission of signs and symptoms.

**Discussion**

Titanium and its alloys are used as biocompatible material for various purposes, like knee implants, pacemakers and are often used for manufacturing dental implants from last 2–3 decades. Dental implants have been manufactured using commercially available pure titanium (CPTi) and titanium alloy, commonly the CPTi grade 4 titanium. However, the biocompatibility of any material cannot be considered universal.[8] The occurrence of metal sensitivity following exposure to titanium implants has been reported to be about 0.6%.[9] Although titanium is known for its biocompatibility and thus commonly used for implant alloys, still due to the result of production process nickel is one of the provocative allergen which got impregnated in due manufacturing process. Different titanium manufactures were shown to contain up to 0.034 wt% nickel[10] even in standard titanium alloys (TiAl6Nb7 and TiAl6V4). Delayed-type hypersensitivity reactions in relation to dental implants insertion normally considered first as CD, but their existence is still raised questions due to inconclusive hypersensitivity work up and insufficient patch test preparations. A literature review by Kim et al.[11] reports that titanium implants in the human body enhance the amount after the implantation due to its internal exposure and thus raises titanium ions concentrate in the surrounding tissues, as well as in the regional lymph nodes and pulmonary tissue.[12,13] Titanium implants have been shown to stimulate type I or type IV
hypersensitive responses due to the release of immunogenic protein-metal complexes.[14] Hypersensitivity reactions have also been associated with various problems such as atopic dermatitis and impaired fracture healings, pain, and necrosis.[15] The oral implantology has been documented with the appearance of facial erythema, edematous, and proliferative hyperplastic tissue.[16] Preez et al. in 2007 reported a case of localized severe tissue reaction around the implant sites requiring the removal of the implants.[17] The association of eczema with titanium dental implants was reported by Egusa et al. in 2008.[18] As per the criteria set by Albrektsson et al., such cases are to be categorized under biologic failures and should be included in the discussion as early implant failures.[19] CD is a localized form of delayed hypersensitivity, inducible by a various chemicals and metals. Implant allergies are mostly overlooked in dentistry. The diagnostic tests for allergy include patch test, but so far, there is no standard patch test for titanium. The memory lymphocyte immunostimulation assay test has also been developed, but it lacks specificity in detecting lymphocyte proliferation.[20] Lymphocyte transformation test has been reported to provide many false-positive results. The incidence of titanium sensitivity in dentistry is increasing as its use in dentistry is growing rapidly in the form of titanium plates, dental implants among others. Any history of previous allergy to metals or jewellery should be assessed before implant surgery and should preferably be advised for metal allergy testing. The dental implantologist should be aware about the possibility of a titanium allergy. There are so many limitations in diagnostic uncertainties in evaluating the hyperreactivity of titanium and mostly show it as a rare condition, and above-mentioned findings have been summarized in the literature review by Goutam et al.[21] However, other titanium salts, as suggested by Basketter et al.[22] and Okamura et al.,[23] could prove its usefulness for testing in case of suspected titanium allergy.

**Conclusion**

This clinical report presents a suspected association of an allergic reaction with titanium dental implants, and this always needs a correlation, but normally, it has found to be overlooked by dental clinicians. The rare occurrence of such a response to titanium materials in clinical dentistry should, therefore, be further discussed and investigated.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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