

Zirconium Implant as an Alternative to Titanium Implant in a Case of Type IV Titanium Allergy: Case Report

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Titanium remains the material of choice in the manufacturing of dental implants because of its exceptional biologic and mechanical properties. However, cases of allergy to titanium have been reported in the literature causing skin, mucosal reactions, systemic symptoms, and eventually implant exfoliation. Although the frequency of these cases varied between 0.6% and 5%, undiagnosed or misdiagnosed cases may possibly increase this percentage significantly. Epicutaneous, intradermal inoculation of the allergen or blood tests (LTT, MELISA, IL1 β , IL-6, TNF- α , IL-10) have been used with various degrees of sensitivity and specificity to assess Ti allergy. This case report demonstrated that titanium dental implant allergy caused rapid implant loss following an acute inflammatory reaction and its successful replacement by a one-piece zirconium implant. *Int J Oral Maxillofac Implants* 2020;35:639–644. doi: 10.11607/jomi.7990

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Titanium (Ti) remains the material of choice in the manufacturing of dental implants because of its exceptional biologic and mechanical properties.¹ It has been used for decades in orthopedics for the replacement of hips, knees, and joints. Its high tolerance by the immune system and excellent biocompatibility when used in its purest form with very low residues of iron, copper, and nickel made it the reference material for dental implants. It has great biomechanical properties that resist loading with very low risk of fracture under function. However, no metal can be considered universally biocompatible.² Its high resistance to corrosion due to the formation of a 10- μ m Ti oxide (TiO₂) layer when it comes in contact with air highly favored it in implant dentistry. Its corrosion rate below 0.02 mm per year is well below the corrosion rate acceptable for biomaterials.³ However, Ti implants are placed in the oral cavity, which is one of the most inhospitable electrolytic environments in the body. It is constantly subjected to temperature changes, PH variations, and microbial

attacks.⁴ Corrosion is influenced by PH variations and crevice corrosion.⁵ Galvanic corrosion that results from interaction between Ti and alloys used in prosthetic dentistry may disrupt the TiO₂ layer and cause Ti ion release in the environment. Under normal conditions and because of local and temporal variations in microstructure and the environment,⁴ Ti ions are released in the peri-implant tissues in a range of 100 to 300 ppm.⁶ Presence of Ti ions in the peri-implant tissues are compatible with health,⁷ although Ti ion concentrations higher than 13 ppm have been correlated with a significant decrease in gingival epithelial cell viability and were shown to induce necrosis.⁸ Also, these ions may combine with biomolecules and initiate type IV hypersensitivity reactions.⁹ In cases of infection or because of mechanical friction, a higher proportion of Ti ions are found in the body, including the lungs, regional lymph nodes, blood, spleen, or kidney. The importance of this remains to be precisely determined.¹⁰

Ti allergy has been reported in the orthopedic literature in failed hip and knee prostheses and in patients with Ti osteosynthesis plates and has been believed to represent 5% of implant failures. Clinical signs of intolerance include itching, skin redness, eczema, oral lichen planus, and granulomatous tissue. There have been few reports in the dental literature confirming the possibility of implant loss due to material intolerance. In an extensive report by Sicilia et al¹¹ on Ti dental implant allergy based on 1,500 consecutive patients, Type IV hypersensitivity was described with clinical signs in the hard and soft tissues. Patients with obvious signs of allergy, ie, de-keratinization of the surrounding mucosa, redness, itching, eczema, dermatitis, or unexplained loss of implants or with a history of multiple allergies

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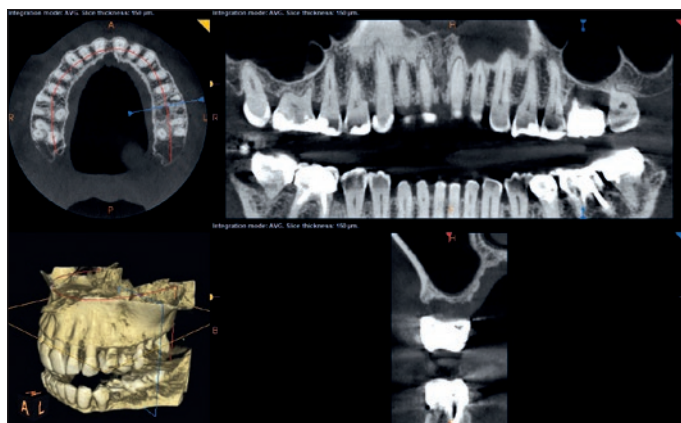


Fig 1 Initial panoramic radiography. The maxillary left first molar shows severe bone loss as a result of endodontic failure. Limited bone height is left in the subsinus area, indicating a sinus floor elevation prior to implant placement.

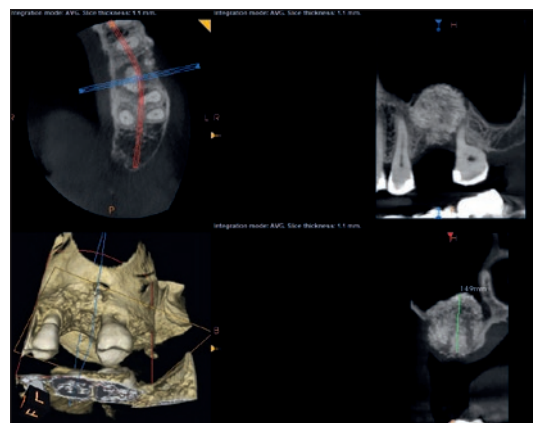


Fig 2 Sectional CBCT following lateral window sinus floor elevation. Note bone height following augmentation and the absence of inflammation in the sinus mucosa.

or patients with intensive exposure to Ti due to multiple implant placement or several episodes of peri-implantitis and implant loss were investigated; 0.6% implant failure was related to allergic reactions. Yan et al¹² reported a 6.3% prevalence of Ti allergy based on the examination of 217 patients exhibiting positive allergic reactions to at least one type of metal allergen. De Graaf et al¹³ reported a 5.7% frequency of Ti allergy in a selected population referred for allergy testing, a result that may not be directly extrapolated to the general population.

Here, a case of implant loss due to a strongly suspected Ti allergy and its successful replacement with a zirconium implant is reported.

CASE REPORT

A female patient 46 years of age with a history of Hashimoto disease, an autoimmune disease that causes gradual destruction of the thyroid gland and currently being treated with levothyroxine (euthyrox) and daily vitamin supplement, consulted in June 2016 for pain on the maxillary left first molar following a failed endodontic treatment (Fig 1). It was decided to extract the tooth and replace it, since implants are today the best treatment option for a single tooth loss with sound adjacent teeth. The patient's overall periodontal condition was good. She was under regular dental care with good oral hygiene. The maxillary left first molar was extracted; an external sinus elevation to augment bone height and delayed implant placement were indicated because of the limited subsinus bone height. In July 2016, sinus elevation was done using the lateral approach and window repositioning.¹⁴ It was grafted with anorganic bovine bone (Cerabone, Botiss Dental), and the site

was left to heal for 6 months (Fig 2). Six months later, a sectional cone beam computed tomography (CBCT) scan was taken to confirm the sinus graft healing, and a 5 × 11.5-mm select conical implant (Nobel Biocare) was placed in type 2 bone via a limited crestal incision with excellent primary stability. A healing abutment was immediately connected. The patient was given a course of antibiotics (Amoxicillin/Clavulanic Acid 1 g b.i.d. for 5 days) and a painkiller (diclofenac 50 mg) as needed.

A few days following the surgery, the patient reported severe pain with a burning sensation in the palate adjacent to the implant site that was barely controlled by the prescribed analgesic. Clinical examination revealed a zone of 1 cm of de-keratinization on the palatal mucosa resembling a chemical burn that was initially attributed to a hot food burn. A periodontal dressing was placed over the area to alleviate the pain. The patient was seen a week later. The inflammation persisted. Two weeks later, the implant was found mobile. It was removed with a plier. The site was curetted, and all granulation tissues were removed. A sectional CBCT scan was taken and showed inflammatory thickening of the sinus mucosa (Figs 3 and 4). The patient was covered with moxifloxacin 400 mg (1 tab/day for 1 week). A week later, the pain subsided totally, and the mucosa healing was progressing normally. This clinically unexplained failure was suspicious.

The patient was referred to a dermatologist (C.I.) to test for allergy to Ti. Patch testing was performed with the TRUE test (SmartPractice Canada), an epicutaneous test used in the diagnosis of allergic contact dermatitis to 35 allergens, a general panel that showed, in the current case, sensitivity to phenylenediamine, nickel, cobalt, gold sodium thiosulfate, balsam of Peru, and dispersed blue. The dermatologist concluded that there was a Ti cross reactivity to cobalt and nickel, both

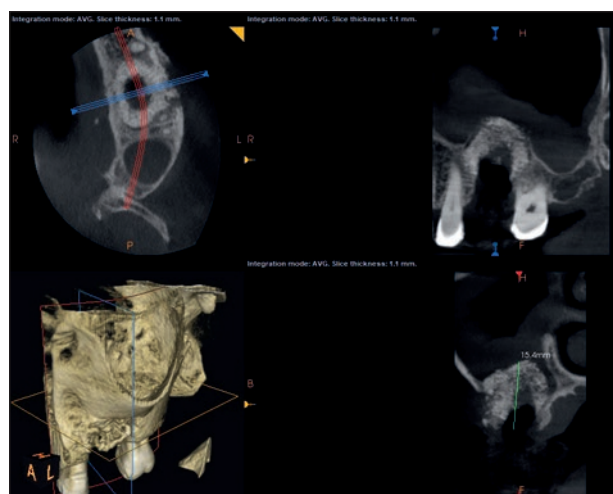
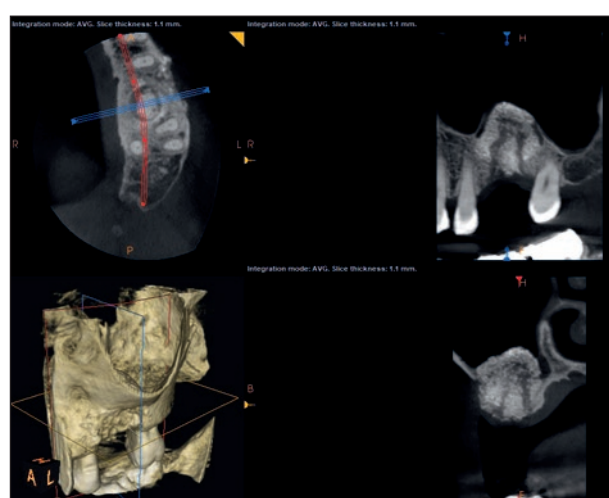
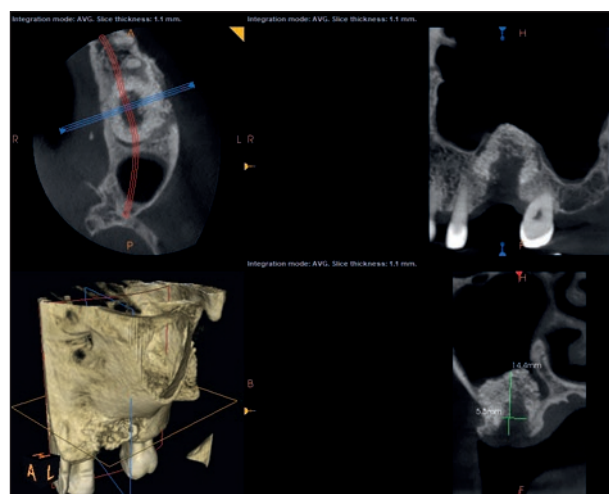


Fig 3 (above left) Sectional CBCT taken following Ti implant removal. Note the amount of bone loss at the implant site and the inflammatory thickening of the sinus mucosa in regard to the site of the maxillary left first molar.

Fig 4 (above right) Sectional CBCT taken 1 month following the inflammatory episode. Note the resolution of the sinus mucosa inflammation and the presence of an alveolar defect at the previous implant site, which necessitated socket grafting.

Fig 5 (right) Sectional CBCT taken 4 months following socket grafting. Note the total bone reconstruction at the implant site and the absence of inflammatory reactions on the adjacent structures.



known to be co-reactants to Ti. However, in order to confirm Ti allergy, a patch test using a sterile Ti implant cover screw was performed using a test chamber that allowed the placement of the allergen in contact with the skin (AllergEaze, SmartPractice Canada). Patch test chambers were removed from the back of the patients after 48 hours of exposure, and readings were performed on days D2 and D3. Positive reactions rated as +, ++, or +++ in accordance with the European Society of Contact Dermatitis reading criteria were regarded as allergic, whereas doubtful reactions were not. The present patient showed severe 3+ sensitization to the Ti patch test. In addition, a skin prick test with Ti oxide in Vaseline was performed to provide more evidence of Ti allergy. The test was also positive (wheal/flare: 4 to 5) compared with a negative saline control and a positive histamine control.

The patient insisted on having the tooth replaced. A zirconium implant was proposed as an alternative to Ti. The patient agreed on the treatment. In April 2017, an-organic bovine bone was added to fill the socket defect

that followed implant failure. The site was left to heal for 4 months (Fig 5). In July 2017, a one-piece zirconium implant (Straumann), 4.1 × 12 with a 5.5-mm abutment height, was placed flapless with excellent primary stability. The postoperative course was uneventful. Implant healing progressed normally with no signs of pain or inflammation. Five months later, a zirconium crown was placed. The postoperative control 18 months later confirmed the excellent integration of the implant in hard and soft tissues (Figs 6a to 6h).

DISCUSSION

This unusual case of Ti allergy caused a rapid implant exfoliation following a severe type IV allergic reaction. It was successfully replaced by a one-piece zirconium implant after the resolution of all clinical signs of inflammation and site reconstruction. The authors' initial interpretation of the palatal gingiva de-keratinization was hot food burn, and the inflammatory reaction that

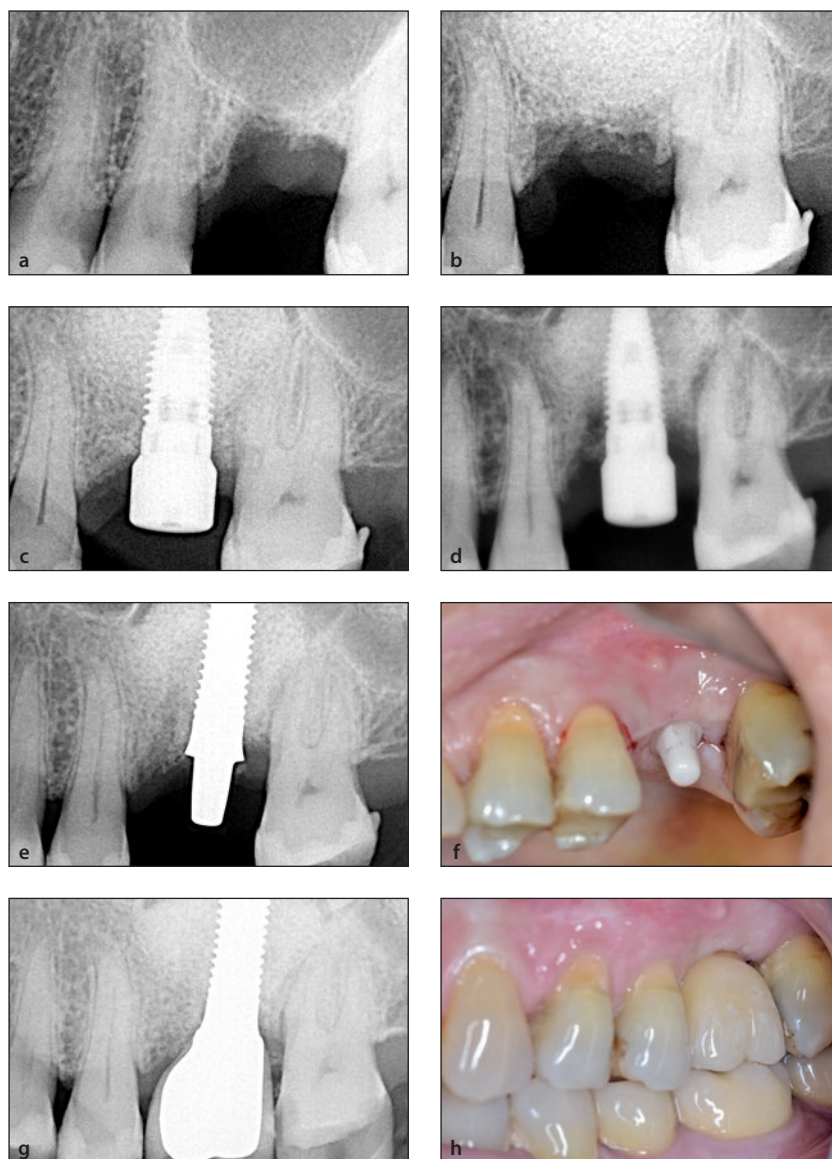


Fig 6 (a) Periapical radiograph prior to sinus floor elevation. (b) Periapical radiograph following sinus floor elevation. (c) Periapical radiograph following Ti implant placement with healing abutment connected. (d) Periapical radiograph 1 week following implant placement; acute inflammatory reaction causing peri-implant bone loss. (e) Periapical radiograph following one-piece zirconium implant placement. (f) Clinical image 3 months post-zirconium implant placement. (g) Periapical radiograph at definitive zirconia crown placement. (h) Final clinical situation 18 months postoperative.

followed implant placement, in the current case, was believed to be infectious or traumatic in origin. It is important to underline that similar cases of postoperative infection may be misinterpreted, and the diagnosis of allergy to Ti may be overlooked if not properly investigated. In cases of unexpected or unusual reaction to a dental implant, Ti allergy tests must be done for proper diagnosis.

Titanium inertness and biocompatibility have been recently challenged by Trindade et al and Albrektsson et al.^{15,16} According to these authors, osseointegration is not to be viewed as a healing process following the insertion of a chemically and biologically inert material but rather a foreign body

equilibrium between an immune-modulatory foreign body and the immune system. Bone is built around the implant to wall it off and isolate it from the body, and the osseointegration remains as long as the equilibrium is not ruptured. Otherwise, peri-implantitis starts as an immune reaction and develops secondarily due to microbial contamination.

Titanium allergy has been reported in numerous publications, yet the overall prevalence seems to be low. In a study¹³ on 458 patients tested for Ti allergy using a panel of Ti salts, there were 248 with suspected allergy to Ti, 163 with suspected metal allergy other than Ti, and 47 controls with no suspected allergy to Ti; the frequency of Ti sensitivity was 5.7%. In a survey of 1,500 patients evaluated for Ti allergy, the prevalence was 0.6%.¹¹ Of a total of 270 patients with suspected metal allergy who consulted an allergy clinic and were tested using patch tests that include 28 metal and Ti allergens,¹² 80.4% exhibited positive allergic reactions to at least one type of metal and 6.3% tested positive to Ti allergens. Sixteen patients had dental implants and reported allergy symptoms following implant placement. Eleven exhibited positive allergic reactions to one of the metals tested and four of them to Ti allergens. Five patients had a negative reaction to all allergens tested. No patient exhibited allergic reactions to only Ti allergens. Allergic reactions disappeared completely after implant removal in one patient. In two patients, all metallic restorations and superstructures but not the implants were removed, and all allergy symptoms resolved. One of four patients with minor reactions recovered without implant removal, suggesting individual Ti sensitivity levels.

Proinflammatory cytokines and potential tolerance to Ti were tested in healthy individuals, 14 with

no dental implant placement and 6 with complication-free dental implants.¹⁷ Proliferation index in lymphocyte transformation test (LTT), production of interleukin (IL)1 β , IL-6, and tumor necrosis factor alpha (TNF- α) linked to innate immune response, and immune regulation (IL-10) were assessed in response to TiO₂ particles and Ti disks. No enhanced T lymphocyte proliferation was seen in any of the individuals examined. Individuals without implants showed higher cytokine response than individuals with symptom-free implants. Five of six symptom-free individuals showed production of IL-10 and none of the 14 controls. The authors concluded that IL1 β , IL-6, and TNF- α production reflect normal un-specific immune response to Ti.

Allergy patch tests to Ti have been widely used, but it does not seem that an unequivocal test is available, as many of them proved to be unreliable. In a retrospective review of 458 patients who underwent patch tests with one to five different Ti salts, Ti oxalate hydrate had the highest yield and the Ti dioxide the lowest, and it was concluded that the medical history and clinical picture remain crucial in the diagnostic workout.¹³ Positive tests in the control group highlight the possibility of false positive results.

In the present case, three allergy tests were used. The TRUE test confirmed a severe allergy to nickel and cobalt, which have been demonstrated to be cross-reactants with Ti. However, since metal allergy to nickel, chromium, and cobalt has not been shown to necessarily equate with Ti allergy,¹² although the risk of metal allergy is more prevalent in patients with sensitivity to other metals,⁴ an epicutaneous test using Ti as allergen in a Ti chamber and a prick test using Ti oxide with Vaseline showed severe allergic reaction to Ti. Commonly used patch tests are not quite reliable because of low epidermal penetration of Ti salts.⁹ According to Fage et al,¹⁸ given the inconsistencies of the diagnostic tests currently used to determine Ti allergy, diagnosis of this condition should be primarily based on clinical evaluation. Recently, inflammatory markers such as IL-17 or IL-22 have been used as immunologic assay.

LTT and memory lymphocyte immune-stimulation assay (MELISA) are available as alternative diagnostic tools. However, it seems that LTT is more appropriate for people who are sensitized and currently exposed to allergens and seems less appropriate for people who are sensitized but not currently exposed to allergens.¹³ Patients with clinical symptoms after receiving Ti-based implants who tested negative with patch tests elicited a positive response using MELISA.¹⁹ However, it is important to note that among those who tested positive to metals, 33.9% were negative to Ti allergen. Yet, after implant removal, all patients showed clinical improvements in their clinical symptoms. Also, a high number

of false positive results using these tests compromise their validity.²⁰

Type I allergy occurs very shortly after metal exposure to the humoral response. Type IV allergy is cell-mediated and occurs a few hours to days after exposure to immunogens. Most of the allergy reports come from the orthopedic literature, but some include dental material.²¹ They are mostly related to implants made of alloys containing nickel and cobalt and may be the cause of implant loosening, but also from Ti. Du Preez et al²² reported a case of suspected allergy to Ti causing a severe tissue reaction at the implant site. Egusa et al²³ reported a concomitant face eczema with a Ti implant overdenture that completely recovered following dental implant removal. In the same line, a contact stomatitis was diagnosed in regard to a Ti nitride-coated abutment that totally subsided after the removal of the abutment and its replacement with an uncoated abutment.²⁴ In an interesting case report of facial eczema following orthopedic surgery on a patient who concurrently had dental implants with no local signs of allergy or inflammation, eczema signs improved after the removal of the metal prosthesis but only disappeared totally following the explantation of the dental implants.²⁵ Zirconium implants were successfully used to rehabilitate a patient with severe metal allergy including Ti.²⁶

In the present case, the diagnosis of Ti allergy was based on the TRUE test and the epicutaneous and prick tests, but more so on the adverse clinical signs following implant placement, on the resolution of the signs after implant removal, and on the excellent asymptomatic healing following the placement of the zirconium implant. Although the frequency of allergy to Ti is considered very low either because of a low prevalence or no diagnosis, the need to develop noninvasive highly sensitive and specific tests to confirm unequivocal Ti allergy remains of importance to identify these unusual clinical situations.

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