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SHORT REPORT



Suspected allergy to titanium after anterior cervical discectomy and fusion using a Zero-P device: a case report

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ABSTRACT

Purpose: Cases of allergy to large surgical implants have been reported. However, few studies have reported allergy to small titanium-containing implants (e.g. Zero-P device).

Methods: We reported the case of a 51-year old male patient who underwent the anterior cervical discectomy and fusion (ACDF) procedure using a Zero-P device and exhibited allergic symptoms 1 month after the surgery.

Results: The allergic symptoms included intermittent tingling and itches in the throat induced by speaking. Systemic rashes over the skin surface and congestion of the eyeball, and dysphagia were also present. Anti-allergic treatment did not resolve the symptoms. Patch tests revealed negative reactions to the rested reagents including titanium. Radiographic results showed solid bone fusion and no signs of chronic inflammation or hypotoxic infection in the surrounding tissues. Upon the patient's request, we removed the titanium screws and plate of the Zero-P device. No allergic reactions were observed after the surgery and at a 6-month follow-up.

Conclusions: Even with a small implant such as the Zero-P device, allergy to titanium may still occur. This case demonstrated the need to screen for the presence of allergy to metals including titanium before the surgery.

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Cervical spine; rash; titanium; hypersensitivity; ACDF

Introduction

Many of the metals in surgical implants are potentially immunogenic and allergic reactions to them have been reported.^{1,2} Hypersensitivity to orthopedic implants has been the commonest.³ In orthopedics surgery, titanium is commonly used. It is highly resistant to corrosion due to the formation of a thermodynamically stable and adherent oxide layer on its surface.^{4,5} Therefore, titanium may provoke a few allergic reactions.^{6,7} For patients with metal sensitivity, titanium has been particularly recommended.⁵ Nonetheless, titanium implants are typically made of titanium alloy, which contains traces of other metals. Theoretically, allergy to titanium might still occur.⁸

Allergy to titanium-containing implants has been reported. Thomas et al. reported a patient who developed eczema upon titanium-based osteosynthesis.⁹ Egusa et al. reported facial eczema associated with a titanium dental implant.¹⁰ Allergy to titanium implants used in orthopedics surgery has rarely been observed.^{11,12} Here, we reported a patient who received anterior cervical discectomy and fusion (ACDF) procedure using a Zero-P device which is much smaller than those used in other surgeries (e.g. knee and heart surgery).

Case presentation

A 51-year-old male patient who had never experienced contact-hypersensitivity to metals presented with neck and right arm

pain for 10 years combined with unstable walking for 1 year. Preoperative magnetic resonance imaging (MRI) showed severe compressions of the spinal cord at the C5/6 level (Figure 1). ACDF was performed using a Zero-P device. The surgery was successful and postoperative outcomes (e.g. pain and disability) were satisfactory. Postoperative X-ray and MRI were also satisfactory. Radiographs of the patient at his first surgery are shown in Figure 1.

One month after the surgery, the patient complained of intermittent tingling and itches in the throat. The symptoms were induced after talking. He also developed congestion of the eyeball (Figure 2(a)), systemic rashes over the skin surface (Figure 2(b)), and dysphagia. There were no ulcers and pigmentations on the skin. The patient was prescribed antiallergic agents (e.g. steroids) for several months, which only afforded short-term benefit. The symptoms still occurred intermittently thereafter. The patient had skin patch tests in the dermatology department for general allergens. The results, however, did not reveal any allergy to the metals including titanium.

Three years after the operation, the patient came back to our hospital. The patient's job is teaching. Because the symptoms he had experienced impaired his daytime functioning, he requested to have the implants removed. A radiographic examination confirmed complete bone fusion and no inflammation or infection signals on MRI (Figure 3(a–c)). Full blood count, erythrocyte sedimentation rate, C-reactive protein level, and levels of antibodies against cytomegalovirus IgM were normal. Only the IgE



Figure 1. Radiographs of the patient at his first surgery. (a–c) Preoperative X-ray and magnetic resonance imaging (MRI) showed cervical spondylosis at C5-6 level and severe compression of the spinal cord at this segment. (d) This patient was treated with ACDF using a zero-P profile device. (e) Radiologic evaluation at over 6 months post-operation showed solid fusion. (f) Postoperative MRI images showed complete decompression of the spinal cord.

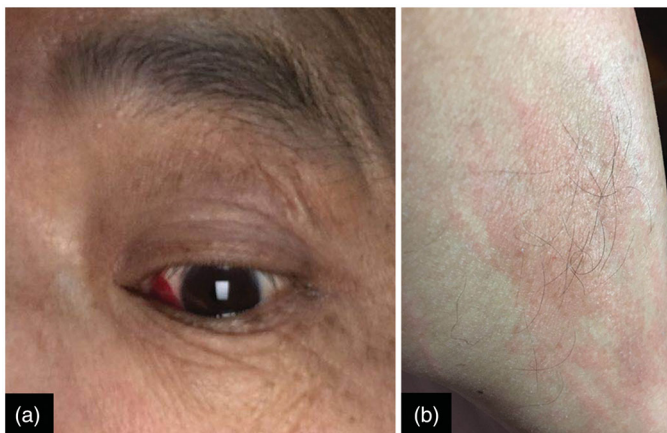


Figure 2. Clinical manifestations of the patient after his first surgery. A physical examination revealed (a) congestion of the eyeball and (b) red rashes over the skin surface of the legs.

was raised. Barium swallow cine X-ray showed normal functions of the pharynx and esophagus. No stenosis was observed (Figure 3(d)).

The symptoms indicated a possible allergy to the implants. At the patient's request, we re-operated and removed all titanium implants (Figure 4) leaving the PEEK part in place. This was confirmed on X-ray (Figure 3(e)). A computed tomography (CT) scan and lateral X-ray 3 months postoperatively demonstrated the range of osteotomy and confirmed that the cage was well maintained (Figure 3(f–g)). No further anti-allergic medications were given. After the surgery, the allergic symptoms resolved and had not recurred at a 6-month follow up. Figure 5 shows the normal skin and eyeball after the removal surgery.

Discussion

The Zero-P implant consisted of a cage made of poly-ether-ether-ketone (PEEK) and a plate with four screws made of



Figure 3. Radiographs of the patient at his second surgery. (a,b) A lateral X-ray and computed tomography (CT) scan confirmed complete bone fusion after 3 years of his ACDf surgery. (c) MRI imaging showed no more compressions of the spinal cord and no inflammation or infection signals surrounding the device. (d) Barium swallow X-ray showed normal function of the pharynx and esophagus. (e) This patient underwent a second surgery and the titanium plate and screws were removed from the patient. (f,g) CT scan and lateral X-ray 3 months postoperatively demonstrated the range of osteotomy and confirmed that the cage was well maintained.

titanium alloy. The alloys are Ti-6Al-4V and Ti-6Al-7Nb. Ti-6Al-4V contains aluminum (5.50–6.75%), vanadium (3.50–4.50%), and iron (0.40%). Ti-6Al-7Nb contains aluminum (6%) and niobium (7%) (DePuy Synthes Mitek, Raynham, MA). Allergic reactions to titanium have been reported in patients receiving much larger implants than the Zero-P device. In this case report, we described possible allergies to titanium in a patient receiving a Zero-P device, the titanium part of which is very small. Allergic symptoms included tingling and itches in the throat after talking, accompanied by difficulties in swallowing and rashes over the skin surface. The patient did not exhibit a positive reaction for a titanium reagent, but the allergic symptoms disappeared after the removal of the titanium implant.

Metal allergy can lead to adverse reactions (e.g. hypersensitivity or tissue damage). The clinical presentation of metal allergy varies widely, which can be manifested in the extremities, limbs, and even on the skin. On the skin surface, the manifestations may be presented as eczema, contact dermatitis, and plantar palm rash.^{13,14} In our case, the patient reported allergic symptoms of skin rashes and throat tingling and itches. In several

other studies, contact dermatitis around titanium products has been reported.^{8–10} In one case of suspected titanium allergy, the patient exhibited eczema on the general skin surface after dental implantations using titanium screws.¹⁵ Impaired wound healing and local eczema occurred in another case who received treatment of a right metacarpal fracture using a pure titanium mini-plate and screws.⁹

Among the commonly used materials, titanium may provoke few allergic symptoms due to its compatibility with human bodies and high corrosion-resistance.⁵ Therefore, titanium has been widely used.^{3,7} However, the titanium implant used in surgery is not completely pure and contains a small amount of other metals (e.g. aluminum, vanadium, beryllium, cobalt, chromium, copper, iron, and nickel).¹⁶ Based on previous evidence, the most important allergens include nickel, cobalt, chromium, and bone cement.³ Thus, it could be metals other than titanium in alloys that cause allergic reactions. In this case, the titanium alloys were made from Ti6Al4V and Ti-6Al-7Nb which contain iron, aluminum, vanadium, and niobium, any of which may have caused the reactions observed in this patient.

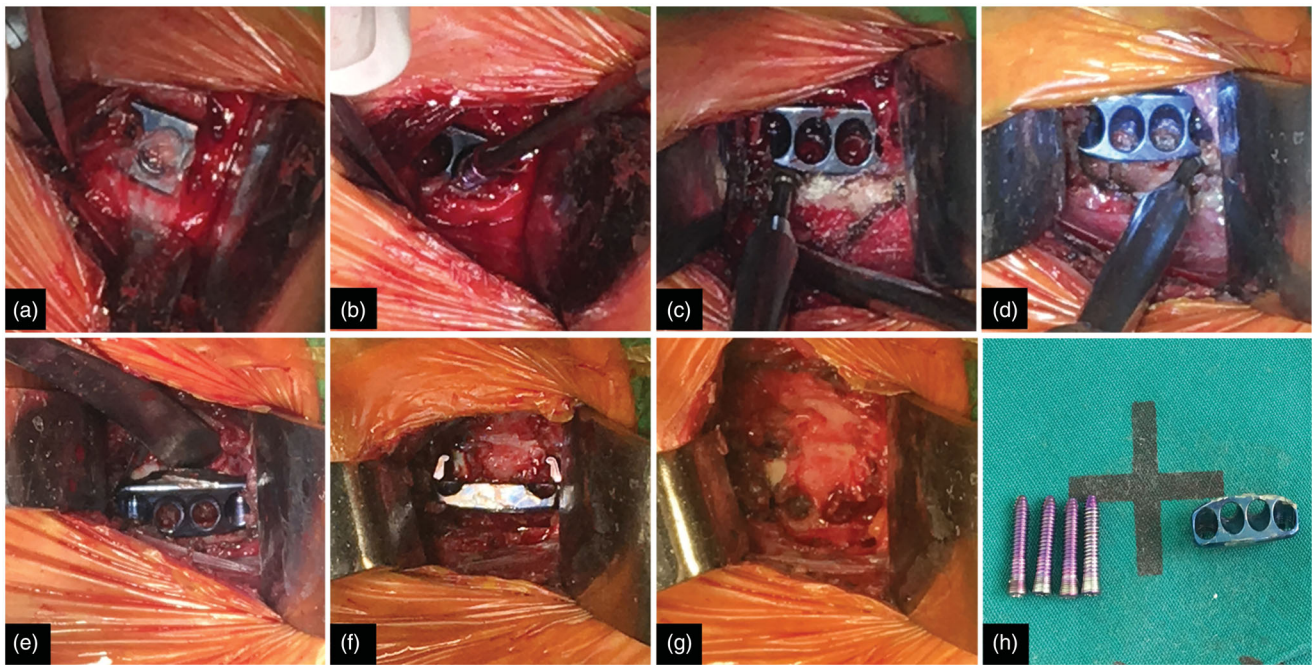


Figure 4. Procedures of the zero-P device removal. (a) Using an anterior approach, the C5/6 vertebrae body and zero-P device were exposed. No signs of chronic inflammation or hypotoxic infection were observed in the surrounding tissues. (b) The four screws were removed using a driver. (c) An osteotomy was performed using a high-speed burr to remove the anterior and inferior margin of the C5 vertebral body and the anterior and superior margin of the C6 vertebral body. (d) The depth of the osteotomy was controlled to expose the interface of the plate and cage. (e,f) A Cobb was then used to separate the plate and the cage. (g) All the titanium parts were removed and the cage was exposed. (h) Removed four screws and zero-P plate.

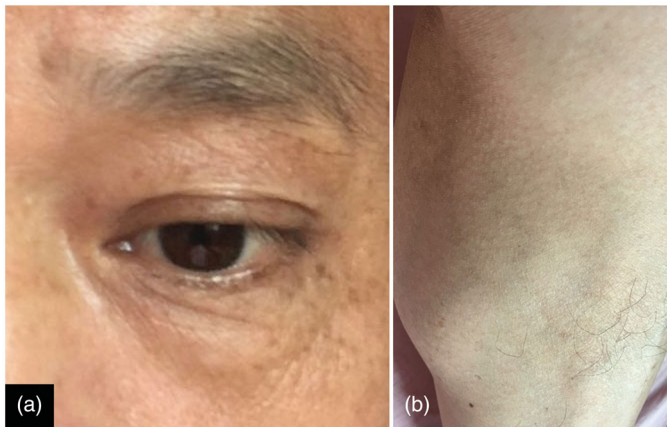


Figure 5. Clinical manifestations of the patient after his second surgery. A physical examination revealed (a) normal eyeball and (b) skin surface of his legs after the titanium screws and plate removal.

In our patient, skin patch tests were performed using various reagents (e.g. compositions in the titanium and stainless-steel bars). However, the results were negative. This finding was consistent with previous case reports. Specifically, in two brothers aged 17 and 23 years,¹⁷ high fever, chest pain, and pleural effusion appeared after repair of pectus excavatum using titanium bars. There were no signs of infection. The two patients had a history of metal allergy, but skin patch tests to titanium were negative. The symptoms disappeared after the titanium bars were removed 2 years later. Similarly, in an 86-year-old male patient¹⁸ who received a pacemaker, poor healing of the wound was observed after the surgery. There was no evidence of infection. The skin patch test to titanium was negative, but the wound healing problem resolved after the removal of the titanium-containing pacemaker. The diagnosis of titanium allergy has been challenging due to its low incidence and occult manifestation. It

might be misdiagnosed as other conditions (e.g. wound infection and foreign body inflammation).¹⁹ When metal allergy is suspected, skin patch tests have been commonly used. However, there has been no worldwide standard patch test reagent for titanium. A previous study examined the form and density of patch-test reagents for titanium.²⁰ It was suggested that reagents composed of pure titanium powder and petroleum jelly were suboptimal as they are non-specific stimulants. In comparison, a titanium tetrachloride (0.1%) may be preferable. The prevalence of positive reactions against titanium reagents is very low and no patient has exhibited positive reactions only for a titanium reagent.¹⁵ Thus, skin patch tests do not always reveal a metal allergy and a negative result does not exclude the possibility.¹⁹ Collectively, both our case and the previous reports suggested that allergic reactions to titanium may occur even with negative results of the skin patch tests.

In summary, even with a small implant such as the Zero-P device, allergy to titanium may still occur. In our case, the allergic reactions included rashes and symptoms in the surgical areas (e.g. throat). This report has implications for clinical practice. For instance, a detailed history of allergic reactions to metals should be documented prior to the surgery. For patients with a history of metal sensitivity, a patch test should be recommended. Spine surgeons should also keep in mind that titanium allergy might still occur with a negative skin patch test. Surgeons should routinely inform the patients of possible allergic reactions so that the symptoms can be detected early. In the case of titanium allergy, treatment of allergic symptoms should be a primary step. Removal of the titanium materials should be performed once complete fusion has been achieved.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

- Kelly RE, Goretsky MJ, Obermeyer R, *et al.* Twenty-one years of experience with minimally invasive repair of pectus excavatum by the Nuss procedure in 1215 patients. *Ann Surg* 2010;252:1072–81.
- Rushing GD, Goretsky MJ, Gustin T, Morales M, Kelly RE Jr, Nuss D. When it is not an infection: metal allergy after the Nuss procedure for repair of pectus excavatum. *J Pediatr Surg* 2007;42:93–7.
- Pacheco KA. Allergy to surgical implants. *Clinic Rev Allerg Immunol* 2019;56:72–85.
- Kononen M, Rintanen J, Waltimo A, Kempainen P. Titanium framework removable partial denture used for patient allergic to other metals: a clinical report and literature review. *J Prosthet Dent* 1995;73:4–7.
- Siddiqi A, Payne AGT, De Silva RK, Duncan WJ. Titanium allergy: could it affect dental implant integration? *Clin Oral Implants Res* 2011;22:673–80.
- Oluwajana F, Walmsley AD. Titanium alloy removable partial denture framework in a patient with a metal allergy: a case study. *Br Dent J* 2012;213:123–4.
- Kim KT, Eo MY, Nguyen TTH, Kim SM. General review of titanium toxicity. *Int J Implant Dent* 2019;5:10.
- Siddiqi A, Payne AG, Zafar S. Bisphosphonate-induced osteonecrosis of the jaw: a medical enigma? *Oral Surg Oral Med Oral Pathol Oral Radiol* 2009;108:e1–e8.
- Thomas P, Bandl WD, Maier S, Summer B, Przybilla B. Hypersensitivity to titanium osteosynthesis with impaired fracture healing, eczema, and T-cell hyperresponsiveness in vitro: case report and review of the literature. *Contact Dermatitis* 2006;55:199–202.
- Egusa H, Ko N, Shimazu T, Yatani H. Suspected association of an allergic reaction with titanium dental implants: a clinical report. *J Prosthet Dent* 2008;100:344–7.
- Bouguennec N, Colombet P, Graveleau N, Jambou S. The migratory cortical button: a rare case of hypersensitivity to titanium after an anterior cruciate ligament reconstruction. *Knee Surg Relat Res* 2019;31:132–6.
- Vijayaraghavan V, Sabane AV, Tejas K. Hypersensitivity to titanium: a less explored area of research. *J Indian Prosthodont Soc* 2012;12:201–7.
- Feller L, Wood NH, Khammissa RA, Lemmer J. Review: allergic contact stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2017;123:559–65.
- Yanagi T, Shimizu T, Abe R, Shimizu H. Zinc dental fillings and pal-mopplantar pustulosis. *Lancet* 2005;366:1050.
- Hosoki M, Nishigawa K, Miyamoto Y, Ohe G, Matsuka Y. Allergic contact dermatitis caused by titanium screws and dental implants. *J Prosthodont Res* 2016;60:213–9.
- Thomas P. Allergic reactions to implant materials. *Der Orthopade* 2003;32:60–4.
- Sakamoto K, Ando K, Noma D. Metal allergy to titanium bars after the Nuss procedure for pectus excavatum. *Ann Thorac Surg* 2014;98:708–10.
- Syburra T, Schurr U, Rahn M, Graves K, Genoni M. Gold-coated pace-maker implantation after allergic reactions to pacemaker compounds. *EP Europace* 2010;12:749–50.
- Wang LF, Wu J, Zheng C, Li SL, Huang RR, Zhang JK. Long-term fever after Hallux Valgus Surgery secondary to titanium allergy: a case report and review of the literature. *J Foot Ankle Surg* 2016;55:1282–6.
- Nakajima K. [Study on patch test reagent for titanium]. *J Stomatol Soc Jpn* 2007;74:92–8.