Orthopedic and Cutaneous Reactions to Nickel after Total Hip Replacement

Domagoj Delimar[1], Ivan Bohaček[1], Zrinjka Paštar[2], Jasna Lipozenčić[3]

[1]Department of Orthopedic Surgery, Clinical Hospital Centre Zagreb and School of Medicine, University of Zagreb, Zagreb, Croatia; [2]Department of Health Studies, University of Zadar, Zadar, Croatia; [3]Croatian Academy of Medical Sciences, Zagreb, Croatia

Corresponding author:
Assist. Prof. Zrinjka Paštar MD, PhD
Department of Health Studies
University of Zadar
Splitska 1
23000 Zadar
Croatia
zpastar@hotmail.com

Received: September 11, 2016
Accepted: October 18, 2017

ABSTRACT Implant degradation products have shown signs of a cutaneous allergic response after implantation of a metal orthopedic replacement, loosening and failure of the joints as well as skin rashes, general fatigue, pain, and impaired wounds and bone healing. The prevalence of contact skin sensitivity in patients with a joint replacement device is higher than that in the general population. This delayed hypersensitivity to metallic orthopedic implants is more clearly defined and is a contributing factor to implant failure. Nickel was associated with hypersensitivity responses as the first cause in metallic orthopedic implants as early as 1966 by Foussereau and Laugieru and is a commonly used metal in alloys because it grants necessary strength and durability to the implant. Herein we report on delayed hypersensitivity to nickel sulfate in a patient with pain, fatigue, and contact allergic dermatitis in both inguinal regions, with instability of the left acetabular part and with five hip replacements from 1987 to 2013. The findings of this report support that primary sensitization to a metal due to an implant itself might develop. Proper investigation in patients with history or prior hypersensitivity reactions to metals and test evaluation before orthopedic device implantation is needed.

INTRODUCTION

Cutaneous and systemic hypersensitivity reactions to implanted metals are not so rare (1-5). Over the past twenty years, the use of metallic and other implants, mainly as orthopedic, cardiovascular, plastic surgery, and dental implants, has increased, and so has the number of studies on allergic reactions to metallic compounds (1-11). The most commonly used orthopedic implants are joint replacement implants; e.g. hip, knee, shoulder and elbow endoprostheses. Foussereau and Laugier described a case of metallic orthopedic implants on nickel in 1966 (6). Nickel, cobalt, and chrome were classic contact allergens in the implants (2,3,5,7,8).

Total hip prostheses are made of metal alloy, which has better mechanical properties than pure metal such as titanium. Cobalt-chrome alloys, where the base metals are cobalt (>34%) and chrome (>19%), are mixed with smaller quantities of other metals, including nickel.

Orthopedic grades of alloys such as stainless steel and cobalt-chromium alloys contain relatively

Acta Dermatovenerol Croat
2018;26(1):39-43

high levels of nickel compared with pure titanium or titanium alloy implants (12). Therefore, titanium implants or titanium alloy implants are often used as an alternative for patients suffering from nickel, chrome, or cobalt allergies (5,8). However, all metallic alloys corrode, especially in contact with biological fluids (7). Patients who have had an allergic reaction to a metallic device or to jewelry are more likely to have this kind of a reaction than those with no history (7). Many researchers suggest the importance of patch testing in patients with a clinical history of metal hypersensitivity before prosthetic device implantation (4,7,13-16). In addition to causing host hypersensitivity, the problems of osteolysis and late aseptic loosening can also be associated with the potential of cobalt-chrome particles to release metal ions that may be toxic to cells, inducing deoxyribonucleic acid damage (17).

CASE REPORT

We report the case of a 59-year-old man with a history of five surgical procedures, all performed on the left hip between 1987 and 2014. The first symptoms appeared at the age of 18 when the pain in the patient's left hip started. Hip dysplasia was later diagnosed at the age of 21.

In 1987, at the age of 32 and because of the left-hip coxarthrosis, total hip arthroplasty was performed (endoprosthesis model Lubinus, cemented prosthesis; alloy: CoCrMo, polyethylene acetabulum). The operation as well as the postoperative course and rehabilitation were remarkable (Figure 1, A, B) and the patient was without symptoms until 1993.

In 1993, because of intensive pain in the left hip that interfered with walking, the instability of the

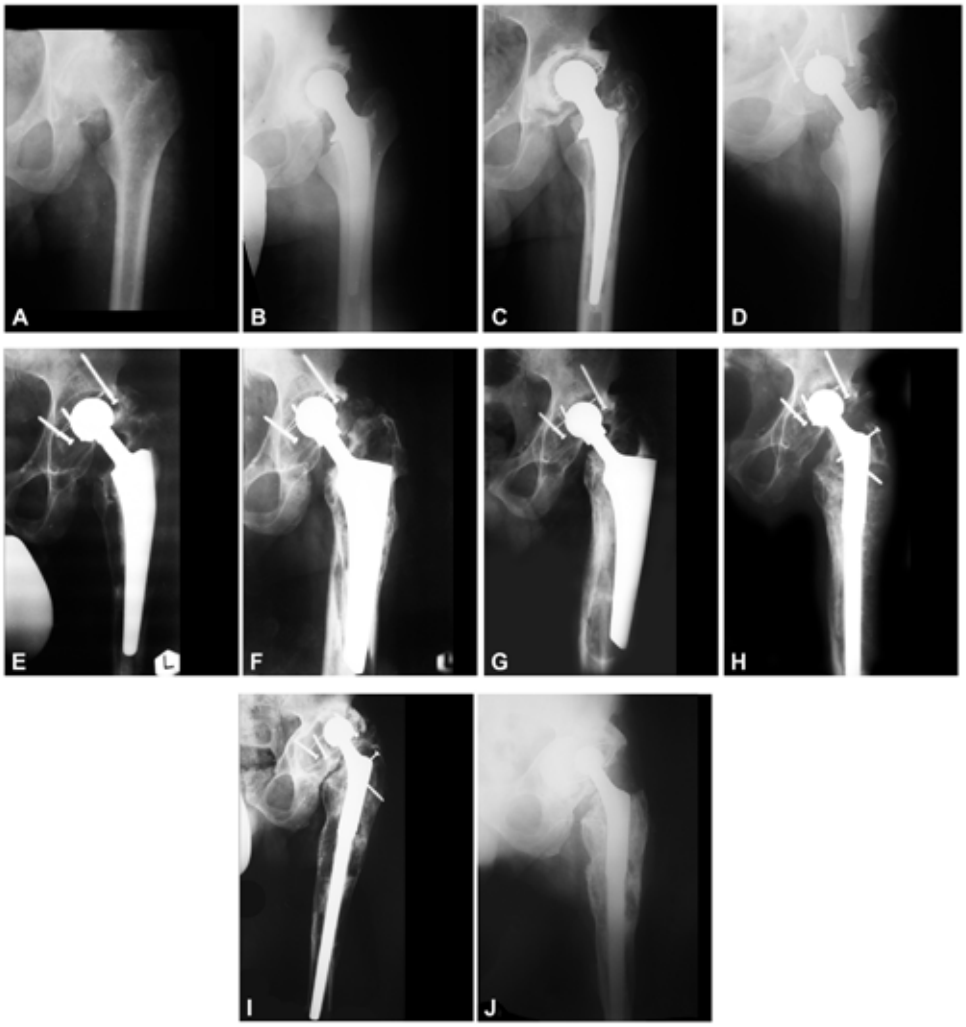

Figure 1. Plain radiograph (anteroposterior view) before the first surgery (A) and after the first surgery (B). Plain radiograph (anteroposterior view) before the second surgery (B) and after the second surgery (C). Plain radiograph (anteroposterior view) before the third surgery (E) and after the third surgery (F). Plain radiograph (anteroposterior view) before the fourth surgery (G) and after the fourth surgery (H). Plain radiograph (anteroposterior view) before the fifth surgery (I) and after the fifth surgery (J).

Acta Dermatovenerol Croat
2018;26(1):39-43

total endoprosthesis was diagnosed. Therefore, extraction of the total prosthesis was performed, followed by immediate left hip re-arthroplasty (femoral part model Müller-Crystal, alloy: CoNiCrMo, acetabular part model Morscher; chemical ingredient: polyethylene). Acetabular component stability was additionally reinforced with three screws (alloy unknown). The operation as well as postoperative course and rehabilitation were remarkable (Figure 1, C, D).

In 1999, following the manifestation of pain in the left hip, loosening of the endoprosthesis was diagnosed. Left hip partial re-arthroplasty was performed with a femoral component (Intraplant, model KS, alloy: Ti6Al4V) (Figure 1, E, F). Suspicion of a metallic allergy, patch testing revealed allergy to nickel, gold, and steel. Two months later, because of periprosthetic fracture of the femur, operative revision of the left hip was performed. Since callus had formed and femoral stem stability was preserved, no endoprosthetic components were replaced.

In 2001, because of loosening of the prosthesis, partial re-athroplasty was performed with revision of the femoral component (modular femoral component of total endoprosthesis LIMA, model Revision, alloy: Ti6Al4V) (Figure 1, G, H).

The patient remained stable until 2010, when he presented with erythema and desquamation accompanied by itching in the bilateral inguinal regions that lasted for 11 years. Skin lesions partially regressed on topical corticosteroids.

Patch test to the European Standard Series was positive to nickel sulfate, fragrance, and hydroxycitronellal as a part of an additional series of allergens.

In 2013, instability of the acetabular part of the endoprosthesis of the left hip was diagnosed. The patient had experienced pain for the last three years; there was subluxation of the acetabula component. Therefore, the extraction of the acetabular part of the endoprosthesis of the left hip together with three screws was performed. Pathologic examination of the tissue below the polyethylene acetabular component and around the great trochanter revealed massive fibrosis and metalosis, without remarkable inflammatory findings. Furthermore, acetabular re-arthroplasty of the left hip (acetabulum: type Muller; ceramic head: LIMA, model Biolox forte; acetabulum consisted of polyethylene, cemented) was performed (Figure 1, I, J).

DISCUSSION

Skin rashes, localized or generalized eczemas, exacerbation of atopic dermatitis, severe eczema, pacemaker dermatitis, urticaria, vasculitis, persistent swelling, sterile osteomyelitis, aseptic implant loosening and failure, impaired wound and bone healing, or delayed healing of fractures and as well as general fatigue and pain can present as allergic reactions to metal implants (1,2,4,5,8,12,14-16,18-29). Therefore, these symptoms can necessitate the removal of the implant (1,2,4,5,8,12,14-16,18-29). Our patient experienced pain in the left hip accompanied with aseptic implant loosening, contact allergic dermatitis on both inguinal regions, and five operations of the left hip.

Possible components besides implanted metals associated with hypersensitivity are plastic that acts as artificial cartilage, or cement components (methyl methacrylate, an N,N-dimethyl-p-toluidine and a benzoyl peroxide activator), which can be also impregnated with antibiotics (gentamicin, neomycin, bacitracin) (4,11,13,29-31). Our patient had positive patch test to nickel sulfate, fragrance, and hydroxycitronellal. The degree to which a known condition of metal hypersensitivity may elicit an over-aggressive immune response remains unpredictable (18). Skin reactions to implanted devices are primarily delayed hypersensitivity reaction (14,18,32,33). Peri-implant reactions seem to be Th1-dominant with increased levels of interferon (IFN)-γ and interleukin (IL)-6 in metal-allergic patients with joint arthroplasties; minimal IFN-γ but a significantly elevated level of IL-17 in nickel-allergic patients with symptomatic joint implants but not in nickel-allergic patients with well-functioning joint implants (18,24,28,32,34-36).

Metal ions have also been found in capsular and periprosthetic tissues, in extracutaneous sites (liver, spleen, and lymph nodes) and in urine/serum of hip arthroplasty patients (5,24,34,35). In our patient, pathologic examination of the tissue below polyethylene acetabul and around the trochanter revealed massive fibrosis and metalosis without remarkable inflammatory findings.

Several studies have shown that titanium alloys may contain traces of nickel as a result of the production process. Under certain circumstances, these small amounts may be sufficient to trigger allergic reactions in patients suffering from the corresponding allergies, such as a nickel, palladium, or chrome allergy (5,12). Although, the "Nickel Directive", which applies to items that have a direct and prolonged contact with the skin, determines that a maximum of 0.5 μg nickel/cm^2/week can be released, limiting the nickel contents in piercing metals to 0.05%, such guidelines do not yet exist for implants or implant materials (5,10). Consequently, there have been numerous case reports reporting incompatibility reactions to titan materials in orthopedic implants or

pacemakers, such as skin contact allergies or aseptic prosthesis loosening (5,20,23-25,37-40). Additionally, hypersensitivity cutaneous reactions in these cases may be falsely attributed to the titanium itself. There is also a possible toxic, non-allergic, reaction to implanted metals with irritant contact dermatitis with negative patch test (37).

CONCLUSION

Patch testing is the gold standard for evaluation of type IV hypersensitivity reactions, which can be a cause of implant loosening in orthopedic and other patients with implants. Appropriate patch testing is indicated in patients with implanted metal devices and suspected metal hypersensitivity reactions. Although routine pre-implant patch testing is not yet routinely used, there is a subset of individuals with a prior history of reported cutaneous metal hypersensitivity who should be patch tested with implant components prior to device implantation. Positive patch test results or metal hypersensitivity should influence the decision of the referring surgeon in all pre-implantation cases. The management decision whether or not to remove implant requires decisions on a case-by-case basis.

Prospective trials are needed to closely examine the patients with metallic allergy and provide sufficient evidence for an evidence-based approach. Until then, the current knowledge in this field should be valuable to health care providers who manage the patients, and positive patch test results or metal hypersensitivity should influence the decision of the referring surgeon in pre-implantation cases.

References:

1. Buchet S, Blanc D, Humbert P, Girardin P, Vigan M, Anguenot T, *et al.* Pacemaker dermatitis. Contact Dermatitis. 1992;26:46-7.
2. Merle C, Vigan M, Devred D, Girardin P, Adessi B, Laurent R. Generalized eczema from vitallium osteosynthesis material. Contact Dermatitis. 1992;27:257-8.
3. Rostoker G, Robin J, Binet O, Blamoutier J, Paupe J, Lessana-Liebowitch M, *et al.* Dermatitis due to orthopaedic implants. A review of the literature and report of three cases. J Bone Joint Surg Am. 1987;69:1408-12.
4. Atanaskova Mesinkovska N, Tellez A, Molina L, Honari G, Sood A, Barsoum W, *et al.* The effect of patch testing on surgical practices and outcomes in orthopedic patients with metal implants. Arch Dermatol. 2012;148:687-93.
5. Harloff T, Hönle W, Holzwarth U, Bader R, Thomas P, Schuh A. Titanium allergy or not? "Impurity" of titanium implant materials. Health. 2010;2:306-10.
6. Foussereau J, Laugier P. Allergic eczemas from metallic foreign bodies. Trans St Johns Hosp Dermatol Soc. 1966;52:220-5.
7. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am. 2001;83-A:428-36.
8. Gawkrodger DJ. Metal sensitivities and orthopaedic implants revisited: The potential for metal allergy with the new metal-on-metal joint prostheses. Br J Dermatol. 2003;148:1089-93.
9. Kreibich DN, Moran CG, Delves HT, Owen TD, Pinder IM. Systemic release of cobalt and chromium after uncemented total hip replacement. J Bone Joint Surg Br. 2006;78:18-21.
10. Liden C, Norberg K. Nickel on the Swedish market. Follow-up after implementation of the Nickel Directive. Contact Dermatitis. 2005;52:29-35.
11. Granchi D, Cenni E, Tigani D, Trisolino G, Baldini N, Giunti A. Sensitivity to implant materials in patients with total knee arthroplasties. Biomaterials. 2008;29:1494-500.
12. Schuh A, Thomas P, Kachler W, Göske J, Wagner L, Holzwarth U, *et al.* Allergic potential of titanium implants. Orthopade. 2005;34:327-8, 330-3.
13. Schalock PC, Menné T, Johansen JD, Taylor JS, Maibach HI, Lidén C, *et al.* Hypersensitivity reactions to metallic implants - diagnostic algorithm and suggested patch test series for clinical use. Contact Dermatitis. 2012;66:4-19.
14. Adala R, Chakravarthy M, Srinivas V, Pai S. Orthopaedic surgery in a patient with metal sensitivity. J Cutan Aestet Surg. 2011;4:67-8.
15. Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systematic hypersensitivity reactions to metallic implants. Dermatitis. 2011;22:65-79.
16. Basketter DA, Briatico-Vangosa G, Kaestner W, Lally C, Bontinck WJ. Nickel, cobalt and chromium in consumer products: a role in allergic contact dermatitis? Contact Dermatitis. 1993;28:15-25.
17. Brown C, Fisher J, Ingham E. Biological effects of clinically relevant wear particles from metal-on-metal hip prostheses. Proc Inst Mech Eng H. 2006;220:355-69.
18. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am. 2001;83-A:428-36.
19. Tan M, Suzuki H. Usefulness of titanium implants

for systemic contact dermatitis due to orthopaedic prostheses. Contact Dermatitis. 1995;33:202.

20. Yamauchi R, Morita A, Tsuji T. Pacemaker dermatitis from titanium. Contact Dermatitis. 2000;42:52-3.
21. Pigatto PD, Guzzi G. Systemic contact dermatitis from nickel associated with orthodontic appliances. Contact Dermatitis. 2004;50:100-1.
22. Song H, Yin W, Ma Q. Allergic palmoplantar pustulosis caused by cobalt in cast dental crowns: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011;111:e8-10.
23. Bircher AJ, Stern, WB. Allergic contact dermatitis from "titanium" spectacle frames. Contact Dermatitis. 2001;45:244-5.
24. Thomas P. Impaired fracture healing and eczema from titanium based osteosynthesis with corresponding T-cell hyperresponsiveness in vitro: A case of titanium hypersensitivity? Contact Dermatitis. 2006;55:199-202.
25. Willert HG, Buchhorn GH, Fayyazi A, Flury R, Windler M, Koster G, *et al.* Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. J Bone Joint Surg Am. 2005;87:28-36.
26. Breton JL, Louis JM, Garnier G. Asthma caused by hard metals: Responsibility of titanium. Presse Medicale Journal. 1992;21:997.
27. Host L. A case of severe metal hypersensitivity post tibial plating. The Internet Journal of Orthopedic Surgery. 2008;11(2).
28. Christiansen K, Holmes K, Zilko PJ. Metal sensitivity causing loosened joint prostheses. Ann Rheum Dis. 1980;39:476-80.
29. Schuh A, Thomas P, Holzwarth U, Reinhold R, Zeiler G, Mahler V. Allergic reaction to components of bone cement after total knee arthroplasty. Zentralbl Chir. 2006;131:429-31.
30. Haddad FS, Cobb AG, Bentley G, Levell NJ, Dowd PM. Hypersensitivity in aseptic loosening of total hip replacements: the role of constituents of bone cement. J Bone Joint Surg Br. 1996;78:546-9.
31. Treudler R, Simon JC. Benzoyl peroxide: is it a relevant bone cement allergen in patients with orthopaedic implants? Contact Dermatitis. 2007;57:177-80.
32. Hallab NJ, Epstein R, McAllister K, Jacobs JJ. In vitro reactivity to implant metals demonstrates a person-dependent association with both T-cell and B-cell activation. J Biomed Mater Res A. 2010;92:667-82.
33. Chaturvedi TP. An overview of the corrosion aspect of dental implants (titanium and its alloys). Indian J Dent Res. 2009;20:91-8.
34. Baur W, Hönle W, Schuh A. Pathological findings in tissue surrounding revised metal/metal articulations. Der Orthopäde. 2005;34:225-33.
35. Doorn PF, Mirra JM, Campbell PA, Amstutz HC. Tissue reaction to metal on metal total hip prostheses. Clinical Orthopaedics. 1996;329:S187-205.
36. Hallab NJ, Anderson S, Stafford T, Glant T, Jacobs JJ. Lymphocyte responses in patients with total hip arthroplasty. J Orthop Res. 2005;23:384-91.
37. Suhonen R, Kanerva L. Allergic contact dermatitis caused by palladium on titanium spectacle frames. Contact Dermatitis. 2001;44:257-8.
38. Merritt K, Rodrigo JJ. Immune response to synthetic materials. Sensitization of patients receiving orthopaedic implants. Clin Orthop. 1996;326:71-9.
39. Yang J, Merritt K. Production of monoclonal antibodies to study corrosion of Co-Cr biomaterials. J Biomed Mater Res. 1996;31:71-80.
40. Basketter DA, Whittle E, Monk B. Possible allergy to complex titanium salt. Contact Dermatitis. 2000;42:310-1.
41. Walsh G, Mitchell JW. Free surface nickel in CE-marked and non-CE-marked spectacle frames. Ophthalmic and Physiological Optics. 2002;22:166-71.
42. Tamai K, Mitsumori M, Fujishiro S, Kokubo M, Ooya N, Nagat Y, *et al.* A case of allergic reaction to surgical metal clips inserted for post-operative boost irradiation in a patient undergoing breast-conserving therapy. Breast Cancer. 2001;8:90-2.