

Hypersensitivity Reactions in Total Hip Arthroplasty

Christoph H. Lohmann, MD; Jakob V. Nuechtern, MS; Hans-Georg Willert, MD†;
Sabine Junk-Jantsch, MD; Wolfgang Ruether, MD; Gerald Pflueger, MD



Christoph H. Lohmann

Hypersensitivity and allergic reactions to total hip arthroplasty (THA) are rare phenomena that were observed with the first generation of metal bearings^{1,2} and have reappeared with the second-generation of metal-on-metal joint replacements currently in use.^{3,4} Such reactions are considered to represent a local hypersensitivity reaction type IV and also are known as aseptic lymphocytic vasculitis-associated lesions.⁴

Although hypersensitivity or allergy reactions are uncommon, they are clinically

relevant. Potential allergens or haptens are components of metal alloys or bone-cement constituents such as benzyl peroxide.⁵

In Central Europe, the clinically relevant incidence of metal allergies in total joint replacement is estimated to be 1% to 2%, and for some alloy components such as cobalt and chromium, the incidence is estimated to be as high as 5%.⁶ For the treatment of hip disease with THA, preoperative evaluation of patients is imperative. Thus, the main treatment option is prevention.

For patients who have a known allergy, a dermatologic report is necessary and will guide the implant choice. Patients with suspected metal allergies or adverse skin reactions to metals should be referred to a dermatologic department for testing. However, currently there is no reliable cutaneous test to identify a deep-tissue metal allergy.⁷

In our experience, most of the allergies that are clinically

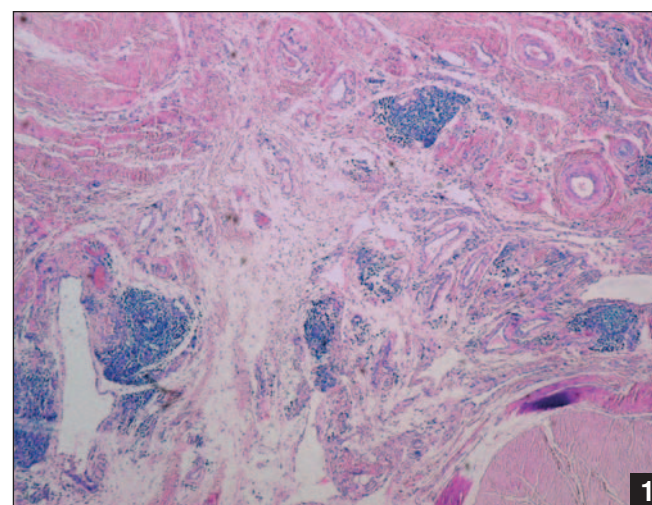


Figure 1: Photomicrograph of retrieval tissue showing diffuse follicular and perivascular lymphocyte infiltrations. No foreign-body reaction was observed (hematoxylin-eosin).

relevant are sensitivities to constituents of the metal alloys. In these cases, most patients are allergic to nickel or cobalt. In such patients undergoing THA, ceramic-ceramic or ceramic-polyethylene bearing surfaces can be used. If necessary, special titanium stems may be used for cemented fixation.

DOES A HYPERSENSITIVITY REACTION REALLY EXIST?

Since 1995, in >200 retrieval tissues from aseptic re-

vision arthroplasties that were sent to our groups, distinct changes in histomorphology were observed: The tissues of the capsules were characterized by lymphocytic infiltrations, fibrin exudation, eosinophilic granulocytes, and mast/plasma cells, but no foreign-body reactions with multinuclear cells or macrophages storing particles were observed (Figure 1).

In addition, the immunohistochemistry was positive for B and T lymphocytes, sig-

Drs Lohmann and Ruether are from the Department of Orthopedics, University of Hamburg-Eppendorf, Hamburg, and the Rheumaklinik Bad Bramstedt, Bad Bramstedt, Germany; Mr Nuechtern is from the Department of Orthopedics, University of Hamburg-Eppendorf, Hamburg, Germany; and Drs Junk-Jantsch and Pflueger are from Evangelisches Krankenhaus Wien, Vienna, Austria.

†Deceased.

Correspondence should be addressed to: Christoph H. Lohmann, MD, Dept of Orthopedics, University of Hamburg-Eppendorf, Martinistr 52, D-20246 Hamburg, Germany.

nifying an active proliferating reaction (data not shown). In some instances, lymphocytic infiltration was diffuse, with follicular structures being observed, and lymphocytes also appeared perivascularly. Furthermore, high-endothelial venules were seen. The metal allergy is associated with a type IV response, which is considered to induce an aseptic osteolysis.^{8,9}

Clinical symptoms are typical. Most patients exhibit symptoms early after their primary surgery, within 10 months to 5 years. They report thigh and groin pain, clicking noises, and recurrent instability.

Radiographic findings do not follow specific patterns. Osteolysis may be observed in the proximal femur (Figure 2) or around the acetabulum that does not represent the typical proximal femur atrophy occurring with certain cementless devices.

We also analyzed another series of patients with failed metal-on-metal THAs that were manufactured from low carbon hydride alloys.¹⁰ Histology, serum metal concentrations, and component wear as well as joint fluid were analyzed.

Component wear was similar to other metal-on-metal systems. Histology revealed diffuse as well as follicular lymphocytic infiltrations. In cases of metallosis, a macrophage-dominated reaction was observed.

Low and high tissue metal content seemed to induce a macrophage response in the capsules, whereas a medium

metal content of 200 µg/g tissue correlated with a lymphocytic response. Further, there was no correlation between serum metal contents and local tissue reactions.

The phenomenon of hypersensitivity to metal-on-metal THA is a peri-implant reaction. Currently, there is no method that allows preoperative prediction of implant failure due to hypersensitivity reaction. However, analysis of preoperative joint aspirates may hold some potential.

Fluids from hips of patients with osteoarthritis, ceramic-polyethylene failures, and metal-on-metal failures with and without lymphocytic reactions have shown expression of markers for osteoclast activation and differentiation as well as markers associated with hypersensitivity type IV. In patients with metal allergy, type IV allergy markers were highly expressed, and granulocyte macrophage-colony stimulating factor as well as interleukin-6 were selectively expressed in patients with lymphocytic infiltration.

IS METAL-ON-METAL TECHNOLOGY A DANGER?

Hypersensitivity reactions to metal in THA has a low incidence. There is no correlation between local allergy and skin hypersensitivity. Changing the articulating system rather than reusing a metal-on-metal articulation is recommended in revision of cases with a potential hypersensitivity reaction.

Hypersensitivity reaction may be prevented by careful preoperative evaluation of patients. In cases of metal allergies, various alternatives exist. Modularity on the acetabular side may make revision easier than in hypersensitivity cases in total knee arthroplasty. In cases with suspected allergy, osteolysis in the proximal femur or around the acetabulum may be diagnostic hints after ruling out infection or malpositioning of the implant. □

REFERENCES

1. Elves MW, Wilson JN, Scales JT, Kemp HB. Incidence of metal sensitivity in patients with total joint replacements. *Br Med J*. 1975; 4:376-378.
2. Evans EM, Freeman MAR, Miller AJ, Vernon-Roberts B. Metal sensitivity as a cause of bone necrosis and loosening of the prosthesis in total joint replacement. *J Bone Joint Surg Br*. 1974; 56:626-642.
3. Park YS, Moon YW, Lim SJ, Yang JM, Ahn G, Choi YL. Early osteolysis following second-generation metal-on-metal hip replacement. *J Bone Joint Surg Am*. 2005; 87:1515-1521.
4. Willert HG, Buchhorn GH, Fayyazi A, 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.
5. Granchi D, Cenni E, Trisolino G, Giunti A, Baldini N. Sensitivity to implant materials in patients undergoing total hip replacement. *J Biomed Mater Res B Appl Biomater*. 2006; 77:257-264.
6. Thomas P, Summer B, Sander CA, Przybilla B, Thomas M, Naumann T. Intolerance of osteosynthesis material: evidence of dichromate contact allergy with concomitant oligoclonal T-cell infiltrate and TH1-type cytokine expression in the periparticular tissue. *Allergy*. 2000; 55:969-972.
7. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. *J Bone Joint Surg Am*. 2001; 83:428-436.
8. Hallab NJ, Vermes C, Messina C, Roebuck KA, Glant TT, Jacobs JJ. Concentration- and composition-dependent effects of metal ions on human MG-63 osteoblasts. *J Biomed Mater Res*. 2002; 60:420-433.
9. Hallab NJ, Anderson S, Stafford T, Glant T, Jacobs JJ. Lymphocyte responses in patients with total hip arthroplasty. *J Orthop Res*. 2005; 23:384-391.
10. Lohmann CH. Can metal-metal total hip arthroplasty induce hypersensitivity reactions? In: D'Antonio JA, Dietrich M, eds. *Bioceramics and Alternative Bearings in Joint Arthroplasty: Proceedings*. Darmstadt, Germany: Steinkopff; 2005:33-37.



Figure 2: Postoperative radiograph 3 years after an uncemented total hip arthroplasty showing progressive osteolysis in the proximal femur.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.