

# Hypersensitivity to metallic implants: pathophysiologic and diagnostic considerations

Nicholas G. Kounis, Ioanna Koniari

Department of Cardiology University of Patras Medical School, Rion, Patras, Achaia, Greece

Metals are ubiquitous in the surrounding environment and constitute an important class of substances that can act as allergens. Consumer products such as earrings, zip, jewellery, cosmetics, paints, dental and body implants as well as endovascular, intracardiac and orthopedic devices are made from metals. Metal anions eluted from various metals are common allergic sensitizers. In Europe nickel, chromium and cobalt induce allergic skin reactions in about 20%, 4%, and 7% while in the United States 14%, 4%, and 9% respectively (1).

In the very interesting published in *Acta Biomedica* (2) the authors concluded that for total knee arthroplasty nowadays, the hypersensitivity to metals has to be considered as possible preoperative risk or a postoperative cause of failure and not as a "fiction". The patient's information and the medical history, associated, in suspect cases, with laboratory testings seems to be crucial. Furthermore, in today's commercial market several knee implants are available and safe for allergic patients.

Indeed, this review delineates important issues as far as metal allergy, its diagnosis and treatment:

1. All metals implanted in the human body either in orthopedics or cardiology and elsewhere undergo some kind of corrosion. Metal ions circulate with the blood stream and come in touch with the blood proteins and in total knee arthroplasty, in particular, may form complexes with native proteins intraarticularly acting as haptens. Haptens behave as antigens and can cause immunologic responses in the human body or in the synovial joint. The implant-related hypersen-

sitivity is generally a type IV allergic reaction, a delayed cell-mediated response, that activates specific T lymphocytes. The prevalence of metal sensitivity in patients with well-functioning implants, mostly of the hip, seems to be high (3) and it is estimated to be approximately 25%. In patients with a failed, loose, or poorly functioning implants, the average prevalence of metal sensitivity could be as high as 60% (range, 13% to 71%), but is not known whether this phenomenon is a cause or an effect (4). In a recent paper (5), concerning a patient with allergy to nickel sulphate and cobalt chloride and bone cement, zirconium and titanium alloys were used during re-operation for total knee arthroplasty. However, since these alloys are not anymore regarded as inert materials (6, 7), the patient was advised that should be followed up for any consequences for more than 3 years.

2. Detection of metal or drug allergens and corroboration of any immune response and the protein interaction can be achieved by ordering skin patch testing and measuring total IgEs. In acute systemic manifestations or relapse, serum histamine, serum tryptase and eosinophil count could be helpful. Furthermore, the followings could be of additional value for metal anion hypersensitivity where and when are appropriate:

- Lymphocyte proliferation assay that measures the ability of lymphocytes to undergo a clonal proliferation when stimulated in vitro by a foreign molecule, antigen or mitogen.
- Serum specific IgE measurements for the suspected metal anion

3. We must always remember that patients are frequently sensitized to multiple metal anions. This can occur to any practice using metallic implants either in cardiology or in orthopedics and elsewhere. Concurrent sensitization, cross-reactivity, or both seem to be possible. It has been shown that sensitization to one metal anion increases the possibility of being sensitized to additional metals. Metals seem to “join forces” to sensitize individuals (8).

Therefore, as Innocenti et al (2) have suggested, hypersensitivity to metals should be considered as a possible preoperative risk or a postoperative cause of failure of total knee arthroplasty and not as a “fiction” (2). Crucial is the information of patients and the medical history, associated in suspect cases to laboratory testing.

We suggest, therefore, that taking careful and detailed previous histories of diseases and adverse drug reactions as well as hypersensitivities and to apply specific laboratory testing in susceptible individuals is of paramount importance

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Correspondence:

Nicholas G. Kounis

Queen Olga Square, 7 Aratou Street,

Patras 26221, Greece

E-mail: ngkounis@otenet.gr