Cutaneous Metal Hypersensitivity Reaction

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Keywords
Metals · Implant · Implant hypersensitivity · Allergic contact dermatitis · Patch test

Abstract
A 53-year-old lady underwent a left total knee arthroplasty. She developed a dermatitis over the left knee on postoperative day 5, which worsened over the next 2 weeks and spread to the trunk despite regular topical corticosteroids and oral antihistamines. Physical examination revealed an erythematous plaque over the left knee and urticated plaques over the neck. She was given a course of oral and topical corticosteroids with resolution. Subsequent patch testing showed a showing ++ reactions to gold and nickel, and + reactions to copper, palladium, rhodium, titanium, vanadium, zinc, and hydroquinone. Orthopedic implants contain metal alloys, which may include nickel, cobalt. Hypersensitivity to implants allergy may arise from the metal alloy or bone cement. Metal hypersensitivity reactions (MHR) can manifest as a local or systemic contact dermatitis weeks to months following exposure. The role of MHR in contributing to prosthesis failure is conflicting. In patients with no history of metal allergy, pre-implant patch testing is not routinely recommended as a positive patch test does not consistently predict in vivo metal-induced complication. MHR may be managed conservatively with good outcomes. However, in patients with MHR and implant failure, or in a preoperative patient with a proven and clinically relevant hypersensitivity, replacement of the implant, or implant with a titanium or oxidized zirconium alloy should be considered.
Introduction

Hypersensitivity to orthopedic implants may arise from the metal alloy (e.g., nickel and cobalt) or bone cement (e.g., methyl methacrylate, N, N-dimethyl-p-toluidine, added antibiotics such as gentamicin). Metal implant hypersensitivity reactions (MHR) have been reported in approximately 0–5% of implanted devices [1] and may manifest as a local or systemic contact dermatitis weeks to months following exposure [1].

Case Report/Case Presentation

A 53-year-old lady underwent a left total knee arthroplasty. She subsequently developed a dermatitis over the left knee on postoperative day 5, which worsened over the next 2 weeks and spread to the trunk despite regular topical corticosteroids and oral antihistamines. She had stopped plaster dressings and did not use any other topicals from postoperative day 3. She also had a history of chronic urticaria. Physical examination revealed an erythematous plaque over the left knee (Fig. 1) and urticated plaques over the neck (Fig. 2). She was treated with a course of oral and topical corticosteroids with resolution of her dermatitis.

Patch test to the metal series, methyl methacrylate, and beprosone cream (which she had been using over the affected areas) was performed 8 weeks after the course of oral steroids. Patches were applied over the patient's upper back, removed at 48 h, and read by a dermatologist at 48 and 96 h following the International Contact Dermatitis Research Group reading scale. Patch testing results at 96 h showed ++ reactions to gold and nickel,

Fig. 1. Erythematous urticated plaques with vesiculation over the site of the knee replacement.
and + reactions to copper, palladium, rhodium, titanium, vanadium, zinc, and hydroquinone (Table 1).

The metal implant was confirmed to contain nickel, cobalt, chromium, molybdenum, aluminum, titanium, and vanadium. On further questioning, the patient gave a history of localized rashes triggered with certain earrings. Based on the clinical context and patch test results, she was diagnosed with contact dermatitis secondary to the metal implant with nickel, titanium, and vanadium being of current relevance. As she did not have further dermatitis after the course of oral corticosteroids and there was no clinical or radiological evidence of implant failure (last follow-up 10 months post-knee replacement), the implant was left in-situ.

**Discussion/Conclusion**

The role of MHR in contributing to prosthesis failure is conflicting. A systematic review showed that patients with a failed implant had more than double the odds of a metal allergy compared to a stable implant [2]. However, the presence of metal hypersensitivity could not predict likelihood of a failed implant and there was a high frequency of sensitization in patients with stable implants [2]. Additionally, a matched controlled study showed no difference in reoperation, revision or complication rates in preoperatively allergic and non-allergic patients [3]. It is thus suggested that secondary sensitization to components from an already failing implant may contribute to a higher rate of patch test positivity in patients with a failed implant, as opposed to MHR contributing to implant failure [1, 2].

While the American Society of Contact Dermatitis recommends consideration for pre-implant patch testing in patients with a clear self-reported history of metal allergy, this is more from a humanistic and medicolegal standpoint [4]. In patients with no history of metal allergy, pre-implant patch testing is not routinely recommended as a positive patch test does not consistently predict in vivo metal-induced complications [4].

The presence of a MHR in a symptomatic patient is not an indication for removal of the implant. As in this patient, MHR may be managed conservatively with good outcomes. However, in patients with MHR and implant failure, removal or replacement of the implant should be considered [4].

![Fig. 2. Urticated plaques over the neck.](image-url)
Table 1. Results of patch testing, showing ++ reactions to gold and nickel

| Substance                          | Concentration, vehicle, % | 48 h | 96 h |
|------------------------------------|---------------------------|------|------|
| Aluminum (III) chloride hexahydrate| 2.0, pet                   | –    | –    |
| Calcium titanate                   | 10.0, pet                  | –    | –    |
| Cobalt (II) chloride               | 1, pet                     | –    | –    |
| Copper (II) sulfate pentahydrate   | 2.0, pet                   | +    | +    |
| Copper (I) oxide                   | 5.0, pet                   | –    | –    |
| Ferric chloride                    | 2.0, pet                   | –    | –    |
| Gold (I) sodium thiosulfate dihydrate| 0.5, pet                 | +    | +    |
| Gold (I) sodium thiosulfate dihydrate| 2, pet                    | ++   | ++   |
| Iridium                            | 1.0, pet                   | –    | –    |
| Iridium (III) chloride trihydrate  | 1.0, pet                   | –    | –    |
| Manganese chloride                 | 2.0, pet                   | –    | –    |
| Mercury                            | 0.5, pet                   | –    | –    |
| Mercury (II) chloride              | 0.1, pet                   | –    | –    |
| Molybdenum                         | 5.0, pet                   | –    | –    |
| Nickel sulfate                     | 2.5, pet                   | ++   | ++   |
| Palladium (II) chloride            | 2.0, pet                   | –    | +    |
| Rhodium (III) chloride hydrate     | 2.0, pet                   | +    | +    |
| Silver nitrate                     | 1.0, aq                    | –    | –    |
| Tin                                | 50.0, pet                  | –    | –    |
| Titanium                           | 10.0, pet                  | –    | –    |
| Titanium (III) nitride             | 5.0, pet                   | –    | –    |
| Titanium dioxide                   | 10.0, pet                  | –    | –    |
| Titanium (III) oxalate decahydrate| 5.0, pet                   | –    | +    |
| Tungsten                           | 5.0, pet                   | –    | –    |
| Vanadium                           | 5.0, pet                   | –    | +    |
| Zinc                               | 2.5, pet                   | –    | –    |
| Zinc chloride                      | 1.0, pet                   | –    | +    |
| Zirconium (IV) chloride            | 1.0, pet                   | –    | –    |
| Hydroquinone                       | 1.0, pet                   | +    | +    |
| 4-Tert-butylphenol-formaldehyde resin| 1.0, pet                 | +    | –    |
| Methyl methacrylate                | 2.0, pet                   | +    | –    |
| Benzoylperoxide                     | 1.0, pet                   | –    | –    |
| Betamethasone dipropionate cream (patient’s own) | – | – |

++ Reactions highlighted in grey.

Pet, petrolatum; Aq, water.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. Ethics approval was not required for this study in accordance with our local IRB guidelines.
Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding was provided for this case report.

Author Contributions

Dr. Ellie Choi and Dr. Yau Hong Ng contributed to the conception of the report. Dr. Sun Yang and Dr. Ellie Choi wrote the first draft. Dr. Yau Hong Ng vetted the final manuscript. All authors approved of the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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