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Hypersensitivity to orthopaedic implant manifested as erythroderma: Timing of implant removal☆

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ABSTRACT

INTRODUCTION: Incidence of hypersensitivity to orthopaedic implant, once estimated in less than 1% of population, recently has increased to 10%. Controversies about the timing of implant removal remain, especially due to the fact that implant hypersensitivity may be a contributing factor to implant failure. We present a case report and literature reviews to establish the decision making for the timing of implant removal in the presence of implant hypersensitivity.

PRESENTATION OF CASE: Female, 42 years old with nonunion of mid-shaft tibia and fibula which was treated with ORIF with conventional SAE16 stainless steel plate and bone graft. A week after, she developed a generalized rash, which is later diagnosed as erythroderma, that relapsed despite adequate systemic corticosteroid. Poor healing of surgical site wound were marked. After the implant removal, the cutaneous condition improved and no relapse were found.

DISCUSSION: Management of hypersensitivity to implants involved corticosteroid administration, removal or replacement of implants, or implants coating with polytetrafluoroethylene. Currently there are no specific guidelines regulating the management of implant allergy based on the timing of the onset, especially in fracture cases. The decision-making would be straightforward if union was already achieved. Otherwise, controversies would still occur. In this paper, we proposed an algorithm regarding the steps in managing metal allergy due to implant in fracture cases.

CONCLUSION: Despite the concerns regarding implant survival in hypersensitivity cases, the decision whether the implant should be removed or replaced should be based on the time and condition of the fracture healing process.

1. Introduction

The incidence of hypersensitivity to orthopaedic implant is relatively high in general population. Once, the incidence was estimated to be less than 1% of population, but now it has reached around 10–17% of general population [1–4]. The main concern of implant hypersensitivity were whether it might affect implant survival [2,3]. As it still remains a controversial issue, many researchers have concluded that implant hypersensitivity may be a contributing factor to implant failure due to shorter lifespan of implants in patients with positive patch reaction to metal [5,6]. We presented a case of implant hypersensitivity which was treated by watchful observation with low dose corticosteroid to control the skin lesions. This paper has been reported in line with the SCARE criteria [7].

2. Case presentation

Forty-two years old female came to our outpatient clinic with 9-month-neglected fracture of her right shaft tibia and fibula. She had a motor vehicle accident previously and had a closed fracture of her tibia and fibula. Then she was treated by a bonesetter for 9 months with no significant result. There were no comorbidities and she was mobile (using a crutch). On initial examination, there was no skin defect or signs of infection at the fracture site. Radiograph showed well-demarcated oblique fracture line at the middle shaft of her tibia and fibula, suggesting a nonunion. After that, a decision was made to treat the tibia with open reduction and internal fixation using a conventional narrow plate and standard anterior

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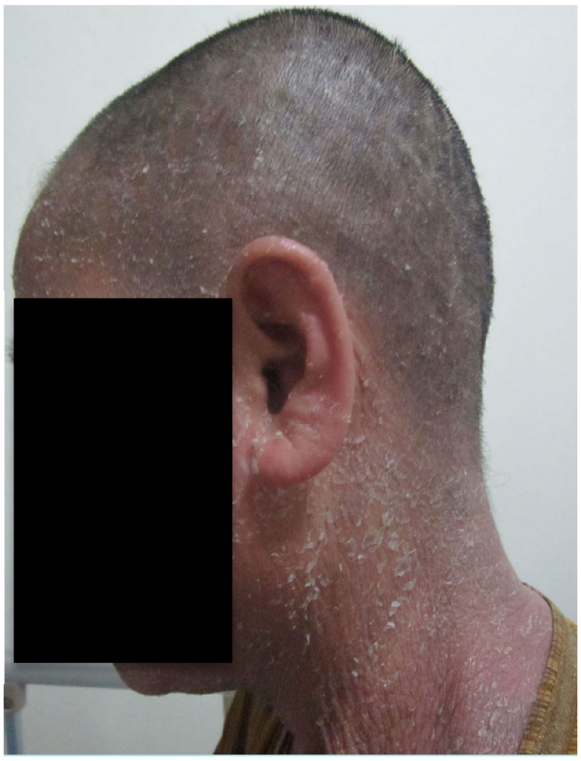

Fig. 1. Generalized scaly erythema on head and neck one week after surgery.

tibia approach. Removal of the intervening fibrosis and preparation of non-union fracture site was performed in surgery, as well as autologous bone grafting harvested from the iliac crest.

A week after surgery, extensive skin lesions developed on her scalp, trunk, upper and lower extremities especially around the surgical wound. Skin examination showed generalized scaly erythema (exfoliative dermatitis with diffuse skin involvement and ill-defined margin) as showed on Fig. 1. The patient was consulted to the dermatologist and was diagnosed as psoriatic erythroderma. By that time, the information about her history of metal allergy (ear pierces) was obtained. Systemic corticosteroid (methylprednisolone 2 mg/day) was administered to treat the lesions and the patient responded well to the treatment after several days. The surgical wound healed well and the suture was removed 14 days after surgery.

But a week after the suture removal, the erythroderma relapsed and wound dehiscence occurred along the previous surgical incision (Fig. 2). There was no sign of infection such as pus at the surgical wound. The white blood count was still within normal limit despite some elevation in ESR and CRP. After discussion the dermatologist, we decided to observe the fracture healing or implant loosening by serial plain radiograph examinations, (AP and lateral view of the cruris every 4 weeks) while treating the skin lesions with topical (triamcinolone cream 0.025%) and low dose systemic steroid (methylprednisolone) to control the skin eruption. The steroid administration was intermittent, as a dosage of 2 mg/day was given during the relapse and was tapered off to 0,5 mg/day (maintenance dose) in a week after the resolution of skin lesions. Oral calcium and calcitriol supplements were also given throughout the course of treatment. The wound was treated using moist dressings until re-epithelization was achieved. During the observation period, the risk for secondary complications such as infection, fluid-electrolyte imbalance, and thermoregulatory disturbance, were carefully monitored.

Eight weeks after the surgery, as the callus were visible from radiological examination, a decision was made to preserve the plate

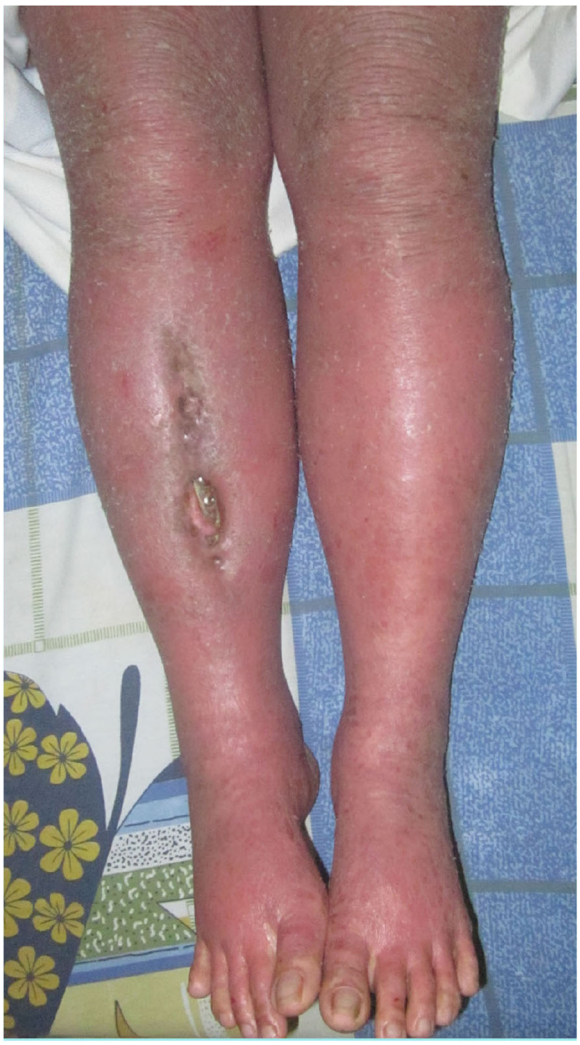

Fig. 2. Generalized erythema on both legs with surgical wound breakdown of the right tibia.

fixation until more calluses were produced and clinical union was achieved. During seven months of postoperative follow-up, the patient had five relapses (including the two previously-mentioned incident), which resolved in several days (7–10 days) after the low dose steroid treatment.

Seven months after surgery, the plate was removed and a week later, the skin condition improved (Fig. 3). At the last follow up (one year after implant removal), no further relapse occurred, complete union was achieved and the patient had completely returned to her daily activities.

3. Discussion

Hypersensitivity due to orthopaedic implants usually manifested as poor wound healing, local reaction and rarely systemic dermatitis reaction [3,4]. Our case matched 6 of 9 criteria to diagnose hypersensitivity due to metal (chronic dermatitis beginning weeks to months after metallic implantation, eruption overlying implant, morphology consistent with dermatitis, systemic allergic dermatitis reaction in rare instances, dermatitis resistant to therapy and complete recovery after removal of the offending implants) [8]. Women are more susceptible to metal hypersensitivity. Verma et al. reported that in 28 cases of metal hypersensitivity after TKA, 23 of

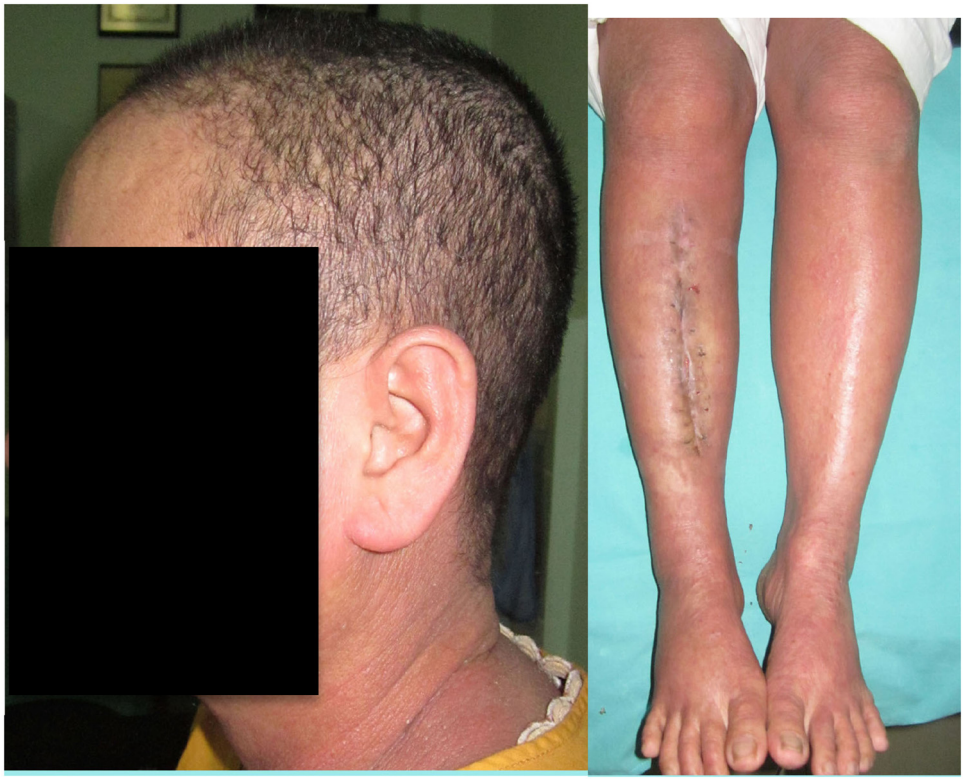

Fig. 3. Improvement of the skin lesions one week after implant removal.

patients were female [3,4]. Even in recent years; the female-male proportion of metal hypersensitivity is reaching 10:1 [1].

The implant used in our patient was made of standard SAE 316 stainless steel. Stainless steel contains iron in a balance percentage, nickel (8.3–35%), chromium (20%), manganese (2%), molybdenum (2–3%), nitrogen (0.1%), carbon (0.03%), sulfur (0.03%), silicon (0.75%) and phosphorus (0.045%). With contact to body fluids, nickel was reported to be released in the greatest amount from aforementioned metals [8]. Nickel was the most common sensitizer in humans with prevalence of nickel hypersensitivity between 8 and 25% [9–11]. Only 1–2% of the population was allergic to cobalt, chromium or both [1].

Titanium alloy implants generated less metal hypersensitivity problem compared to stainless steel or cobalt alloy implants, but there were some reports indicating the association of metal sensitivity with titanium implants. In a case series of five-revision total hip replacement after a failed titanium implant, negative results were found in all patients after skin patch testing with diluted titanium salts solution. However, two gave a positive result to titanium-containing ointment [12]. Intraoperative finding showed the evidence of metallosis in the joint capsule of all five patients and after analyzing the tissue, the presence of macrophages, few T-lymphocytes and the absence of B-lymphocytes were well corresponded to delayed type hypersensitivity reaction.

In recent year, the prevalence of implant hypersensitivity is 25% in patients with functioning prosthesis but it is 60% in patients with implant failure [5]. Although it still remains a disputable issue, many researchers have concluded that implant hypersensitivity may be a contributing factor to implant failure. Shorter implants lifespan was observed in patients with positive patch reaction to metal [6]. Despite these facts, it was still unclear if there were causal relationship between these two factors in symptomatic patients. It was suggested that some combination phenomenon occurred whereby implant-loosening promoted immunogenic reaction which would potentiate the loosening process [5]. Cadosh et al. performed a bio-corrosion model of stainless steel by osteoclast and showed that osteoclast precursors were able to grow and differentiate to mature osteoclast on the surface of stainless steel [13]. These mature osteoclasts then could erode the surface material and released metal debris into the surrounding tissue or circulation, which may bind with endogenous protein thus initiate an immune reaction.

Management of symptomatic hypersensitivity to metal implants involved admission of corticosteroid, removal of implants, replacement of implants, or coating of implants with polytetrafluoroethylene [14–17]. The timing of the removal is debatable, as most surgeons will recommend immediate removal in symptomatic metal hypersensitivity. While removing of the cause of allergy is the mainstay of all hypersensitivity treatment, direct implant removal and revision may jeopardize the bone healing process especially nonunion cases that were treated with autologous bone graft. Corresponding to the pathophysiology of implant corrosion and the nature of the delayed type of hypersensitivity, onset of symptoms may be varied, ranged from 3 days until 1 year after metal implantation [15–17]. According to our knowledge, currently there is no guideline regulating the management of implant allergy based on the timing of the onset, especially in fracture cases. The decision-making would be straightforward if union was already achieved by the time of the onset, but if otherwise, controversies would still occur. Michelson et al. has proposed an algorithm in management of implant hypersensitivity based on the patch test for total knee replacement. In cases that has positive patch test after TKR, it is recommended that implant revision should be performed with the best implant (hypoallergenic) available to the patient [18,19]. Unfortunately, in our case, the titanium implants were not available at that time, thus watchful waiting was chosen to observe whether the healing process or implant loosening would occur first. After which, a definite decision would follow. We proposed an algorithm regarding the steps in managing metal allergy due to implant in fracture cases in Fig. 4.

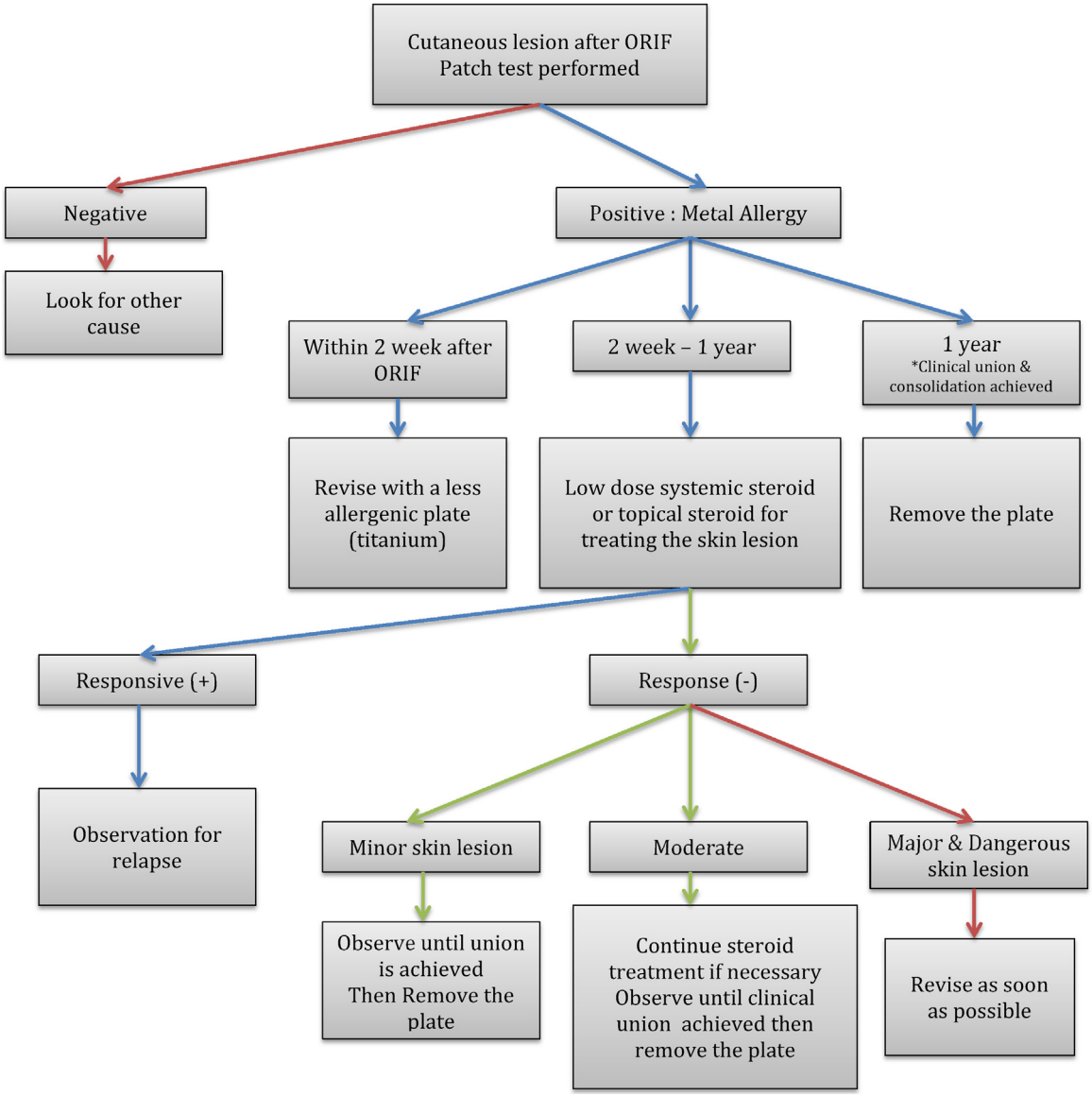

Fig. 4. Proposed algorithm of Implant Removal/Revision in cutaneous Implant allergy.

Cutaneous allergic reaction is one of the rare manifestations of metal allergy to orthopaedic implants. In a two-year-prospective study of cutaneous problem in implant recipients, orthopedic-implant-associated skin eruption occurred in 19 patients. There were two clinical patterns observed; transient "exanthematic" dermatitis and persistent reaction dermatitis. Even though the causal relationship was unclear, the likelihood of the cutaneous lesion being allergic in nature is slightly greater if: (1) the implant was static; (2) there was a history of metal hypersensitivity; (3) cutaneous eruption showed a predilection for the anatomic zone of the implant; (4) the eruption is eczematous, developed late and persisted [21]. According to the extent of skin lesions, eruption associated with orthopaedic implant can take two forms: localized and generalized. There were no correlations between the types of implant (static or joint prostheses) with the extent of eruption [22]. The cutaneous lesion in our case, which was generalized and transient dermatitis, fulfill all aforementioned criteria of implant-associated-allergic skin lesions.

The gold standard test for diagnosing orthopaedic implant hypersensitivity is still open to debate. Both in-vivo patch test and in vitro lymphocyte transformation test (LTT) have a quite similar sensitivity and specificity, but each has its own advantages and limitations. Patch test was less expensive and didn't need special laboratory services thus it is more suitable for preoperative screening. Moreover, patch test may be less suitable for titanium allergy, since either titanium metal or salts are not soluble and therefore cannot penetrate the skin. Muller reported that in LTT test, more than half yielded positive result in response to titanium dioxide, despite negative results on patch test [22]. Frigerio et al., recommended the usage of both methods for screening metal allergy prior to arthroplasty intervention to allow the surgeon to select which implant is best to the patient [24].

The use of corticosteroid during bone healing is controversial. The in vitro effect of corticosteroid on bone healing is well documented as it may lead to osteoblast and osteocyte apoptosis and also decreases the production of osteoblast resulting the inhibitory effect of bone healing [25,26]. However, animal studies had failed to show consistent result. Several studies even failed to prove inhibitory effect on bone healing [27]. One of the possible explanation was that cortisone may have a dose related effect on the bone [28]. It might also be related to the findings of Duthrie and Baker that only endochondral ossification affected by the inhibitory effect

of steroid [29]. Regarding the duration of the steroid use, almost all papers stated that even in the short term use (<30 days) of normal-dosed-steroids, the bone-related risk increases significantly [30]. However, to our knowledge, there are limited evidence about the use of short-term low-dose steroid in the conjunction with the bone-related-complications. In our proposed algorithm, we suggest the use of low dose steroid administration within intermittent duration based on the relapsing symptoms of the cutaneous lesion.

4. Conclusion

Hypersensitivity to orthopaedic implants may manifest as not only mild local but also severe generalized dermatitis and life threatening condition. Despite the concerns regarding implant survival in hypersensitivity cases, the decision whether the implant should be removed or replaced should be based on the time and condition of the fracture healing process.

Conflict of interest

There is no conflicts of interest.

Funding

There is no funding that paper.

Ethical approval

This study is exempt from ethical approval in our institution.

Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Author contribution

Conceptualization: PP YPD IS. **Data curation**: PP YPD IS DRB. **Formal analysis**: PP YPD IS DRB MW JS **Writing – original draft**: PP YPD IS. **Writing – review & editing**: PP YPD IS DRB MW JS. This manuscript has been read and approved by all authors and represents a honest work.

Registration of Research Studies

None, because it is not a human trial, but a case report about the outcome of hypersensitivity after implant placement.

Guarantor

Yoshi Pratama Djaja and Phedy Phedy.

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