

Severe Metal Hypersensitivity Following Internal Fixation of an Ankle Fracture

A Case Report

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Abstract

Case: A 67-year-old woman underwent internal fixation of an ankle fracture. Ten days postoperatively, the patient developed systemic hives, difficulty breathing, and oral swelling. At 8 weeks postoperatively, the hardware was removed because of a suspected metal hypersensitivity. Despite experiencing perioral edema and difficulty breathing after the hardware removal, she had complete resolution of the symptoms at the 2-week, 6-week, and 12-month follow-up appointments.

Conclusion: Hypersensitivities to metal-based implants can develop and cause local and systemic reactions. Orthopaedic surgeons should inquire about a history of metal allergies, and possibly perform allergy testing for patients with a history suggestive of metal hypersensitivities. Consideration should be given for hospital admission following hardware removal for patient monitoring.

Ankle fractures are one of the most common traumatic injuries seen by orthopaedic surgeons^{1,2}. When open reduction and internal fixation (ORIF) is indicated, metal implants are most commonly used³. The development of corrosion-resistant biocompatible metal alloys makes it possible for internal fixation to be used successfully.

Reactions to metal implants have been documented in the literature; cutaneous hypersensitivity reactions to implanted metals have been reported to occur in 1% to 5% of orthopaedic cases⁴. Nickel is the most common metal sensitizer in humans, followed by cobalt and chromium^{4,5}. The incidence of sensitivity reactions to implants is not dependent on their composition, but on the release rates of chemically active metal ions under normal use⁶. These cellular interactions may lead to an unregulated immune response that results in a clinical picture similar to a hypersensitivity reaction.

We describe a rare case of a systemic type-IV delayed hypersensitivity reaction secondary to a stainless steel plate that was used for internal fixation of an ankle fracture.

The patient was informed that data concerning the case would be submitted for publication, and she provided consent.

Case Report

A 67-year-old woman, who presented with no known allergies and no recollection of previous allergic reactions,

underwent an ORIF of an ankle fracture using a distal fibular locking compression plate, which was composed of chromium, nickel, and manganese stainless steel (18Cr-14Ni-2Mn, ASTM F138), and stainless steel syndesmosis screws (DePuy Synthes, a Johnson & Johnson company).

Ten days postoperatively, hives developed on the patient's torso, bilateral upper and lower extremities (Fig. 1), lips, and mouth. She also noted perioral swelling and difficulty breathing. The rash was initially attributed to the Lovenox (enoxaparin) injections and/or antibiotics that had been administered, and she was given a 10-day course of prednisone, diphenhydramine, and triamcinolone cream. The symptoms persisted despite the discontinuation of the Lovenox and the use of steroids, antihistamines, and cream. At the 6-week follow-up appointment, the patient recalled a previous history of a severe allergy to nickel earrings, which had been diagnosed more than 30 years ago. She was referred to an allergy immunologist who agreed that the current symptoms were consistent with a hypersensitivity to nickel.

Hardware removal was performed 8 weeks after the initial internal fixation. There were no complications during the surgery. However, the patient developed acute, severe facial and lip edema and had difficulty breathing in the post-anesthesia care unit (Fig. 2). She was admitted to the hospital for monitoring, and subsequently developed hives and pruritic lesions overnight.

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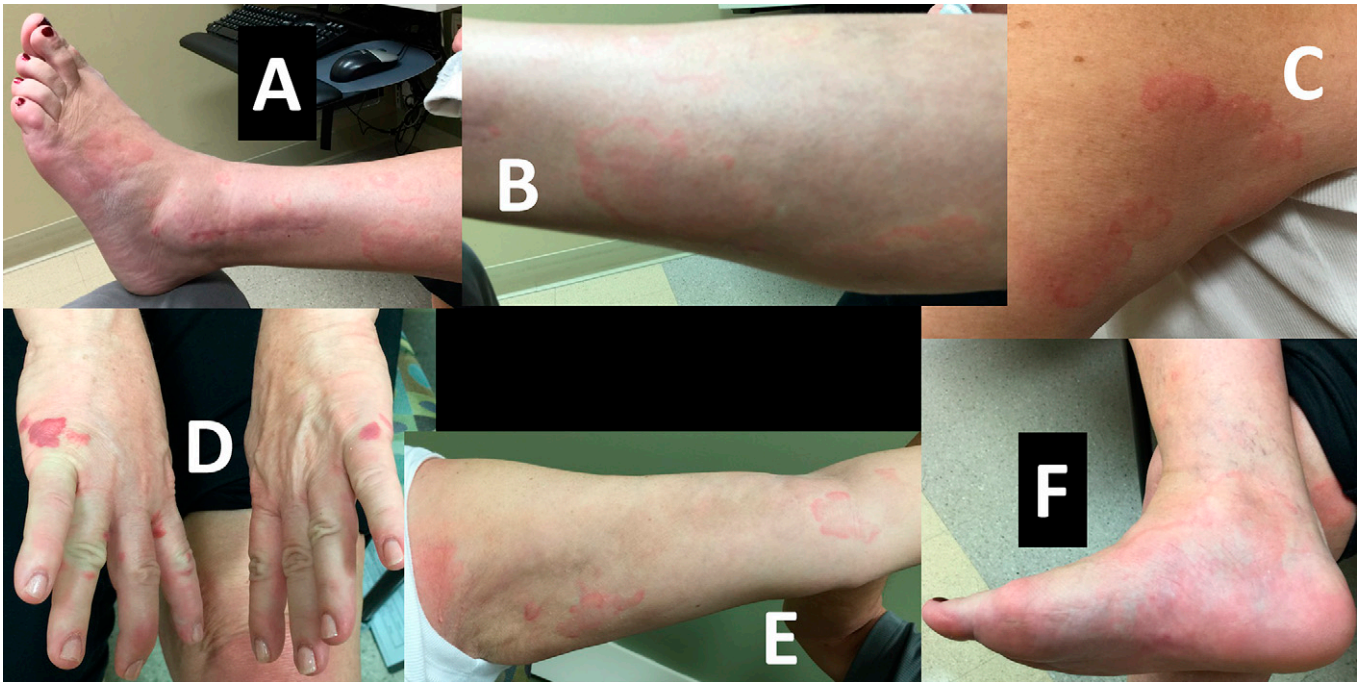


Fig. 1

Figs. 1-A through 1-F Systemic skin lesions, prior to hardware removal, on the left leg at the surgical site (**Fig. 1-A**), on the lateral aspect of the left leg (**Fig. 1-B**), on the posterior aspect of the left shoulder (**Fig. 1-C**), on both hands (**Fig. 1-D**), in the axilla and on the posterior aspect of the right arm (**Fig. 1-E**), and on the medial aspect of the right foot and ankle (**Fig. 1-F**).

The patient received diphenhydramine and methylprednisolone throughout the evening, and the following morning, the symptoms had almost completely resolved, with the exception of some general pruritus. At the 2 and 6-week follow-up appointments after hardware removal, there was full remission of the systemic symptoms (Fig. 3). The patient's latest follow-up was 12 months after hardware removal, and she reported no recurring symptoms throughout the postoperative period and did not display signs of an ongoing hypersensitivity reaction.

Discussion

Implant-related metal hypersensitivity reactions are unpredictable and remain poorly understood⁴. Although cutaneous hypersensitivity reactions to implanted metals are reported in 1% to 5% of orthopaedic cases, the prevalence is most certainly higher since cases involving implant-related metal sensitivity are likely underreported because of difficulty of diagnosis⁴. One study that used an in vitro blood-cell migration test to determine immune sensitivity found that 20% to 25% of patients without prior exposure to implant materials developed implant-induced metal sensitivity without any allergic skin manifestations⁶. Furthermore, the prevalence of metal hypersensitivities is not static because it is influenced by changes and developments in the surrounding environments and society⁷. For example, it is reported that the incidence of nickel contact allergy and dermatitis is decreasing in European countries because of regulations that limit the amount of nickel in trade products⁸. Despite changes in policy, studies

have shown that the proportion of nickel contact allergy to overall contact allergy has increased over the past 50 years⁷. This is primarily explained by the increased exposure with clothing buttons and zippers, as well as the use of imitation jewelry⁷. Because the likelihood of allergic reaction increases with exposure, one can conclude that the general population is at greater risk for allergic reactions to orthopaedic implants



Fig. 2

Following hardware removal, the patient developed facial and lip edema and had difficulty breathing in the post-anesthesia care unit, requiring hospital admission for monitoring and steroid treatment.

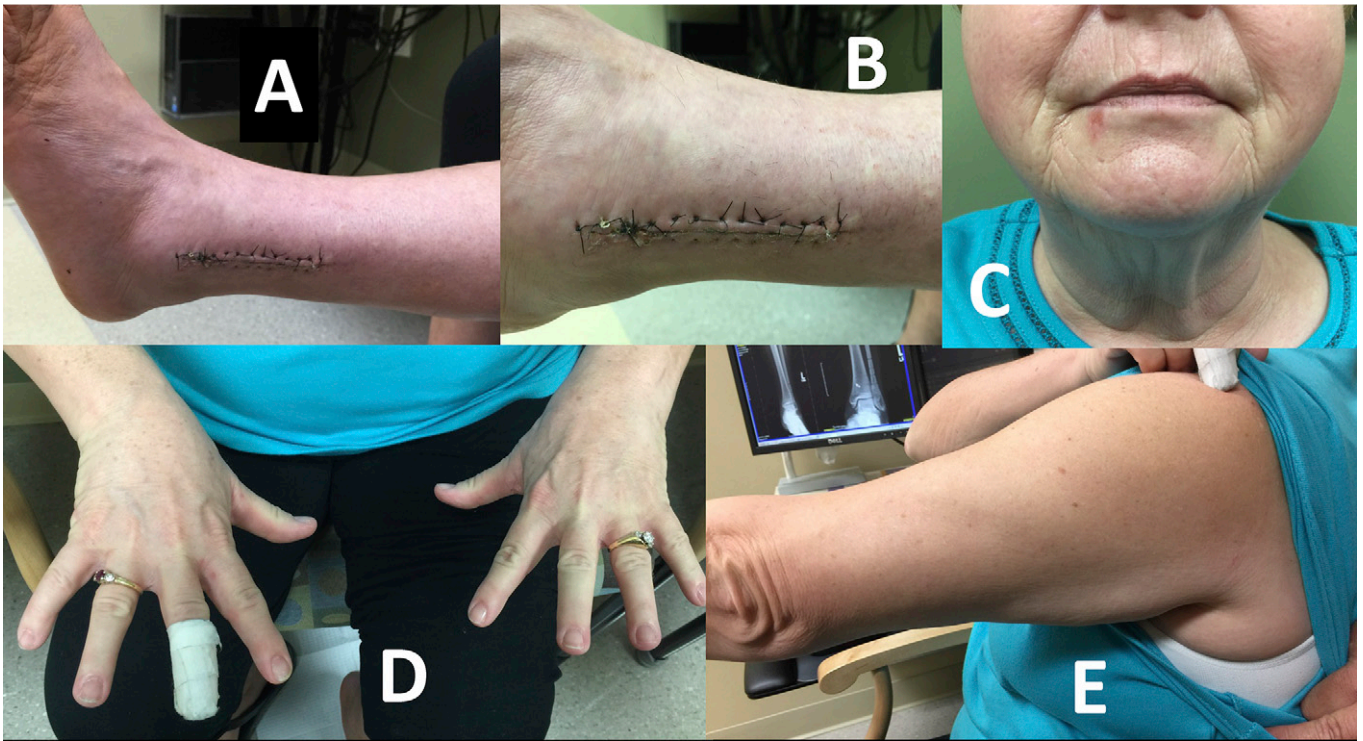


Fig. 3

Figs. 3-A through 3-E At the 2-week follow-up after hardware removal, the patient had full remission of the systemic symptoms on the left leg at the surgical site (**Figs. 3-A and 3-B**), resolved perioral edema (**Fig. 3-C**), remission of the lesions on both hands (**Fig. 3-D**), and remission of the lesions in the axilla and on the posterior aspect of the left shoulder (**Fig. 3-E**).

with nickel because of an increase in nickel exposure over recent decades.

Metal implant-related hypersensitivity reactions are generally type-IV delayed hypersensitivity reactions, with Ni^{2+} -induced allergic dermatitis being the most common⁴. Degradation of metal-alloy implants may decrease the structural integrity of the implant and release chemically active metal ions into the tissue⁹. Nickel sensitivity is acquired through intimate and prolonged skin exposure to nickel metal or nickel salts¹⁰. This interaction describes the sensitization phase, when the antigen is processed, displayed on the surface of dendritic cells, and taken to regional lymph nodes to interact with T lymphocytes^{9,11,12}. The result is cytokine-induced T-cell proliferation bearing receptors specific to that antigen¹². The sensitization phase is followed by the elicitation phase, which occurs with re-exposure to the antigen, and leads to cytokine-induced activation of T lymphocytes and the release of inflammatory mediators¹². The result is Ni-induced contact dermatitis, which leads to swollen, reddened, and itchy skin. Periarticular dermatological eruption and chronic dermatitis beginning weeks to months after implantation are associated more often with metal hypersensitivity reactions¹³. In most cases, the resulting rash occurs only at the site of contact, although it may be found on other parts of the body as well¹⁰. This may provide a possible explanation for the acute exacerbation in our patient following hardware removal. The reintroduction of nickel during hardware removal may have triggered an acute release of

inflammatory mediators that were recognized by previously sensitized T cells, leading to bronchospasms and difficulty with breathing.

Superficial allergic reactions are the most common reactions associated with metal implants, and the degree that metal sensitivity contributes to implant failure remains highly controversial^{4,14}. Specifically, degradation products of an implant can cause increased metal hypersensitivity, but it remains unclear as to whether these products contribute to implant failure⁴. Thyssen and Menné determined that the risk of surgical revision was not increased in patients with metal allergies, and the risk of metal allergy was not increased in patients who were operated on when compared with control groups¹⁵.

In our patient, the implant did not fail, and removal of the device resulted in complete and rapid symptom resolution following an immediate exacerbation of the symptoms. Prevention of patient discomfort and additional surgery resulting from these reactions would be ideal, but a reliable screening tool for metal sensitivity has yet to be developed. Obtaining an accurate patient history may be most important in primary prevention. When performing a preoperative assessment, the orthopaedic surgeon should specifically inquire about metal allergies. Consideration should be given to asking specific information about reactions to jewelry and/or watches as patients may be unaware of their own metal allergy. Patch testing is considered the gold standard for diagnosing contact allergy, but its validity in detecting systemic hypersensitivity reactions has

been questioned⁵. Although routine preoperative implant screening is not recommended, some individuals with a history of reported metal sensitivity should be patch-tested prior to implantation¹⁶. In the event that metal sensitivity is detected, alternative implants should be considered.

There are several important questions to ask. How can these hypersensitivity reactions affect patient outcomes and, if outcomes are poor, how can they be prevented? Our patient experienced severe cutaneous manifestations and respiratory difficulties prior to hardware removal. Moreover, immediately following hardware removal, there was an increased reaction, which manifested as facial edema, perioral edema, and difficulty breathing. This required hospital admission, steroid treatment, and monitoring. The integrity of the implant was not compromised, and the fracture healed uneventfully.

When orthopaedic hardware is implanted, undiagnosed metal allergies may result in increased perioperative morbidity and cost. Orthopaedic surgeons need to be mindful of the importance of screening for metal allergies preoperatively with a thorough history. Routine patch testing remains controversial, but may be required in the event of a patient history suggestive of

metal allergies. Hardware removal results in symptom resolution but, as seen with our patient, symptom exacerbation may result immediately following the removal. Surgeons should strongly consider careful postoperative monitoring after hardware removal in patients with metal hypersensitivity. Prospective studies and additional research are needed to provide reliable screening methods and cost-effective treatments, and to determine the role of hypersensitivity reactions in implant failure. ■

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