

Case report

EXTENSIVE DERMATITIS DUE TO HYPERSENSITIVITY TO ORTHOPEDIC SYNTHETIC MATERIALS: CASE REPORT

ABSTRACT

Aims: The present case report aims to describe a rare case of hypersensitivity to orthopedic synthetic materials, an adverse event that developed following surgical intervention for the correction of an open fracture of the radius and proximal ulna.

Presentation of Case: A 63-year-old woman sustained an open fracture of the right olecranon, requiring multiple surgeries, including external fixation and osteosynthesis. Postoperative complications included recurrent infections, cellulitis, acute renal failure, and persistent chronic dermatitis. A Patch Test identified allergies to cobalt chloride, nickel sulfate, and formaldehyde resin, potentially linked to the orthopedic implant. Imaging revealed severe bone rarefaction, non-union of the ulna, and pseudoarthrosis. Despite ongoing treatment and hardware removal, the patient's fracture remained unresolved, with persistent dermatitis and a low-output fistula five months post-injury.

Discussion: Hypersensitivity reactions to metal orthopedic implants, though rare, can cause cutaneous and extracutaneous symptoms, including eczema, urticaria, and implant complications. Diagnosis relies on patch testing, LMIT, and LTT. Treatment includes allergen removal, local therapy for mild cases, or systemic corticosteroids for severe symptoms.

Conclusion: Stainless-steel prostheses are widely used in osteosynthesis to enhance fracture healing and mobility, but their use is associated with hypersensitivity reactions to metals like nickel, cobalt, and chromium. Despite protective coatings, biomechanical stress can release metal ions, triggering immune responses and adverse clinical outcomes. This case highlights hypersensitivity as a potential complication of prosthesis implantation, emphasizing the need for better diagnostic strategies, preventive measures, and further research, particularly given the higher prevalence of nickel hypersensitivity in female patients.

Keywords: Allergic Contact; Dermatitis; Delayed; External Fixators; Hypersensitivity.

1. INTRODUCTION

Fractures of the radial head or neck account for 5% of elbow fractures in adults (Barakat *et al*, 2022). It is important to note that the incidence of fractures in general increases in women aged 65 years or older due to the higher risk of osteoporosis (Rundgren *et al*, 2020). To prevent certain complications, surgical intervention on the traumatic elbow should be performed within 24 hours after the initial injury. This procedure is necessary due to the classification of the elbow as a complex joint and the narrow margin for error when dealing with traumatic injuries to the proximal ulna and radius (Rafi & Tiwari, 2022).

In this context, external fixation using instruments made of stainless-steel alloy, composed of chromium, nickel, cobalt, and molybdenum, represents the orthopedic synthetic material commonly used in Brazil today, particularly as an emergency countermeasure. However, it is not the best option for elderly patients as it relies on ligamentotaxis and cannot achieve anatomic reduction of specific fragments (Medda *et al*, 2021). Nonetheless, external fixation is valuable for its rapid initiation of osteosynthesis (Chhabra & Yildirim, 2021).

In summary, the ideal treatment approach depends on individual characteristics, and the choice of a fixation method must be thoroughly evaluated by the surgeon, taking patient-related variations into account. In this regard, different forms of external fixation provide adequate stabilization, as well as satisfactory radiological and functional outcomes for managing fractures of the radius or ulna of varying severity (Ermutluet *al*, 2020).

One of the adverse reactions with low incidence is an allergic reaction to the metallic composition of the fixator, whether internal or external. This allergic reaction, specifically allergic contact dermatitis (ACD), is a type IV hypersensitivity response, accounting for 20% of contact dermatoses. ACD is diagnosed with a gold-standard patch test to confirm the diagnosis in patients with persistent symptoms. Acute ACD typically presents as eczematous erythema, or vesicular dermatitis. Although ACD may manifest as a localized and well-demarcated skin rash, most commonly on the hands or face, it can also be more widespread (Murphy *et al*, 2023).

The present case report aims to describe a rare case of hypersensitivity to orthopedic synthetic materials, an adverse event that developed following surgical intervention for the correction of an open fracture of the radius and proximal ulna.

2. PRESENTATION OF CASE

The patient, a 63-year-old woman, had no history of osteoporosis before being admitted to a hospital unit for surgical treatment of an open fracture of the right olecranon. The initial intervention involved the placement of an external fixator, which was followed by the development of inflammatory signs and suspected cellulitis. Subsequently, the fixator was removed, leading to the progression of diffuse and pruritic dermatitis.

After suffering a fall in early 2021, which resulted in an open fracture of the right olecranon, the patient underwent surgery for the placement of an external fixator and osteosynthesis of the distal third of the right ulna. However, three days after the operation, she developed edema, hyperemia, localized warmth, and suspected erysipelas and cellulitis. After five days, clinical improvement was observed, and she was discharged from the hospital with a prescription for antibiotics and analgesics.

However, four days after discharge, the patient experienced a worsening of symptoms with purulent discharge, leading to readmission due to cellulitis and purulent secretion. Two days later, surgery was performed to remove the fixator and apply a right axillary splint, with a prescription for Ciprofloxacin and Clindamycin. Fifteen days later, osteosynthesis surgery was planned but canceled due to leukocytosis, followed by a prescription for Augmentin (Clavulin) and hospital discharge.

Subsequently, the patient was admitted for surgery to fix the olecranon with a plate and Kirschner wire and was discharged two days later. During a follow-up consultation, postoperative pain and serous discharge from the surgical wound were observed, leading to a prescription of Ciprofloxacin for an additional seven days. The persistence of serous

discharge from the Kirschner wires resulted in their removal, with the prescription for Ciprofloxacin maintained.

Afterwards, an infection was detected in the operative site, requiring rehospitalization and evaluation by internal medicine due to suspected drug-induced dermatitis. Vancomycin and Meropenem were prescribed, and surgical mechanical lavage were performed. Following assessment by an infectious disease specialist, the patient developed acute renal failure. The elbow plate was removed, and shortly thereafter, the patient exhibited intense pruritus disseminated across the body. The patient was discharged from orthopedics and nephrology but remained under investigation by internal medicine regarding drug-induced dermatitis, acute renal failure, and infection, with a prescription for Prednisone for five days.

After the detection of osteomyelitis and erythematous desquamative lesions, the patient was admitted to the ICU and started treatment with Tazocin for a pulmonary infection. She developed an allergic reaction, which was treated with Hydroxyzine while maintaining Hydrocortisone and an antihistamine. A subsequent hospitalization was required to remove the orthopedic synthetic material from the elbow, with a diagnosis of periplate infection and pseudoarthrosis. Three months after the operation, the patient still presents with a low-output fistula and chronic dermatitis that has not responded to dermatological treatment to date. An X-ray examination revealed signs of bone resorption in the humerus, radius, and ulna, as well as non-union of the fracture in the ulna.

Given the persistence of extensive chronic dermatitis, a standardized Patch Test was performed using the PATCHKIT STANDARD NEW GENERATIONS with the Finn Chambers technique from FDA ALLERGENIC. The test revealed positive reactions to Cobalt Chloride, with a possible association with vitamin B12, and to Nickel Sulfate. Positive reactions to the toluenesulfonamide/formaldehyde resin were also identified. The test report highlighted that, due to the extensive dermatitis, the results might have been affected, and it considered the possibility that the allergy was related to the implant of a metallic prosthesis. It recommended the removal or replacement of the prosthesis with one that does not contain chromium and/or nickel. Five months after the operation, the fracture site showed no signs of infection but presented with severe bone rarefaction and bone loss.



Figure 1 - Appearance of the patient's dermatitis

3. DISCUSSION

The implantation of orthopedic devices is a common strategy in various surgical correction treatments (Thomas *et al*, 2024). However, despite being uncommon, there is growing concern about hypersensitivity reactions to implants (HRI), particularly to metals such as nickel, cobalt, and chromium present in these devices. This can occur because such materials are exposed to fluids, biological tissues, and mechanical stresses, making them susceptible to corrosion and ion release, which triggers an immune response that can be characterized as an adverse event (Zemelka-Wiacek, 2022).

In the case of the patient described in this report, an external fixator was initially used to correct the fracture in the right upper limb. Subsequently, a plate and implantable pins were used for osteosynthesis, all of which were orthopedic materials made of stainless steel (a metallic alloy commonly used in orthopedic implants due to its chromium content, which provides greater resistance to corrosion, but also includes other components such as nickel, cobalt, and molybdenum) (Tapscott & Wottowa, 2024). However, despite the high purity of stainless steel, its inherent passive protective layer, and plasma spray coating, friction can still cause the steel to release soluble products into the body (Wozniak *et al*, 2021). According to studies, this may induce the expression of intercellular adhesion molecule-1 (ICAM-1) and cytokine activation, influencing the local environment and, in rarer cases, triggering hypersensitivity in patients, as observed in this case (Toro *et al*, 2020).

The incidence and prevalence of metal allergies to implanted implants can be influenced by various factors. However, they are difficult to determine, as the literature lacks prospective longitudinal studies with clear objective criteria and large cross-sectional studies addressing these questions (Pacheco, 2019). Nonetheless, some relevant findings have been demonstrated in studies, such as the greater sensitivity and development of hypersensitivity to nickel in female patients (a factor also observed in the present case, where the patient

was reported to have nickel hypersensitivity), while male patients exhibit greater sensitivity to cobalt (Silverberg *et al*, 2024).

HRI is generally classified as delayed-type allergies mediated by T lymphocytes (type IV reaction), characterized by increased inflammasome activation induced by metal ions or particles and heightened cytokine (IL-1B) formation (Atwater & Reeder, 2020). Such symptoms and factors characteristic of type IV hypersensitivity reactions were observed in the patient described in this report. Although some studies propose prior exposure to metals at high concentrations as a diagnostic hypothesis for HRI, suggesting sensitization of dendritic cells that could predispose the patient to ACD (Sebastião *et al*, 2020), this was not reported by our patient, and this theory has yet to be proven. Therefore, the most widely accepted hypothesis is that the predisposition to metal hypersensitivity is multifactorial.

The primary clinical symptoms of hypersensitivity to metals include localized cutaneous reactions or systemic allergic dermatitis of an eczematous nature, which may occur over the implanted material. These symptoms can also present as urticaria, blistering eruptions, erythema multiforme, and vasculitis. Additionally, extracutaneous complications associated with orthopedic implants, such as pain and swelling at the implant site, aseptic inflammation, and prosthetic loosening, are common (Gaillard-Campbell & Gross, 2024).

From a laboratory perspective, the most standardized diagnostic tools are the skin patch test, the leukocyte migration inhibition test (LMIT), and the lymphocyte transformation test (LTT), which are the most widely used tests for metal hypersensitivity (Dordunoo *et al*, 2020). The patch test is considered the gold standard for diagnosing metal hypersensitivity and is more commonly used in clinical settings due to its simplicity compared to in vitro tests. The LMIT assesses leukocyte migration inhibition, whereas the LTT evaluates the proliferation of lymphocytes activated by metal ions. Although the LTT is the preferred test, its clinical application is significantly constrained by its high cost and the need for a specialized laboratory (Li & Li, 2021).

For treatment, allergen removal is consistently the most effective approach for all types of hypersensitivity. However, if the patient presents with only mild eczema or less severe dermatitis, local dermatological treatment is generally preferred. When systemic allergic symptoms occur, the prescription of oral prednisolone is also indicated (Ramcharan *et al*, 2023).

4. CONCLUSION

The fixation of a stainless-steel prosthesis as a therapeutic solution aimed at improving osteosynthesis and the patient's mobility is contradicted by the potential for hypersensitivity reactions to implants (HRI) made of metals such as nickel, cobalt, and chromium. Although composed of high-purity stainless steel and coated with plasma spray to inhibit particle oxidation, the release of soluble products into the body is inevitable due to the constant and uninterrupted exposure to the individual's biomechanics.

The literature lacks longitudinal studies that classify the adverse reactions caused by these metallic materials in a way that addresses complications arising from implants used in surgical situations. Therefore, this case report seeks to highlight the occurrence of hypersensitivity to metals as an adverse effect of prosthesis implantation and its possible clinical outcomes. It also aims to explore new evidence bases that contribute to the diagnosis and reduce the incidence of this complication in future cases, such as the finding of a higher prevalence of nickel hypersensitivity in female patients.

Definitions, Acronyms, Abbreviations

ACD: allergic contact dermatitis

ICU: Intensive Care Unit

HRI: hypersensitivity reactions to implants

LMIT: leukocyte migration inhibition test

LTT: lymphocyte transformation test

ACKNOWLEDGEMENTS

We would like to thank our advisor Jalsi Tacon Arruda, for her support throughout the research. We also thank the Universidade Evangélica de Goiás (UniEVANGÉLICA) for providing the IP necessary to access the articles.

COMPETING INTERESTS

All Authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

Each author contributed individually and significantly to the development of this article: MBM Conceived the activities that led to the bibliographic review, interpreted the results of the study, wrote the article and participated in formatting of the article; LPR Planned the activities that led to the study, survey of the medical records, and data collection; ATAM Planned the activities that led to the study, survey of the medical records, data collection, wrote the article; HCS Participated in the review process, formatting of the article and approved the final version; EBS Conceived the activities that led to the bibliographic review; MMM Conceived the activities that led to the bibliographic review; FFS Participated in the review process and approved the final version;JTAParticipated in the review process and approved the final version. All the authors have read and approved the final manuscript.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

This case report was conducted in accordance with the guidelines for research involving human subjects established by the Brazilian National Board of Health and the principles outlined in the Declaration of Helsinki. It was approved by the Ethics Committee of

Evangelical University of Goiás(CAAE: 80274824.1.0000.5076, protocol: 7.097.797), and ethical agreements with the hospital institution were signed. A waiver for informed consent was requested because the outcome involved a death unrelated to the therapeutic intervention or the subject of this study. To minimize inconvenience and protect the patient's identity, the waiver was requested and approved by the ethics department to which this work was submitted.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with ethical standards.

DISCLAIMER (USE OF ARTIFICIAL INTELLIGENCE)

The authors acknowledge the use of GTP-4 for rewriting and editing this manuscript, specifically for refining the English grammar of the translated text, which was originally written in Brazilian Portuguese. The AI's role was strictly limited to improving the grammatical accuracy and ensuring alignment with academic language standards, without adding any new information to the text. The details of AI usage are as follows:

1. The original manuscript, written in Brazilian Portuguese, was translated into English, and AI was employed to enhance the grammatical quality of the final version, adhering to academic English conventions.
2. Carefully designed prompts were used to guide the AI in making grammatical corrections and verifying the translation's consistency with academic norms.

REFERENCES

1. Barakat, A., McDonald, C., & Singh, H. (2022). Current concepts in the management of radial head fractures: a national survey and review of the literature. *The Annals of the Royal College of Surgeons of England*. <https://doi.org/10.1308/rcsann.2022.0109>
2. Rundgren, J., Bojan, A., Mellstrand Navarro, C., & Enocson, A. (2020). Epidemiology, classification, treatment and mortality of distal radius fractures in adults: an observational study of 23,394 fractures from the national Swedish fracture register. *BMC Musculoskeletal Disorders*, 21(1). <https://doi.org/10.1186/s12891-020-3097-8>
3. Rafi, B. M., & Tiwari, V. (2022). Forearm Fractures. PubMed; StatPearls Publishing. <https://pubmed.ncbi.nlm.nih.gov/34662094/>
4. Medda, S., Aneja, A., & Carroll, E. A. (2021). Distal Radius Fractures: Setting Yourself Up for Success in the Active Geriatric Patient. *Journal of Orthopaedic Trauma*, 35(5), S16–S20. <https://doi.org/10.1097/bot.0000000000002226>
5. Chhabra, A. B., & Yildirim, B. (2021). Adult Distal Radius Fracture Management. *Journal of the American Academy of Orthopaedic Surgeons*, 29(22), e1105–e1116. <https://doi.org/10.5435/jaaos-d-20-01335>
6. Ermutlu, C., Mert, M., Kovalak, E., Kanay, E., Obut, A., & Öztürkmen, Y. (2020). Management of Distal Radius Fractures: Comparison of Three Methods. *Cureus*. <https://doi.org/10.7759/cureus.9875>

7. Murphy, P. B., Atwater, A. R., & Mueller, M. (2023). Allergic Contact Dermatitis. PubMed; StatPearls Publishing. <https://pubmed.ncbi.nlm.nih.gov/30422461/>
8. Thomas, P., P. Arenberger, Bader, R., Bircher, A. J., M. Bruze, N. de Graaf, Hartmann, D., Johansen, J. D., A. Jowitz-Heinke, Krenn, V., Kurek, M., A. Odgaard, Rustemeyer, T., Summer, B., & Thyssen, J. P. (2024). A literature review and expert consensus statement on diagnostics in suspected metal implant allergy. *JEADV. Journal of the European Academy of Dermatology and Venereology/Journal of the European Academy of Dermatology and Venereology*. <https://doi.org/10.1111/jdv.20026>
9. Zemelka-Wiacek, M. (2022). Metal Allergy: State-of-the-Art Mechanisms, Biomarkers, Hypersensitivity to Implants. *Journal of Clinical Medicine*, 11(23), 6971. <https://doi.org/10.3390/jcm11236971>
10. Tapscott, D. C., & Wottowa, C. (2023). Orthopedic Implant Materials. StatPearls. <https://pubmed.ncbi.nlm.nih.gov/32809340/>
11. Woźniak, A., Staszuk, M., Reimann, Ł., Bialas, O., Brytan, Z., Voinarovych, S., Kyslytsia, O., Kaliuzhnyi, S., Basiaga, M., & Admiak, M. (2021). The influence of plasma-sprayed coatings on surface properties and corrosion resistance of 316L stainless steel for possible implant application. *Archives of Civil and Mechanical Engineering*, 21(4). <https://doi.org/10.1007/s43452-021-00297-1>
12. Toro, G., De Cicco, A., Braile, A., Landi, G., & Schiavone Panni, A. (2020). New insights on metal allergy in total joint arthroplasty. *Journal of Biological Regulators and Homeostatic Agents*, 34(5 Suppl. 1), 125–130. IORS Special Issue on Orthopedics. <https://pubmed.ncbi.nlm.nih.gov/33739017/>
13. Pacheco, K. A. (2019). Allergy to Surgical Implants. *Clinical Reviews in Allergy & Immunology*, 56(1), 72–85. <https://doi.org/10.1007/s12016-018-8707-y>
14. Silverberg, J. I., Patel, N., Warshaw, E. M., DeKoven, J. G., Belsito, D. V., Atwater, A. R., Taylor, J. S., Sasseville, D., Reeder, M. J., Houle, M.-C., DeLeo, V. A., Maibach, H. I., Fowler, J. F., Zug, K. A., Pratt, M. D., Yu, J., Mowad, C. M., Botto, N. C., & Adler, B. L. (2024). Patch Testing With Nickel, Cobalt, and Chromium in Patients With Suspected Allergic Contact Dermatitis. *Dermatitis*, 35(2), 152–159. <https://doi.org/10.1089/derm.2023.0139>
15. Atwater, A. R., & Reeder, M. (2020). Hypersensitivity reactions to orthopedic implants: what's all the hype? *Cutis*, 105(2), 68–70. <https://pubmed.ncbi.nlm.nih.gov/32186530/>
16. 16. Sebastião, A. I., Ferreira, I., Brites, G., Silva, A., Neves, B. M., & Teresa Cruz, M. (2020). NLRP3 Inflammasome and Allergic Contact Dermatitis: A Connection to Demystify. *Pharmaceutics*, 12(9), 867. <https://doi.org/10.3390/pharmaceutics12090867>
17. Gaillard-Campbell, D. M., & Gross, T. P. (2024). Hypersensitivity to metals in metal-on-metal hip arthroplasty: a prospective study of one hundred and thirty five lymphocyte transformation tests. *International Orthopaedics*, 48(3), 693–698. <https://doi.org/10.1007/s00264-023-05992-7>

18. Dordunoo, D., Anaman-Torgbor, J., Smith, C., Shaik, A., Hass, M., Gordon, C., An, M., Aviles-G, M. L., & Weinzierl, M. (2020). Hypersensitivity in patients receiving metal implants: a scoping review protocol. *JBI Evidence Synthesis*, 19(6), 1404–1411. <https://doi.org/10.11124/jbies-20-00171>
19. Li, Y., & Li, L. (2021). Contact Dermatitis: Classifications and Management. *Clinical Reviews in Allergy & Immunology*, 61(3), 245–281. <https://doi.org/10.1007/s12016-021-08875-0>
20. Ramcharan, D. N., Alaimo, K. L., & Tiesenga, F. (2023). Diagnosis and Management of a Hypersensitivity Reaction to Titanium-Containing Surgical Clips: A Case Report. *Cureus*. <https://doi.org/10.7759/cureus.34929>

UNDER PEER REVIEW