

Case Report

A rare case of delayed hypersensitivity reaction to metal ions secondary to a remnant pedicle screw fragment after spinal arthrodesis

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Delayed hypersensitivity reaction to metal ions is rare and has been mostly documented among patients undergoing total joint arthroplasty with metal-on-metal bearing surfaces. Nonetheless, to our knowledge, only a few cases associated with spinal arthrodesis have been reported in the literature. The aim of this case report was to describe the clinical features of a rare case of delayed-type hypersensitivity reaction to nickel that occurred after an extraordinarily long period of time (approximately 15 years) after spinal arthrodesis. Here, we present a 38-year-old patient who was referred to us with a diagnosis of delayed-type hypersensitivity reaction to nickel that was established by a skin patch test. The chief sign and symptoms of the patient were allergic contact dermatitis along with intractable, generalized itching that started several months ago. The medical history revealed that the patient had undergone spinal arthrodesis using rods and pedicle screws approximately 15 years ago, followed by revision surgery to remove the implants. Radiological examination showed a remnant pedicle screw fragment at the third lumbar vertebra that had broken off during the removal of implants nine years ago. However, the signs and symptoms of metal hypersensitivity started shortly before the patient was referred to our hospital. We decided to remove the screw fragment as allergic contact dermatitis was refractory to medical treatment. On postoperative day one, the itching was completely resolved, although the skin patch test remained positive.

Metal hypersensitivity following arthroplasty is rare (0-5%) (1-5) and often underreported owing to unpredictable occurrence and the lack of a diagnostic guideline (2, 6). Metal hypersensitivity is mostly documented among patients with total joint arthroplasty, whereas a small number of cases are reported after spinal arthrodesis (2). There is very little clinical information about implant-related metal hypersensitivity because of its extremely low incidence, vague clinical manifestations, and diagnostic difficulty (1).

Metal hypersensitivity has been mainly associated with arthroplasty involving metal-on-metal bearing surfaces and has been attributed to immunologic effects and cell toxicity mediated by exposure to wear debris (2, 6-8). It is generally believed that wear debris particles, in conjunction with native proteins, form haptens that elicit delayed-type hypersensitivity reactions (type IV) in the local tissue (2, 6, 7, 9). In most cases, it takes weeks to months (<2 years) for

this process to complete and for the symptoms of metal hypersensitivity to occur (1, 2, 4, 9-11).

Although spinal arthrodesis is distinctly different from total joint arthroplasty in degree and pattern of motion, loading environment, and tissues adjacent to the prostheses (7, 9), hypersensitivity after spinal metallic implantation also presents within weeks to months in almost all cases (2, 9-11). However, in comparison with previously reported cases our patient had an extremely long (15 years) symptom-free interval.

In this report, we present a patient with allergic contact dermatitis, who was sensitive to nickel (Ni) on the skin patch test. The metal hypersensitivity was apparently due to a remnant pedicle screw fragment, and the patient's symptoms improved immediately after removal of the screw fragment. This case is unique because the patient's metal allergy developed 15 years after the spinal arthrodesis.

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Case Presentation

The case review was conducted according to all guidelines outlined in the Declaration of Helsinki. Written informed consent for publication was obtained from the patient. A 38-year-old patient visited the dermatologist with a chief complaint of intractable generalized itching, which had started several months ago. Crusted patches were noted on the trunk and arms. A skin patch test revealed hypersensitivity to Ni, but the patient did not wear any metallic articles and did not have any known routine contact with such materials.

The patient had undergone spinal arthrodesis with rods and pedicle screws for lumbar disc herniation approximately 15 years ago. Despite the surgery, the low back pain persisted, and the patient underwent three subsequent revisions to remove the pedicle screws. The most recent surgery for screw removal had been performed nine years ago and was incomplete, which resulted in one broken pedicle screw being left at the third lumbar vertebra (Figure 1). During the 15 years after the first arthrodesis, the patient had had no itching, only the persistent low back pain.

After determining the medical history, we believed that the remnant pedicle screw fragment was a plausible cause of the allergic dermatitis. Because the remnant pedicle screw was located deep in the vertebral body, it appeared that it would be technically very challenging to remove it without damaging the facet and aggravating the low back pain, persistent since the first arthrodesis. Thus, we tried to use various medications such as steroid, antihistamines, and immunosuppressants. The details are as follows:

- Prednisolone (for 17 months)
- Chlorphenamine (for 19 months), Fexofenadine (for 18 months), Bepotastine (for 16 months), and Cetirizine (for 8 months)
- Methotrexate (for 14 months)

Although we discontinued the steroid for 2 months just before the surgery to exclude steroid-induced allergy, the symp-

toms persisted. Because the symptoms were exacerbated despite medication, we performed the surgery and removed the entire pedicle screw fragment (Figure 2). The next day, the patient's itching was completely resolved without any medication. The patient has never been treated for itching until the last follow-up (25 months after surgery). Skin patch testing at postoperative week 3 indicated that the patient remained sensitive to Ni.

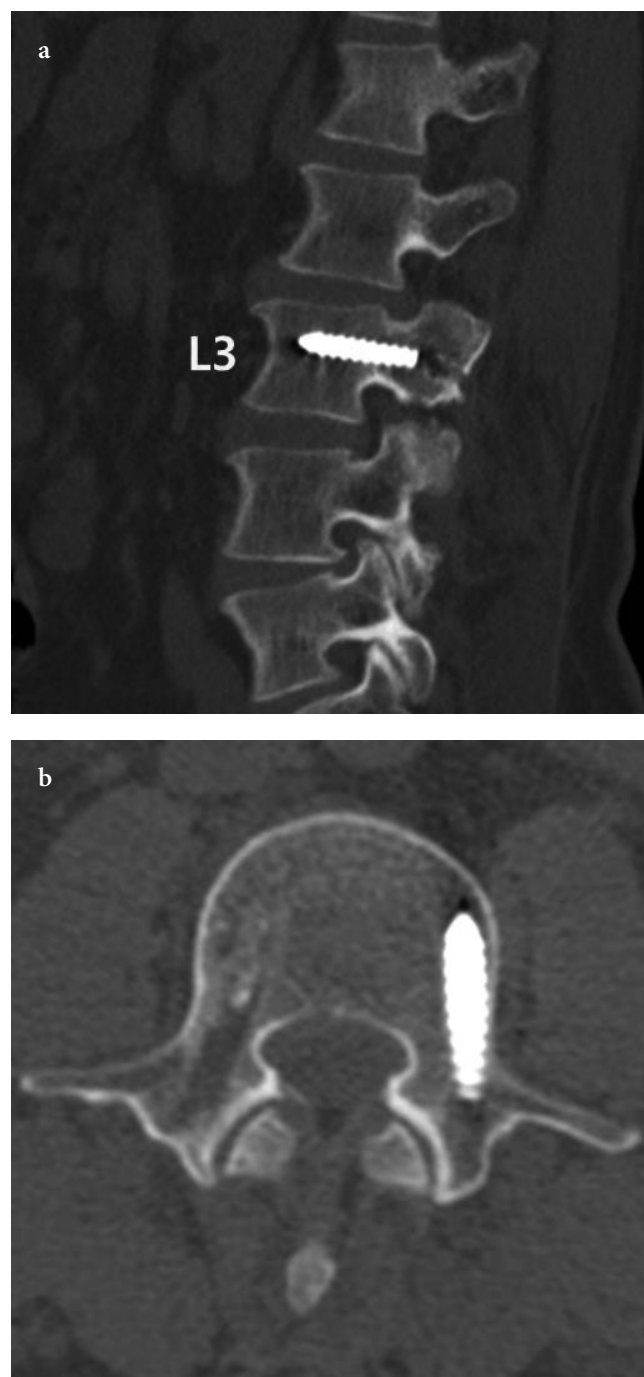


Figure 1. a, b. Preoperative computed tomography showing the remnant pedicle screw fragment in the third lumbar vertebral body (L3) and its left pedicle. (a) sagittal view; (b) axial view

HIGHLIGHTS

- Metallic spinal implants can cause allergic contact dermatitis.
- Metal hypersensitivity can occur even 15 years after the spinal arthrodesis.
- Delayed hypersensitivity should be included as a possible complication of spinal implantation and implant removal can be recommended in these patients.
- Ni is the most frequent allergy-inducing metal and can be confirmed with skin patch test.

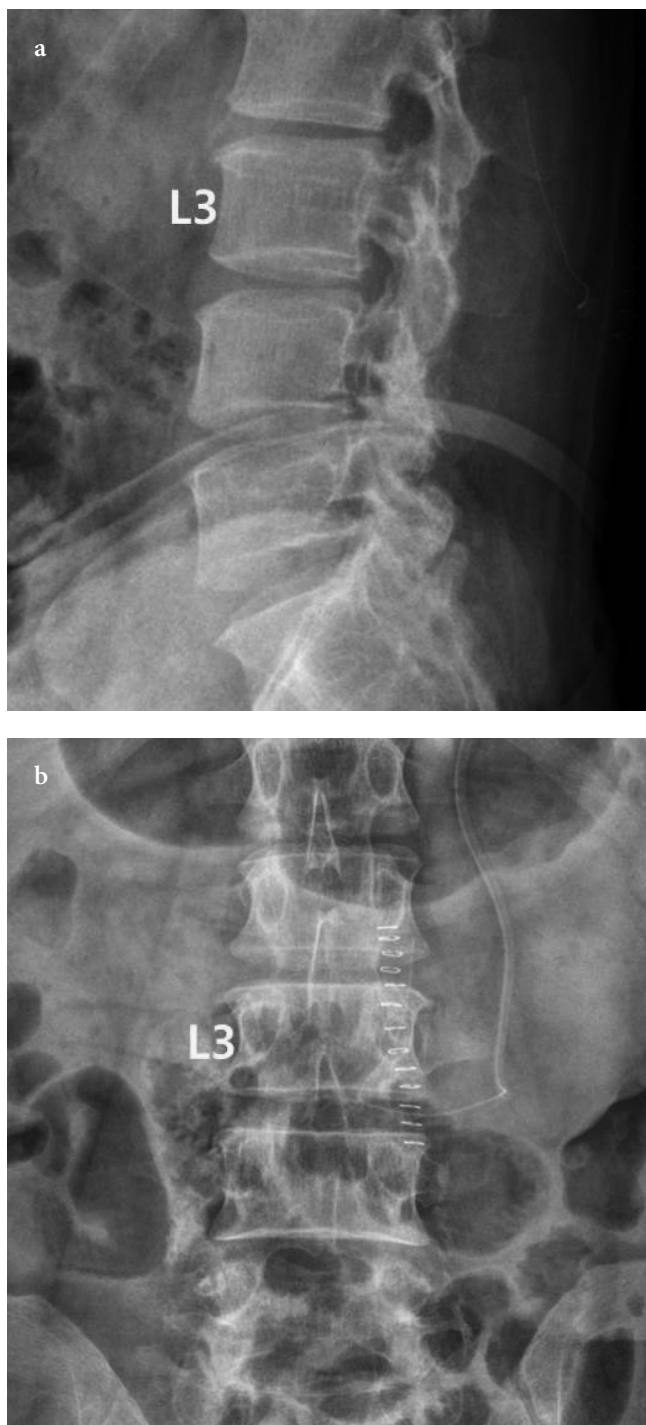


Figure 2. a, b. Postoperative x-ray showing complete removal of the remnant screw fragment (L3: the third lumbar vertebral body). (a) lateral view; (b) anteroposterior view

Discussion

Metals are the most common allergens in contact allergies (12). In the general population, the prevalence of metal hypersensitivity is about 10-15%, and Ni is the most frequent allergy-inducing metal (13-24.4%) (1, 3, 6, 13). We confirmed our patient's Ni allergy by skin patch test and by noting his/

her complete recovery from the itching and improvement of skin lesions after removal of the screw fragment. However, we do not know whether he/she had a preexisting metal hypersensitivity or whether he/she became sensitive after metallic implantation.

The skin patch test is a standard procedure for assessment of hypersensitivity and a necessary step in diagnosis of allergic contact dermatitis (2, 3, 12). Because the patch test is easier to use and cheaper than *in vitro* tests, it is more widely used in clinical settings and is more suitable for large-scale screening (1). Although the patch test has been used for many years with a greater frequency of positivity in patients with metal implants, recommendations for routine testing are still controversial (2-4, 14). According to literature, its sensitivity is as high as 77-100%, but the specificity is quite low (64-71%) (1, 3). For this reason, we are hesitant to utilize it as a routine test to predict postoperative prosthesis-related hypersensitivity. A patient with a positive patch test may not experience postoperative metal hypersensitivity, and a negative patch test cannot guarantee that the patient will not become sensitive to the implanted metal (1). Moreover, the short duration of dermal contact in the patch test is not the same as the long-term closed environment of the metal implant, and the relationship between dermal and deep implant sensitivity is not yet known (2, 6). Concerns that the patch test could possibly induce hypersensitivity in a previously non-sensitive patient also exist (2, 3, 6).

Our patient had an extremely long symptom-free interval compared with that of most reported cases of implant-related metal hypersensitivity (1, 2, 9-11). Although it is difficult to fully understand the mechanism, delayed corrosion and lack of motion may be one explanation for the patient's long symptom-free interval.

All metals that are in contact with biologic systems are subject to corrosion and release metal ions into the body (2, 6, 15). These ions can activate the immune system by forming metal-protein complexes that act as allergens and elicit hypersensitivity responses (1, 2, 6, 7, 15). Although most alloys used for implants rely on an oxidative layer to protect them from corrosion, mechanical factors such as applied stress, fretting, and even micro-motion will cause this protective layer to break down (2).

The broken screw in our patient's body likely provided crevices for prolonged contact with corrosive body fluids. However, because the screw fragment was deeply embedded in the vertebral body and was not involved in any spinal motion, we believe that the mechanical stress was insignificant. Consequently, disruption of the protective layer may have been decelerated by minimal mechanical stress, also minimizing the release of metal ions. Although aseptic prosthetic loosening or periprosthetic osteolysis is

a common complication of arthroplasty, spinal arthrodesis is intended to produce a static environment, releasing relatively fewer debris particles or metal ions (7, 9, 15). However, micro-motion and load-bearing will continue until successful fusion is complete, inducing fretting corrosion (2, 15). Thus, spinal arthrodesis is not free from the corrosive process or the release of metal ions that can cause hypersensitivity reaction.

Although the diagnosis of this case is based on the detailed clinical history and positive patch test reaction, it lacks laboratory tests. First, we did not check the patient's serum or urine Ni level. The corrosion of spinal implants significantly raises Ni level in serum and urine (8). And the serum level also rises after surgery without any evidence of corrosion, and remained above normal levels for 4 years (8, 16). Thus, we think that serial serum and urine Ni levels could offer informative data, although the elevated level of metal itself is not direct evidence of metal hypersensitivity. Second, we did not perform *in vitro* tests such as leukocyte migration inhibition test (LMIT) and lymphocyte transformation test (LTT) because our laboratory did not support them. The LMIT measures the limitation of leukocyte migration by detecting migration inhibitory factor, which can prevent lymphocytes from leaving a site where foreign antigens are present (1). Thus, a positive result indicates an active immune response and metal sensitivity (1). The LTT measures the proliferation of lymphocytes activated by metal ions and indicates the cellular immune function (1, 3, 6). LTT is more reliable than the skin patch test and is currently more widely performed than LMIT, but its clinical practicability is limited by high cost and the need for a specialized lab (1). Moreover, it is not standardized, has inter-laboratory variability, and may produce false negative results if the test is not transported and processed in a timely manner (4).

Conclusion

This case demonstrated that metal hypersensitivity can cause allergic dermatitis even 15 years after spinal arthrodesis. Delayed hypersensitivity should be included in the differential diagnosis of postoperative complications even long after metallic implantation.

Informed Consent: Written informed consent was obtained from the patient for this case.

Conflict of Interest: The author has no conflicts of interest to declare.

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