

Probable delayed-type hypersensitivity to nickel-containing cerebral aneurysm clip associated with neurologic deficits

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Clinical Implications

- Contact allergy to metal is relatively common in the general population. Postsurgical complications and failure of metal-containing devices have been associated with contact hypersensitivity to metal components of implantable devices. This case demonstrates probable delayed-type hypersensitivity to a nickel-containing cerebral aneurysm clip that was associated with neurologic deficits.

TO THE EDITOR:

Contact allergy to metals such as nickel, cobalt, and chromium is common in the general population; it is estimated that up to 17% of women and 3% of men have hypersensitivity to nickel sulfate.¹ Contact sensitization to metals has been associated with prolonged or repeated skin exposure, occupational exposures,² or exposure after corrosion or mechanical wear of metallic implants.³

Most of the patients with nickel hypersensitivity tolerate the insertion of metal implants and reactions to buried nickel are rare.³ However, there have been reports of postsurgical complications, including mechanical failure, infection, and presumed localized hypersensitivity responses manifested by unexplained periarticular swelling and cutaneous eruptions after the insertion of metallic implants such as joint prostheses.⁴ It has been suspected that joint device failure can be caused by local delayed-type hypersensitivity reactions to metal components. A causal relationship between device failure and localized immunologic responses, however, has not been established. Nevertheless, metal contact hypersensitivity associated with failure of joint prostheses^{4,5} and cardiac endovascular devices⁶ has been reported. There is a paucity of cases regarding metal hypersensitivity in association with unexpected complications of neurologic implants.^{7,8}

Herein, we report the case of a nickel-sensitized patient who underwent surgical implantation of a nickel-containing clip for a cerebral aneurysm and experienced bilateral cerebral infarction and disabling neurologic deficits. This case is unique due to the severity of clinical manifestations associated with existing nickel hypersensitivity and the fact that patch testing was performed and supported the diagnosis of metal allergy.

A 33-year-old white female underwent successful endovascular repair of a spontaneous right carotid artery aneurysm rupture using a platinum coil. During her workup, a left posterior communicating artery (PCA) aneurysm was also incidentally found on brain magnetic resonance imaging (MRI). This left PCA aneurysm was electively clipped 9 months after initial

presentation during a second surgical operation, using a nickel-containing fenestrated clip.

The patient presented to the emergency department on postoperative day 10 with altered mental status, aphasia, and fever. She underwent brain MRI, which showed subacute infarction in the left caudate nucleus and left frontal lobe (Figure 1). She subsequently had rapid neurologic decline with status epilepticus. A repeat head computed tomography 6 days later showed a 7-mm midline shift and mass effect on the fourth ventricle, with new hypoattenuation in the left basal ganglia consistent with a new infarction.

On postoperative day 17, a repeat head computed tomography showed another infarction in the right frontal lobe and left cerebellar hemisphere with increased midline shift and downward herniation. Neurosurgery was consulted, and the patient underwent left frontotemporal craniectomy for decompression. Cortical biopsies were taken at the time of surgery, which, as shown in Figure 2, demonstrated scattered eosinophils with perivascular lymphocyte cuffing, more inflammation than would be expected with cerebral infarction.

The patient was started on high-dose methylprednisolone on postoperative day 19 because of concern for cerebral vasculitis. She underwent cerebral angiography on postoperative day 27, which showed near-complete occlusion of the left PCA and short-segment stenosis of several cortical branches of the left middle cerebral artery, which supported a diagnosis of vasculitis. Antinuclear antibody and HIV serology were negative. The erythrocyte sedimentation rate was 33, and C-reactive protein level was 0.8.

On postoperative day 28, the family reported that the patient had previously experienced blistering, erythematous rashes after wearing stainless steel rings and metal earrings. She underwent patch testing (TRUE test panel) on postoperative day 30, which was weakly positive, with a well-demarcated area of erythema without papules or vesicles (1+) to nickel at 48 hours. At that time, she had received high-dose systemic steroids—methylprednisolone 1 g intravenously daily for 5 days followed by prednisone 100 mg *per os* (by mouth) daily for 5 days.

The patient underwent repeat surgery on postoperative day 32 to remove the nickel-containing aneurysm clip and replace it with a titanium clip. It was noted in the operative report that the segment of the carotid artery passing through the fenestrations of the clip was very tightly narrowed and seemed to widen out more proximally and distally consistent with a local inflammatory response. Given the fact that the internal carotid artery gives rise to the anterior cerebral artery, which supplies the caudate nucleus and the frontal lobe, we suspected that the nickel clip may have caused a local inflammatory response, thereby decreasing perfusion, leading to the cerebral infarctions seen initially on postoperative day 10.

The patient did not recover much neurologic function after the removal of the nickel-containing aneurysm clip, and she was discharged to a long-term care facility. At 1 month after discharge, her neurologic status remained unchanged with a Glasgow Coma Scale score of 10 (moderate brain injury) and spontaneous eye opening with intermittently purposeful movements, and she required a tracheostomy for ventilation and tube feeding for nutrition.

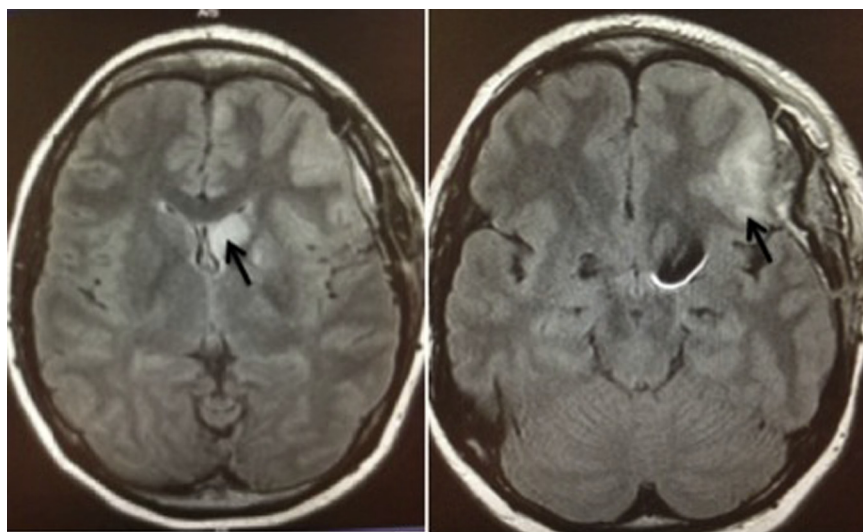


FIGURE 1. Left caudate nucleus infarction (left) and left frontal lobe infarction (right).

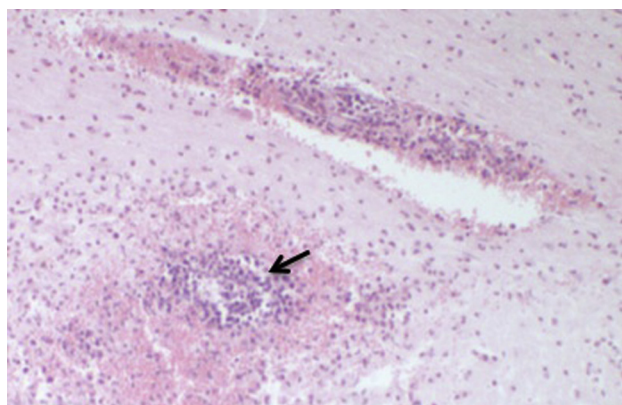


FIGURE 2. Cortical biopsy showing perivascular lymphocyte cuffing (arrow).

With no other obvious explanation for her multiple subacute cerebral infarctions, it was thought that the patient's clinical presentation could possibly be associated with a delayed hypersensitivity reaction to nickel contained in the implant. It was possible that the high-dose systemic steroids she received during patch testing prevented a more strongly positive reaction to nickel on patch testing TRUE test panel at 48 hours.⁹

Review of the literature revealed 2 similar reported cases of adverse neurologic sequelae in patients with nickel-containing neurologic implants.^{7,8} Both cases involved patients presenting with chronic, intermittent headaches 2 months after aneurysm clipping or coiling with a nickel-containing device; however, nickel hypersensitivity was not confirmed with patch testing in either case. In one case, the edema and headaches spontaneously resolved over time,⁸ and the other case required replacement with a titanium clip to resolve the headaches and vasogenic edema seen on brain MRI.⁷

To our knowledge, this is the first report of a possible delayed-type hypersensitivity reaction to a nickel aneurysm clip

that resulted in multiple, bilateral subacute cerebral infarctions leading to permanent neurologic deficits with demonstrated nickel allergy based on positive patch testing. This case demonstrates that presurgical screening for metal allergy should be considered as part of the presurgical workup if a patient has a good clinical history for contact hypersensitivity to metals.

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