

Comment:**Nickel-associated delayed cerebral hypersensitivity—
Recognition is key**

This report of a 60-year-old woman describes an initially uncomplicated coiling of an asymptomatic terminal internal carotid artery aneurysm via endovascular approach.¹ A nickel-titanium guide wire was used to assist placement of platinum coils. In subsequent weeks, she developed recurrent symptoms in the ipsilateral middle cerebral artery/anterior cerebral artery territories, each time associated with multifocal, nonrestricting, T2-hyperintense lesions on MRI. Complete evaluation found no intra-aneurysmal thrombus, CNS emboli, CNS infection, or seizure. After the second event, the patient received steroids, markedly improving her symptoms and resolving her MRI lesions. Skin patch testing revealed strong reactivity to nickel but not to the balloon material.

This is the fourth case report of a delayed cerebral inflammatory syndrome after cerebral coiling and the first to include positive nickel allergy testing. The authors build a strong case for the existence of a delayed reaction due to hypersensitivity to nickel agents (the guide catheter) used transiently during an endovascular procedure.

The strongest predictors of nickel sensitivity are atopy and prolonged contact with jewelry. In patients without ear piercings, filaggrin protein mutations are also associated with nickel sensitivity, since filaggrin chelates free nickel ions in the stratum corneum, preventing allergic responses in the inner skin compartments. The lack of genetic association in pierced patients is likely due to the bypass theory: metal piercings bypass the skin barrier provided by filaggrin, triggering allergic response in the inner skin compartments. Thus environmental exposure is a stronger risk than genetic predisposition. Nickel can also cause systemic hypersensitivity reactions after placement of implants (total knee arthroplasty, arterial stents, atrial septal defect/patent foramen ovale closure devices), sometimes requiring removal. Research is needed to determine whether focused skin patch testing will result in adequate identification of those at risk of developing systemic nickel hypersensitivity.

This case highlights the need for clinicians to have heightened suspicion of a systemic metal reaction in patients with an unusual postprocedural complication, including symptomatic, multifocal, cerebral hyperintensities after a catheter-based procedure. Given the increasing utilization of intravascular procedures, and the high prevalence of nickel allergies (~15%), such cases are likely to become more common.

1. Lobotesis K, Mahady K, Ganesalingam J, et al. Coiling-associated delayed cerebral hypersensitivity: is nickel the link? *Neurology* 2015;84:xxx-xxx.

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