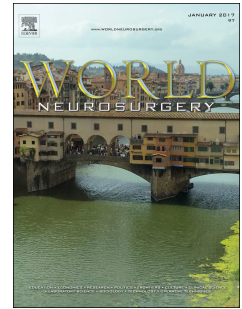


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Use of Pipeline Endovascular Device in Patients with Nickel Allergies

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ABSTRACT

Background: Metal allergies affect a significant portion of the population; intracranial flow diverters contain many of the most commonly allergenic metals. Prior literature has suggested patch testing for all patients with documented or suspected metal allergies prior to intracranial flow diverter placement, however there remains a paucity of reports of patients with documented metal allergies undergoing intracranial flow diversion.

Case Description: We report two patients with documented nickel allergies, confirmed via patch testing by a board-certified allergist, and unruptured intracranial aneurysms that underwent treatment with the PED. Both patients developed contact dermatitis when a PED was affixed to their skin during their preoperative workup. Follow-up arteriography at 12- and 36-months post-PED placement showed no evidence of in-stent stenosis or intimal hyperplasia and both patients never developed systemic allergic reactions.

Conclusions: In two patients with known nickel allergies and intracranial aneurysms treated with the PED there were no clinically- or radiographically-apparent allergic reactions at greater than 2 years of follow-up.

INTRODUCTION

Nickel allergies affect up to 17% of women and 3% of men and are one of the most common causes of allergic contact dermatitis¹, often associated with earrings and jewelry. Metal-related contact dermatitis is most commonly from nickel, cobalt, or chromium and usually begins 12 to 48 hours after exposure with symptoms that include skin rash, itching, redness, and dry skin patches. Prior reports, predominantly in cardiac literature, have demonstrated that inflammatory cell activation and proliferation can occur following coronary stent insertion in patients with metal allergies and as a result metal patch testing has been suggested for all patients with documented or suspected metal allergies prior to intracranial stent placement^{2,3}. However, there remains a paucity of reports of patients with documented metal allergies undergoing intracranial flow diversion.

Implanted, metallic endovascular stents corrode and release metal ions into the circulation that may elicit immune reactions in patients with metal allergies⁴ and metal allergy has been associated with device failure following insertion of hip and knee prostheses and coronary stents, among others¹. It is unknown if this mechanism contributes to in-stent-stenosis of intracranial stents or flow diversion devices such as the Pipeline endovascular device (PED), a braided, multi-alloy, mesh cylinder woven from cobalt-chromium-nickel and platinum/tungsten alloy wires. According to the manufacturer, the PED contains approximately 27% nickel by weight, and a warning regarding allergic reactions is included in the Instructions for Use for the device. In this report we present two patients with documented nickel allergies who underwent positive PED cutaneous patch testing prior to intracranial flow diversion placement and discuss their clinical and radiographic outcomes.

CASE PRESENTATION

Patient 1: A 68-year-old female with a history of nickel allergy, confirmed via patch testing by a board-certified allergist, was found to have an incidental, unruptured, wide-necked and irregular 7 mm left ophthalmic segment internal carotid artery aneurysm (Figure 1). She elected to undergo endovascular aneurysm treatment with a PED. Preoperatively, a PED was affixed to her forearm for 24 hours and she developed local erythema and pruritus consistent with contact dermatitis (Figure 1A). No corticosteroids or antihistamines were given to the patient peri-operatively. After placement of a 4.5mm x 20mm PED in the left internal carotid artery, she showed no systemic clinical signs or symptoms of allergic reaction and follow-up arteriography at 1 year showed no residual aneurysm filling or in-stent stenosis. At her 24-month clinical follow-up she had no complaints and she never experienced evidence of systemic inflammation or allergic reaction.

Patients 2: A 66-year-old female with a history of nickel allergy confirmed via patch testing was found to have an incidental, unruptured, complex 13 mm left ophthalmic segment internal carotid artery aneurysm (Figure 3). She wore a PED affixed to her forearm for 24 hours and developed contact dermatitis with local erythema and pruritis. Her aneurysm was treated with placement of a 4.75mm x 25mm PED in the left ICA; she did not receive antihistamines or corticosteroids in the perioperative period. She showed no clinical signs or symptoms of allergic reaction at any point. Follow-up arteriography 12 months later revealed no evidence of in-PED-stenosis but demonstrated residual opacification and persistent filling of the aneurysm. She therefore underwent placement of a second 4.75mm x 14 mm PED. Follow-up angiography 36 months after initial stent placement showed aneurysm occlusion with no evidence of in-stent

stenosis. She continues to have no complaints, and never developed symptoms of systemic inflammation or allergic reaction.

DISCUSSION

The role of intracranial stents in cerebrovascular neurosurgery has expanded greatly in recent years. Metal allergies are extremely common in the general population and most commonly manifest as a contact dermatitis reaction to nickel, cobalt, or chromium. The role of metal-induced hypersensitivity response and stent restenosis has been extensively studied in cardiac surgery; in one study, of patients with cardiac stents who were patch-test positive, 11.8% were found to have stent restenosis⁵. In a prospective study, Norgaz *et al.* similarly found no significant relationship between bare metal stents and hypersensitivity-mediated restenosis⁶. Conversely, a retrospective study of patients with 316L stainless steel cardiac stents found that ten out of ten patients with positive patch testing had in-stent restenosis on repeat angiography⁷. These contradictory findings have been inadequate to generate a guideline on the use of intracranial stents in patients with metal allergies, but patch testing has been previously recommended to provide better patient counselling prior to intracranial stent placement². Despite this, there is a deficiency of documented reports of patients with cutaneous metal allergies undergoing intracranial flow diverter placement.

We report two patients with documented nickel allergies, confirmed via patch testing performed by a board-certified allergist, who underwent placement of PED flow diverters to treat unruptured intracranial aneurysms. Both patients wore a PED affixed to their arm for 24 hours prior to device placement and both developed local erythema and pruritis, but no evidence of blister formation. Despite this local cutaneous reaction, both patients underwent uncomplicated

PED placement. At over two years of follow-up, neither patient demonstrated radiographic evidence of in-stent stenosis and neither developed any observable allergic reaction.

As the use of intracranial stents and flow diversion devices continues to expand for treatment of complex intracranial aneurysms, larger-scale studies are needed to determine whether patients with metal-induced contact dermatitis are at higher risk for in-stent stenosis or any inflammatory reaction after intracranial stent placement. We report two patients with proven cutaneous nickel allergies and local reactions to cutaneous PED placement, that have not demonstrated any allergic reaction or in-stent stenosis at prolonged follow-up. Although the PED contains in total 27% nickel by weight, only 3-8% is exposed on the surface to actual blood flow, according to the manufacturer, because of the chromium oxide layer that forms on the cobalt chromium wires. This perhaps contributes to the lack of obvious inflammatory response in these two patients with nickel allergies. PEDs may be safe in some patients with intracranial aneurysms requiring vessel reconstruction, even in the setting of dermatitis with PED application to bare skin.

STATEMENT OF ETHICS

Subjects included in this report have given their written informed consent, and the study has been approved by our local Institutional Review Board.

AUTHOR CONTRIBUTIONS

Primary drafting of this report: DAT, JLP, AO, BZ

Critical revision of this report: All authors

Study conception: BTJ, BAG

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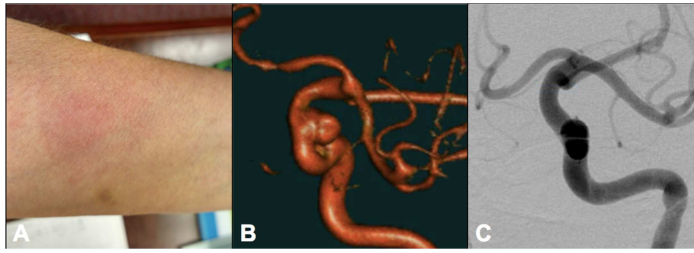
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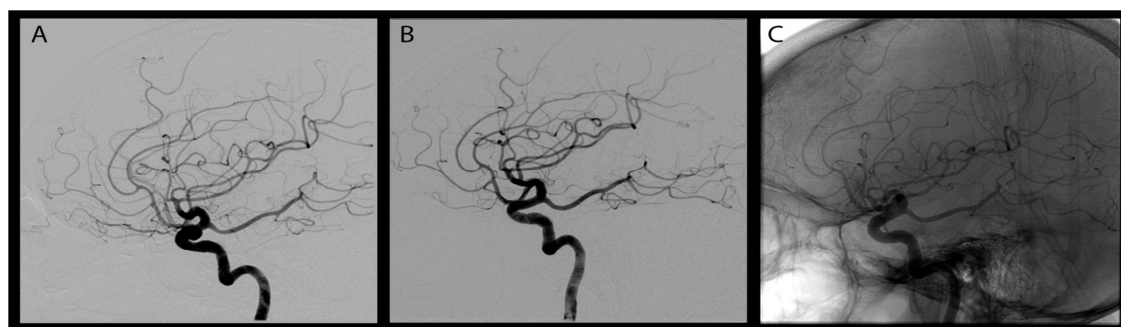
FIGURE LEGENDS

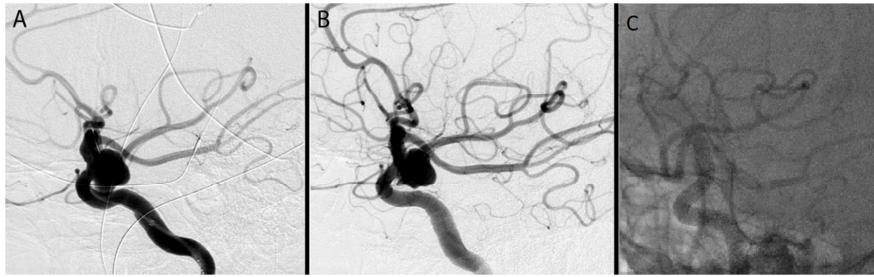
Figure 1. Patient 1: A) Contact-dermatitis secondary to wearing a Pipeline endovascular device affixed to her forearm for 24 hours; B) Pre-treatment arteriography 3-D reconstruction of left ICA injection demonstrating wide-necked left ophthalmic segment aneurysm; C) Follow-up arteriography of left ICA injection demonstrating complete obliteration of the aneurysm and no evidence of in-PED stenosis.

Figure 2. Patient 1: A) Pre-treatment arteriography of left ICA injection demonstrating wide-necked left ophthalmic segment aneurysm; B) 1-year follow-up arteriography of left ICA injection demonstrating complete obliteration of the aneurysm and no evidence of in-PED stenosis.

Figure 3. Patient 2: A) Pre-treatment arteriography of left ICA injection demonstrating an ophthalmic segment internal carotid artery aneurysm; B) 12-month and C) 36-month follow-up arteriography demonstrating aneurysm obliteration and no evidence of in-PED-stenosis.







- 1) The Pipeline endovascular device is composed of cobalt/chromium/nickel and platinum/tungsten alloy wires
- 2) Metal allergies have been associated with device failure in orthopedic prostheses and coronary stents
- 3) The placement of the PED may be safe in patients with a documented nickel allergy

PED: Pipeline endovascular device

ICA: internal carotid artery