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**Durable Polymer Drug Eluting Stent-Induced Kounis Syndrome and
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Short Title: Eosinophilia from Durable Polymer Stent

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Summary

We present a case of in-stent thrombosis and eosinophilia consistent with Kounis syndrome, in the context of metal allergy to durable polymer coated drug eluting stents, requiring long-term immunosuppression.

Abstract

There are no reports of systemic eosinophilic reactions to durable polymer coated drug eluting stents (DP-DES) and a consensus statement indicates that these devices should be considered in nickel allergy. We present a case of in-stent thrombosis, eosinophilia, and rash consistent with allergic myocardial infarction, a presentation of Kounis syndrome, in the context of metal allergy to DP-DES requiring long-term immunosuppression.

Case

An 85-year-old man presented with non-ST elevation myocardial infarction (NSTEMI) and was treated for right coronary artery stenoses with atherectomy and 4 Resolute DP-DES, aspirin and clopidogrel (Medtronic, Fridley, MN, Figure 1). He sustained recurrent NSTEMI 43 days later. Angiography demonstrated in-stent thrombosis in a newly aneurysmal area (Figure 1, Video 1), which was treated with manual thrombectomy and balloon angioplasty. He was discharged on aspirin and ticagrelor. He presented with a diffuse macular pruritic rash accompanied by eosinophilia (2500/ μ L, reference: 100-300/ μ L, Figure 2) 74 days after initial stenting. The patient's only known allergy was "swelling" to penicillin; there were no changes to

his longstanding medications, phenytoin, donepezil, metoprolol succinate and atorvastatin. Sequential elimination, each for >6 weeks, was used to determine if he was reacting to antiplatelets. First, clopidogrel was resumed in place of ticagrelor, but the rash persisted >6 weeks making an allergy to ticagrelor unlikely. Second, aspirin was eliminated for >6 weeks. The rash persisted; therefore, aspirin was restarted and clopidogrel was eliminated. The rash persisted after >6 weeks, shifting attention to the stent. Zotarolimus is 85% eluted after 60 days and is measurable in circulation for up to 180 days.¹ Allergy to zotarolimus was considered unlikely since the reaction did not subside after 180 days. Daily oral prednisone (30 mg) diminished the rash, tapering worsened it. Skin testing 454 days after stenting revealed sensitivity to nickel, manganese, titanium, vanadium, and zinc. He was not a candidate for surgical explant, eosinophilia persisted long-term, and he stayed on steroids for approximately 3 years until his death.

Kounis described allergic MI after coronary artery stenting.² The pathophysiology is driven by release of inflammatory mediators from eosinophils and mast cells reacting to metals, activating platelets which leads to acute thrombosis. Other types are vasospasm of normal epicardial coronary arteries and MI with plaque erosion or rupture. Extra coronary arterial thrombosis in the context of systemic allergic reactions are also manifestations of Kounis syndrome, triggered by various exposures.

While durable polymer should theoretically limit exposure of metals to the circulation, microscopic disruption may be a mechanism for contact between inflammatory cells and the metal surface of the stent leading to eosinophilic reaction and stent thrombosis in this patient. A recent scientific statement indicated that there

are no reports of systemic eosinophilic reactions to DP-DES and that these devices should be considered in patients with nickel allergy, but this case represents a possible exception.³ We cannot eliminate allergy to other stent components, like the polymer, but the finding of skin reactivity to metals in this patient suggests it contributed to the presentation.

Nickel is a component of second-generation DES. Hypersensitivity to nickel is more prevalent (17.5%) as compared to aspirin (2%) and iodinated contrast (0.7%).⁴ Cases of device explant or dysfunction from nickel allergy are exceedingly low as compared to its prevalence, thus there must be other predisposing factors. Nevertheless, user manuals disclaim DP-DES as contraindicated with known metal allergy. Nickel alloys are common in other cardiac implants, such as transcatheter aortic valves, and it is hypothesized that nickel allergy may predispose patients to valve thrombosis.⁵

Why some, but not all, individuals with nickel allergy develop reactions to implanted devices is unclear and operators may wish to share decision-making with allergic patients. Bioresorbable scaffolds or drug-coated balloons may provide a future option, if proven efficacious and safe. While rare, nickel allergy and systemic eosinophilia may be observed with DP-DES.

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Disclosures

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Figure Legends

Figure 1. Severe stenosis of the right coronary artery A) pre and B) post atherectomy and implantation of 4 durable polymer drug eluting stents. C) In-stent thrombosis in an area of a D) new proximal right coronary artery aneurysm 43 days after initial stenting.

Figure 2. Diffuse maculopapular, pruritic rash due to systemic eosinophilia from durable polymer drug eluting stents.

Video 1. New proximal right coronary artery aneurysm associated with stent allergy.









