

Mepolizumab for Treating Systemic Allergic Dermatitis with Hypereosinophilia likely secondary to a Nickel/Cobalt-containing Coronary Artery Stent

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Systemic allergic dermatitis (SAD) to endovascular devices is not uncommon.¹ We present a patient with SAD and hypereosinophilia likely secondary to an unretrievable nickel/cobalt-containing drug-eluting coronary artery stent who responded to anti-interleukin (IL)-5 therapy.

CASE REPORT

A 65-year-old woman with no evident history of atopy or cutaneous sensitivity to non-gold jewelries was referred to our Allergy Center for evaluation of a persistent rash and eosinophilia. The patient had developed an intensely pruritic rash eleven days after coronary angioplasty and placement of two drug (zotarolimus)-eluting stents (DES) for her coronary artery disease. The DES had a non-exposed platinum iridium core with a cobalt alloy shell (35% cobalt, 35% nickel, 20% chromium and 10% molybdenum alloy). After the procedure, her eosinophil count increased from 80 to 210 cells/ μ l (reference range, 0 - 450 cells/ μ l). Since the patient had also started taking metoprolol and clopidogrel around the same time, the former was discontinued and the latter was replaced by ticagrelor, a structurally different P2Y₁₂ inhibitor, without rash resolution. Two weeks after the initial angioplasty, the patient had a third and similar coronary DES placed, and was started on a prednisone taper to treat the ongoing rash. The skin eruption initially resolved, but with decreasing prednisone doses, she had a flare-up of her rash with further spread. Combination of loratadine, cetirizine and topical mometasone 0.1% provided no relief. Resuming prednisone (50 mg/day) resulted in resolution of the rash. Before completing her prednisone taper, she was evaluated by an allergist who noted blood eosinophilia (1,250 cells/ μ l) and suspected SAD in light of the recent endovascular device placement. Prednisone was discontinued for 14 days in preparation for patch testing to selected metals (performed elsewhere, using AllergEAZE patch test chambers and patch test preparations from

SmartPractice, Alberta, Canada). At time of patch placement, a further increase in eosinophil level was noted (2,700 cells/ μ l). Patch testing (occlusion time of 48 hours) revealed sensitization to cobalt (++) and nickel (++) at D2 and D3 post patch placement (**Figure 1A**). Although cobalt and nickel were components of her DES, and SAD was considered likely, stent removal was deemed a last resort as it would require coronary artery bypass surgery. Upon presentation to our institution, a diffuse erythematous papular rash with coalescing plaques involving the trunk and thighs was noted. The eruption was unresponsive to topical corticosteroids (**Figure 1B**). An evaluation for alternative causes of hypereosinophilia was largely non-revealing. We initiated another 30-day prednisone taper starting with 50 mg/day. After initial resolution, the rash recurred as the prednisone dose was tapered to 5 mg/day. A skin biopsy revealed a superficial perivascular and interstitial inflammatory infiltrate with eosinophils, but without spongiosis. The patient was maintained on prednisone 7.5 mg/day and any attempted dose reduction resulted in a prompt flare-up of dermatitis. Concerned about steroid systemic side effects, and because of the concomitant (hyper)eosinophilia, we started the patient on subcutaneous mepolizumab 300 mg monthly, allowing us to taper and successfully discontinue prednisone after her third mepolizumab injection, without any further relapse of dermatitis (**Figure 1C**). Her eosinophil level decreased to 10 cells/ μ L following the fourth mepolizumab dose.

DISCUSSION

To our knowledge, this is the first case of SAD with hypereosinophilia likely due to a nickel/cobalt-containing coronary artery stent. Besides lack of spongiosis and eosinophils on skin biopsy, also the temporal association with stent insertion, exclusion of other likely causes, and positive patch testing might indeed favor SAD in this particular case. While sensitivity to

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zotarolimus discharged from the stent might be another cause, 85% of this drug is discharged by 60 days, making it a less likely culprit. Stent removal was, evidently, not feasible posing a treatment dilemma. The associated hypereosinophilia prompted us to trial mepolizumab, an anti-IL-5 monoclonal antibody, with satisfactory result. Eosinophils can be observed in tissue biopsies of allergic contact dermatitis (ACD)², and both eosinophilia and hypereosinophilia have been reported in SAD patients, also due to endovascular devices^{1,3}; however, the role of eosinophils in ACD and SAD pathogenesis remains unclear. Elevated serum IL-5 levels, a cytokine critical for eosinophil development, were noted in nickel-sensitive individuals indicating type 2 helper T lymphocytes (Th2) activation.⁴ These observations may explain mepolizumab effectiveness in our patient. Joshi *et al.* described a patient with SAD and eosinophilia due to a nickel-containing endovascular stent who responded to dupilumab, a monoclonal antibody that blocks both IL-4 and IL-13 cytokines.¹ Response to anti-Th2 biologics in these patients is intriguing and suggests a pathological role for Th2 cytokines in SAD. Investigating such role may provide a therapeutic avenue when avoiding the culprit allergen(s) is not feasible.

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FIGURE LEGENDS

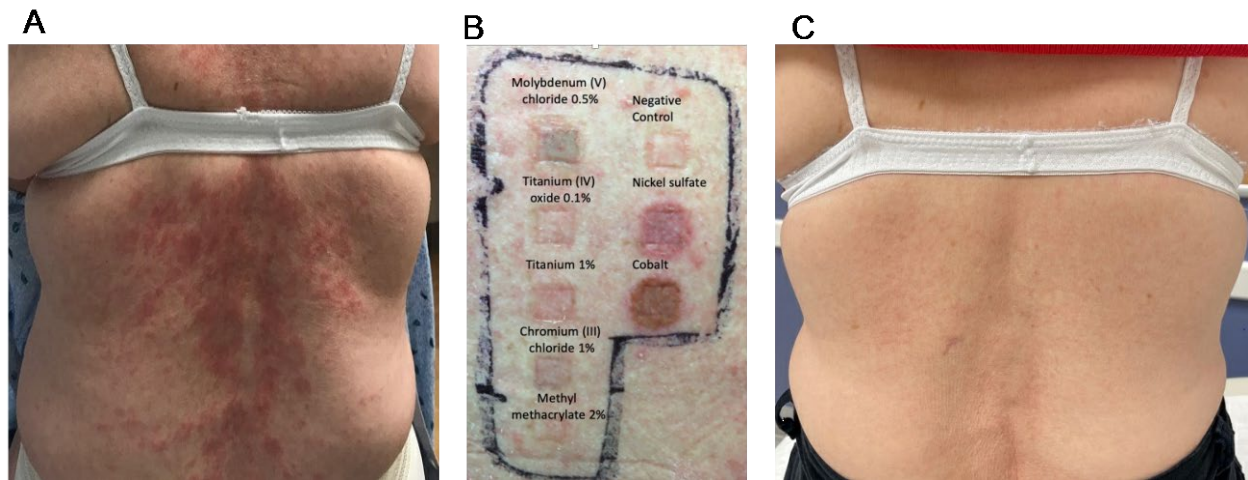


Figure 1. (A) Maculopapular skin rash two months after coronary angioplasty and placement of a nickel/cobalt-containing drug-eluting stent (DES). (B) Patch testing to molybdenum (V) chloride 0.5% pet., titanium (IV) oxide 0.1% pet., titanium 1% pet., chromium (III) chloride 1% pet., methyl methacrylate 2% pet., negative control (uncoated patch that contains neither allergen nor a vehicle), nickel sulfate and cobalt (not further specified) showing a positive (++) result to cobalt and nickel. (C) Resolution of the skin rash 3-months post mepolizumab therapy (patient was off prednisone).