



Cutaneous polyarteritis nodosa resulting from a paclitaxel-eluting balloon angioplasty

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INTRODUCTION

Cutaneous polyarteritis nodosa (cPAN) is a vasculitis of medium-sized arteries in the dermis and subcutaneous tissues. Etiology is currently unknown, although it may be immune complex mediated and has been linked to various infections, drugs, and autoimmune diseases.¹ Dermatologic abnormalities are common at presentation and may include nodules, ulcers, livedo reticularis, or purpura. We describe a rare case of unilateral cPAN that developed after placement of a drug-eluting balloon 4 weeks before the onset of clinical symptoms.

CASE REPORT

A 59-year-old woman with a medical history of multiple catheterizations presented with a unilateral, painful rash on her left leg (Figs 1 and 2). The rash had been present for several weeks. The patient was afebrile without leukocytosis but was undergoing treatment with vancomycin for a presumable infectious etiology. The patient had no history of preceding minocycline or propylthiouracil treatment. She did not have hepatitis. Notably, 4 weeks before presentation, a drug-eluting balloon, LUTONIX (BARD, Tempe, AZ), was placed in her left superficial femoral artery.

On physical examination, painful erythematous nodules were found on her left leg, extending from the ankle to the mid thigh, in the distribution of the superficial femoral artery. Necrosis, ulcers, and livedo reticularis were absent. Sensory and motor examinations were unremarkable, with no signs of neuropathy. Her right leg was spared. A punch biopsy of a nodule from her left leg found a

Abbreviations used:

cPAN:	cutaneous polyarteritis nodosa
IL:	interleukin
pANCA:	perinuclear antineutrophil cytoplasmic antibodies

neutrophilic vasculitis involving a large vessel in the deep dermis with some mild surrounding fat necrosis, most consistent with cutaneous polyarteritis nodosa (Figs 3 and 4).

The rheumatology department was consulted. Laboratory testing found slightly elevated perinuclear antineutrophil cytoplasmic antibodies (pANCA), further supporting a diagnosis of cPAN. Antiphospholipid antibodies, cryoglobulins, and cryofibrinogens were negative. Interleukin 6 (IL-6) levels were not measured. The patient was started on triamcinolone 0.1% topical ointment and prednisone, 1 mg/kg/d initially, which was then tapered. On follow up, clinical improvement with systemic steroids has been steady with marked improvement during the steroid tapering period. The patient has not experienced a flare during the steroid tapering period, although treatment with colchicine and dapsone have been considered if a flare arises.

DISCUSSION

Drug-eluting balloons commonly use paclitaxel, an antiproliferative drug to prevent restenosis after dilating the narrowed artery.² Paclitaxel is locally delivered to the wall of the artery, decreasing growth of the neointima by inhibiting proliferation of vascular smooth muscle cells.³ Carrier molecules are commonly used for delivery of antiproliferative

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Fig 1. Clinical image of anterior aspect of left leg.



Fig 2. Clinical image of medial aspect of left leg.

drugs to the target site.² Our patient received a paclitaxel-eluting balloon coated with polysorbate and sorbitol carrier molecules, both of which are hydrophilic molecules.⁴ In a study performed in a porcine model, 54.4% of initial coating components were found to wash off into distal circulation during balloon inflation, showing a phenomena known as *particulate embolization*.³ Hydrophilic carrier molecules were associated with greater paclitaxel tissue concentrations. The safety of coating compounds is concerning, as the long-term outcome of drug transferred into arterial tissue and entering the bloodstream is largely unknown. There are reports of vasculitis resulting from a superficial femoral artery angioplasty with a paclitaxel-eluting balloon.²

We propose that our patient's cPAN developed from paclitaxel and carrier molecules traveling downstream into circulation, initiating an immune response.

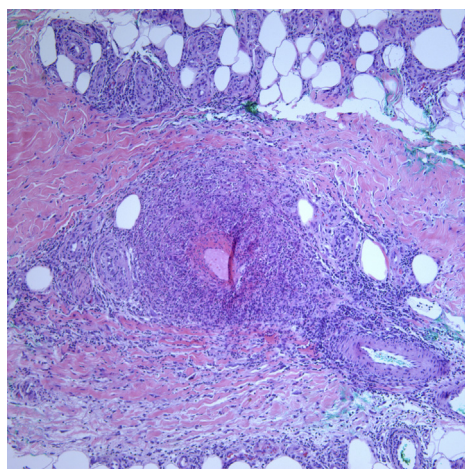


Fig 3. Histopathologic image at 10× magnification.

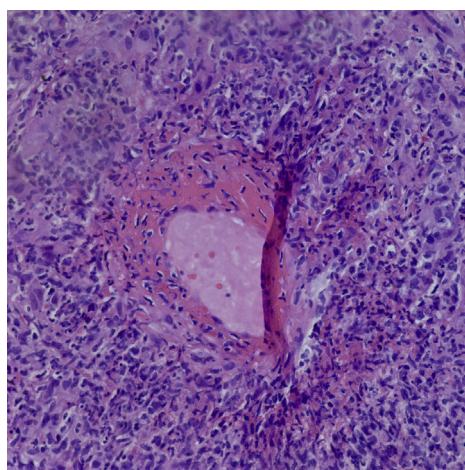


Fig 4. Histopathologic image at 40× magnification.

This finding is substantiated by the fact that the erythematous, painful nodules appeared only in the territory of the superficial femoral artery in her left leg, the symptoms developed 4 weeks after receiving the drug-eluting balloons, and the patient did not have any known risk factors for cPAN development such as infections, inflammatory bowel disease, or commonly implicated drugs. In the aforementioned case by Thomas et al,² a blood screen was negative for an underlying systemic vasculitis syndrome. Despite a slight elevation of perinuclear antineutrophil cytoplasmic antibodies in our patient, no other systemic diseases were implicated, further supporting a diagnosis of cPAN.

A study comparing first-generation paclitaxel-eluting stents with second-generation drug-eluting stents found that the former may be less safe and efficacious.⁵ Vascular lesions were compared from 149 autopsy cases. Paclitaxel-eluting stents showed higher inflammation scores, higher late stent

thrombosis, and higher fibrin deposition, when compared with the second-generation stent.⁵ Another report described severe dermatologic reactions at the treatment site in a patient receiving paclitaxel as a cancer therapy.⁶ The patient had erythematous patches on his extremities 6 weeks after the paclitaxel infusion. These lesions subsequently healed after discontinuation of the drug.

Paclitaxel, primarily used as a chemotherapeutic agent, modulates the immune systems in a positive and negative manner.⁷ Paclitaxel regulates lymphocyte activation, while also upregulating cytokines IL-1, IL-6, IL-8, and vascular endothelial growth factor.^{7,8} In our patient, we propose that treatment with a paclitaxel-coated balloon led to particle wash-off into distal circulation. This action initiated an immune response, creating conditions that allowed cPAN to develop. While we acknowledge that cPAN is generally benign, we present an adverse reaction and clinical sequelae resulting from a drug-eluting balloon.

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