A case of vasculitis after paclitaxel drug-coated balloon angioplasty

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INTRODUCTION

Paclitaxel drug-coated balloon (P-DCB) angioplasty is used to prevent and treat luminal restenosis. Distant embolization of paclitaxel has been documented in both human and animal studies; however, few reports of cutaneous manifestations associated with P-DCB use exist. Here we present a case of unilateral cutaneous vasculitis developing after an ipsilateral P-DCB angioplasty. Though our patient's case spontaneously resolved without complication, this case may help reveal downstream effects of P-DCBs initially thought to be rare and provides warning of potentially serious clinical consequences associated with the widely used procedure.

CASE REPORT

A 53-year-old man with a history of diabetes mellitus, hypertension, aortic aneurysm, thymolipoma, and peripheral artery disease presented to the cardiology clinic with a cutaneous eruption on the right lower extremity following a P-DCB angioplasty (Medtronic's IN.PACT Admiral DCB) of the right superficial femoral artery. Two days after the procedure, the patient developed swelling of the right lower extremity and associated mild pain. Days later, the patient contacted the cardiology office reporting the new skin eruption, prompting a dermatology consultation.

Cutaneous examination demonstrated multiple, erythematous, nonblanching papules on the right thigh, extending to the distal lower extremity (Fig 1). The lesions were mildly tender to palpation but otherwise asymptomatic. No additional cutaneous lesions were found elsewhere on the body. There was no cyanosis, pulses were normal, and there were no sensory changes. The patient had no history of a similar eruption in the past. The patient was started on clopidogrel bisulfate and aspirin immediately prior to the procedure but had not started any other new medications for over a year. The patient denied any application of prescription or over-the-counter topicals prior to the onset of the skin eruption, and he had no known history of allergies. Laboratory test results collected the day before the procedure were all within normal limits, including complete blood count and basic metabolic panel results.

Abbreviation used:

P-DCB: paclitaxel drug-coated balloon

A 4-mm punch biopsy revealed an organizing intraluminal thrombosis with surrounding necrosis and fibrin, as well as mixed inflammatory cell infiltrate composed of lymphocytes, histiocytes, neutrophils, and eosinophils. Clear, nongeometric spaces were found within the thrombus, possibly representing the silhouette of foreign material (Fig 2).

At a 2-week clinical follow-up, the patient's eruption had improved without treatment and completely resolved at the 3-month follow-up.

DISCUSSION

P-DCB angioplasty is widely used to prevent postangioplasty excessive intimal hyperplasia in patients with peripheral artery disease. Paclitaxel, a lipophilic antiproliferative drug, is released upon balloon inflation along with a drug excipient.

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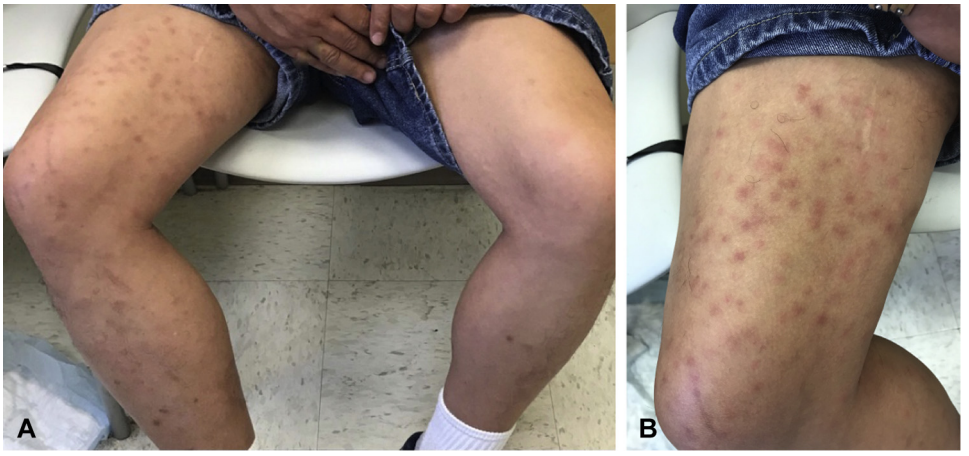

Fig. 1. A, Vasculitic rash on the lower right extremity following paclitaxel drug-coated balloon (P-DCB) angioplasty. **B,** Magnified view of erythematous round papules comprising the rash.

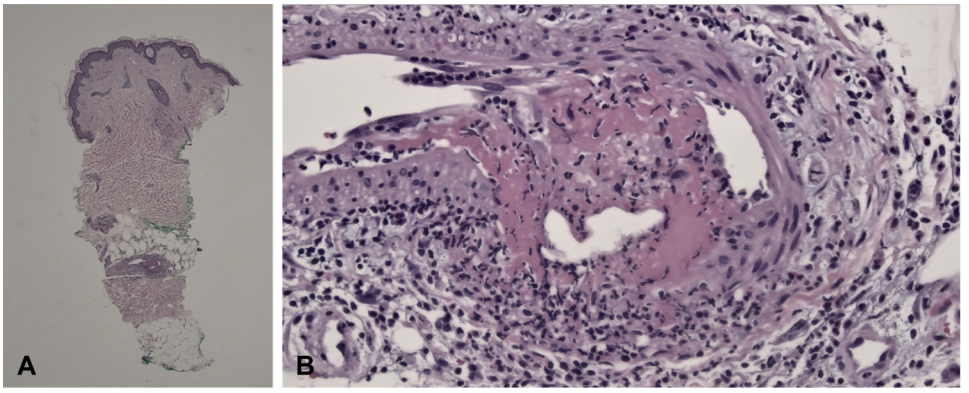

Fig. 2. Histopathologic findings. **A,** Punch biopsy showing intraluminal thrombosis surrounded by lymphocytes and leukocytoclasia. **B,** Vessel with fibrinoid necrosis and thrombosis broken up by clear, nongeometric spaces. (**A** and **B**, Hematoxylin-eosin stain.)

Paclitaxel implants in the arterial wall and serves as a local reservoir; however, evidence suggests that greater than 50% of both drug and excipient involved in P-DCBs may wash off into downstream locations.[1] We suspect that our patient experienced embolization of paclitaxel with subsequent development of a small-vessel vasculitis, given the time course and localization of the eruption. Our patient's eruption was confined to the distal, downstream territory of the treated right superficial femoral artery approximately 1 week after the procedure. Our suspicion is supported by the nongeometric spaces within the thrombus which are likely representative of paclitaxel and excipient. Our patient lacked systemic symptoms, and the eruption resolved without sequela within days, thus there was low suspicion for autoimmune, infectious, or other systemic etiology.

Downstream embolization of P-DCBs following a lower-limb angioplasty has been previously reported in the literature, including 4 reports of ipsilateral cutaneous sequela. Of those 4 reports, 3 were biopsied and revealed panniculitis, polyarteritis nodosa, and small-vessel vasculitis, respectively.[2-4] All 3 cases were treated with systemic steroids with complete resolution within 3-4 months. In the case of polyarteritis nodosa, the patient developed symptoms approximately 1 month after the procedure, suggesting a more delayed immune-related phenomenon in contrast to the more acute-onset manifestation in our patient, which was likely secondary to direct embolic effects. Embolization of polymer coating with subsequent vasculitis has also frequently been reported; however, drug/excipient embolization is far less common. Given that the DCB in our case did not have a polymer coating, this phenomenon can be ruled out.

Interestingly, our patient and the 4 reported patients each had an IN.PACT Admiral DCB, which delivers a paclitaxel concentration of 3.5 $\mu g/mm^2$ with a urea excipient. Hydrophilic excipient molecules such as urea are particularly likely to embolize;

in fact, the main driver of drug migration from DCBs is the chemical makeup of the coating.[1,5]

While no dangerous phenomena stemming from downstream embolic incidences in the lower limb have been reported to date, the long-term effects of drug embolization into systemic circulation and implantation into vital organs is unknown. Cutaneous vasculitis must be considered seriously, as it could be a manifestation of more threatening side effects.

Though a past meta-analysis of paclitaxel-coated devices in femoral and/or popliteal arteries has suggested a significant difference in mortality between P-DCBs and percutaneous transluminal angioplasty.[6] Newer assessments with longer follow-up data have suggested otherwise. In the most recent 3- and 5-year-long follow-up studies, no correlation between paclitaxel exposure and mortality was found.[7,8] In response to the conflicting data, the Food and Drug Administration encourages continued collection of mortality data and recommends continued use of P-DCBs with patients, especially those at risk for restenosis or repeated femoropopliteal interventions. Thus, the long-term safety of P-DCBs is in question, and further analysis with more extensive follow-up data weighing risks versus benefit is ongoing.[9]

Our patient developed this rash after a drug-eluting balloon angioplasty. Though varying levels of paclitaxel have been discovered in distal tissues following a P-DCB, distal vascular lesions resulting from particle embolization have not been well documented. Our case is one of few reported cases of a vasculitic rash secondary to distal embolization of P-DCB drug and excipient.

Conflicts of interest

None disclosed.

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