Case Report

Pulmonary Circulation

Occult catheter rupture causing episodic symptoms in a patient treated with epoprostenol

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Abstract

Infection, thrombosis, and catheter dislodgment are well-recognized potential complications of chronic intravenous prostanoid therapy for pulmonary arterial hypertension. As long-term outcomes of pulmonary hypertension patients improve, novel adverse events are likely to arise. We describe the sudden development of unexplained hypotension and lightheadedness in a patient receiving intravenous epoprostenol for several years, ultimately determined to be due to an unusual catheter complication, not previously described in this population.

Keywords

pulmonary arterial hypertension, epoprostenol, catheter rupture

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Case report

A 61-year-old woman with idiopathic pulmonary arterial hypertension (PAH) managed with intravenous epoprostenol and oral tadalafil was seen for evaluation of recurrent episodes of lightheadedness, nausea, and flushing. Episodes first began one month before current presentation when she noted severe lightheadedness and palpitations upon waking in the morning, leading her to call 911. On evaluation by emergency medical services, her systolic blood pressure was in the 50 s with heart rate in the 80 s in sinus rhythm. She received 500 mL normal saline and was brought to the emergency department. Blood pressure on arrival was 113/67 and she felt markedly improved. She was admitted overnight for observation and telemetry monitoring with no further events. Her episode was attributed to vasovagal symptoms and she was discharged home. Following this event, she had numerous recurrent episodes of more mild, sudden onset lightheadedness, flushing, palpitations, and nausea. Symptoms would last for 5–15 min and then resolve.

There had been no recent changes to her PAH medications, mixing practices, or pump settings. Epoprostenol was infused at 48 ng/kg/min (concentration = 45,000 ng/mL, 77 mL/24 h) using the CADD-Legacy Ambulatory Infusion Pump and a single lumen 9.6 French tunneled silicone catheter, placed in the right subclavian position eight years earlier. There were no recent pump alarms and episodes did not respond to changing out her existing pumps to new ones. Inspections of the catheter, connections, and exit site were unremarkable. There were no fevers or infectious signs or symptoms. A right heart catheterization was planned to further evaluate her symptoms.

On the day of her planned catheterization procedure, the patient was preparing to change her epoprostenol cartridge and tubing when she noticed a focal area of ''ballooning'' of her tunneled catheter adjacent to the clamp. With gentle compression of this area, the dilated area collapsed with immediate reproduction of symptoms of lightheadedness and flushing. She presented to the emergency room for further evaluation. A catheter repair was performed with resection of the dysfunctional portion of the catheter and

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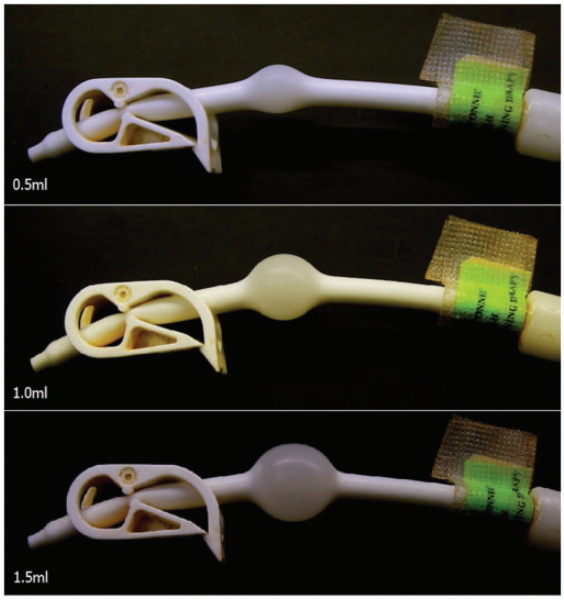

Fig. 1. The resected segment of the patient's tunneled catheter, injected with the indicated amounts of fluid against a closed clamp. This maneuver unmasked an aneurysmal segment of the catheter and the cause of the patient's episodes.

replacement with a new end segment. The patient did very well after catheter repair with complete resolution of symptomatic episodes. The dysfunctional catheter segment was further explored with injection of various volumes of fluid while clamped, revealing a focal aneurysmal segment (Fig. 1).

Discussion

The focal dilatation of catheter, occurring just upstream of our patient's clamp, likely developed secondary to clamp-site damage and stenosis. In the setting of stenosis and upstream increase in intraluminal pressure, the walls of the catheter weaken and dilate, essentially representing a contained partial rupture. As her infusion pump continued to deliver medication uninterrupted, no pump alarms activated despite the fact that the patient experienced several minutes of low or absent drug delivery, with epoprostenol accumulating within the aneurysmal segment. In this case, the elasticity of the catheter was preserved, allowing spontaneous or induced contraction with bolus of the prostanoid, leading to symptoms as described. The external catheter further returned to its normal appearance, with routine inspection of the catheter unrevealing. Though her episodes were suggestive of excess prostanoid, it was challenging to determine the etiology until the aneurysmal segment was visualized.

We would expect this type of catheter complication to be more common with increasing age and use of the catheter. Intravenous epoprostenol and treprostinil have been approved in the United States for PAH since 1995 and 2004, respectively. Many PAH patients on these therapies are surviving 5–10 years or more.[1,2] Our patient, for example, had been treated with epoprostenol for more than 15 years at the time of this event, and her current catheter had been in place for eight years. A tunneled central catheter (TCC) for intravenous prostanoid is considered ''permanent'' and there are no guidelines for (or against) routine replacement; in practice, catheter replacement is only done in situations of infection or malfunction. In other populations using long-term TCCs, guidelines do not recommend routine scheduled catheter replacement.[3–5]

Several studies detail infectious complications for PAH patients receiving intravenous prostanoids, with event rates in the range of 0.03–0.36 per 1000 catheter-days.[1,6–8] However, much less attention has been paid to non-infectious catheter-related complications in this population. Mechanical complications have been noted as relatively unusual events in the controlled trials,[9,10] with few case reports otherwise describing non-infectious catheter-related adverse events.[11]

Permanent TCCs are used for a variety of more common indications, including chronic hemodialysis as well as administration of chemotherapy or parenteral nutrition. In a large study of home infusion catheters, catheter dysfunction preventing normal use occurred at a rate of 0.29 per 1000 catheter-days in those with TCCs; the majority of these events were non-thrombotic. This is compared to the observed infection rate of 0.70 per 1000 catheter-days in these same patients.[12] Other studies in varied populations with TCCs have found mechanical complications (e.g. dislodgment, occlusion, rupture) to be at least as common as infectious complications.[13–15] An investigation involving 584 patients receiving parenteral nutrition studied 99 patients with mechanical complications of a TCC; 65% of mechanical complications were classified as catheter rupture, described by the authors as ''balloon-like'' expansion of the external catheter, most often near the clip.[16] Other data supports that catheter rupture is more likely in silicone (vs. polyurethane) catheters, similar to those used in most intravenous prostanoid patients.[17,18]

The short half-life ($t_{1/2}$) of prostanoids, in particular epoprostenol ($t_{1/2} = 2$–6 minutes), necessitates continuous delivery via ambulatory infusion pump. This short $t_{1/2}$ also means that small errors in dosing can have large effects. In this case, we estimate that the patient was inadvertently bolused 1–1.5 mL of epoprostenol with her current presentation, and possibly much more during her previous hypotensive episode. Depending on rate and concentration, even this small bolus can be substantial. For our patient, this provided her with a bolus dose that was intended to be given over 20 min. The pharmacokinetics and/or lack of vasoactive side effects of most TCC infusions would not create such dramatic symptoms should a similar catheter malfunction occur. It is even likely that a comparable bolus of treprostinil, with longer $t_{1/2}$, could go unnoticed. Thus, this type of catheter damage may certainly be under-recognized. In the systolic heart failure population, chronic

dobutamine infusion could in theory have the same risk with a similar type of malfunction; however, these patients have worse survival and are less likely to be using a catheter for a long duration.[19]

In summary, mechanical catheter complications of chronic intravenous prostanoid therapy, though poorly described in the PAH literature, must be recognized by those caring for PAH patients. As PAH patients enjoy improved survival in the modern treatment era, such events will become more common, particularly for those with older tunneled catheters. While routine replacement of older catheters likely leads to more harm than benefit, close inspection or provocation of the external catheter may reveal surreptitious mechanical problems in symptomatic patients.

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Conflict of interest

The author(s) declare that there is no conflict of interest.

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