CASE REPORT

Erectile dysfunction: a window to the heart

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SUMMARY

Erectile dysfunction (ED) is an early marker of coronary artery disease (CAD) and often manifests before the development of symptomatic CAD. In this case report, we present a 60-year-old man with ED, who demonstrated limited response to the standard management strategies and was subsequently treated with percutaneous pelvic intervention (PPI) of the internal pudendal artery. While on the table for PPI, the patient described a classical history of angina, on which basis he underwent coronary angiography and was found to have narrow proximal left anterior descending stenosis. Coronary artery stent placement was then performed using standard techniques. PPI of pudendal artery stenoses with stents is feasible and can improve cavernosal blood flow and venous leakage as well as erectile function.

BACKGROUND

Erectile dysfunction (ED) is defined as the persistent inability to attain or maintain an erection sufficient for satisfactory sexual performance. ED is a major health problem, affecting more than 150 million men worldwide and expected to rise to 322 million by 2025.[1] ED is common and affects nearly 40% of men over the age of 40 years, and increases in frequency with age.[2]

Successful treatment of ED has a strong impact on improving the quality of life for many patients, particularly in the area of mental health. ED is initially managed by identifying and treating any reversible causes, implementing lifestyle modifications and addressing traditional cardiovascular (CV) risk factors, followed by pharmacological trial with a phosphodiesterase-5 inhibitor (PDE-5I). However, up to 50% of patients with ED have a suboptimal response to PDE-5Is, the reasons for which are not fully understood.[3] Currently available alternatives and adjunctive therapies for patients who are proven non-responders to PDE-5Is include vacuum constriction devices, intracavernous injections, topical and intraurethral applications of prostaglandin E1 and, finally, implantation of penile prostheses.[4] However, many patients and their partners find these other modalities of treatments cumbersome and uncomfortable, and the lack of spontaneity often results in poor long-term compliance. There is, therefore, a growing need for additional and novel therapies for ED.

Vasculogenic ED (VED) accounts for about two-thirds of patients with ED.[2] The erectile-related arteries undergo the same atherosclerotic process as any other vascular bed. This limits the increase in arterial inflow to the cavernosal system needed to achieve an erection and may account for perhaps one-third of patients with VED. Percutaneous pelvic intervention (PPI) using endovascular stents could restore adequate arterial inflow to the penis and, in addition to optimal medical therapy, could correct erectile failure. This is emerging as a promising and exciting area of research in vascular medicine.

CASE PRESENTATION

A 60-year-old man was referred to the ED service with a 5-year history of erectile problems. His sexual health inventory for men (SHIM) score was 5/25, indicating severe ED. Risk factors included type II diabetes, heavy smoking, treated hypercholesterolaemia and a family history of ischaemic heart disease. He had no other relevant history. His drug history included metformin (1 g once daily), gliclazide (80 mg once daily), sitagliptin (100 mg once daily), simvastatin (40 mg once daily) and lisinopril (2.5 mg once daily). Clinical examination was unremarkable. Of relevance was a finding of low total serum testosterone of 7 nmol/L (normal >12 nmol/L).

TREATMENT

Initial management

The patient was initially prescribed sildenafil 100 mg and testosterone replacement therapy using Nebido injections, but this only achieved an initial and brief improvement. Sildenafil was subsequently substituted with tadalafil 20 mg, twice a week, but this was also suboptimal. At this point, the patient was referred to our ED service.

ED service management

Following the initial assessment, the patient was changed to daily tadalafil 5 mg but this was also unhelpful. He was then switched to vardenafil 20 mg twice a week and, in view of a persistently low total serum testosterone (5.8 nmol/L), he was prescribed testogel. This failed to produce a satisfactory result, despite normal testosterone of 18 nmol/L. He was referred to our vacuum pump expert but re-presented 5 months later, frustrated with limited response, and the rather cumbersome vacuum pump. He was switched to daily tadalafil 5 mg with 20 mg top ups once or twice a week. However, after 4 months his condition was unchanged.

Despite the absence of angina, he underwent an exercise treadmill test (ETT) due to his high-CV risk factor profile, including VED. Results from the test proved negative.

Dynamic penile Doppler test was carried out before and after 20 μg of alprostadil injection, achieving partial tumescence with an erection hardness score (EHS) of 2/4. There was a reduction in peak systolic velocity (PSV) in left (22.2 cm/s) and right (26.2 cm/s) cavernosal arteries (normal

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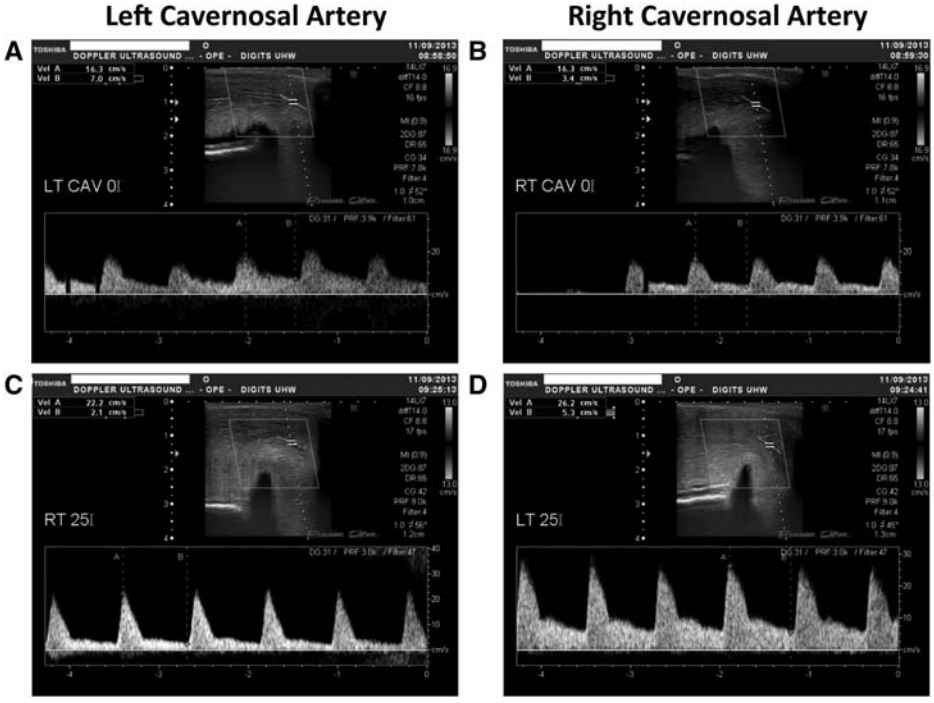

Figure 1 Penile Doppler ultrasound scan of patient's left and right cavernosal arteries before (A and B), and 25 min after Caverject injections (C and D). Each image shows the peak systolic velocity and peak diastolic velocity taken at each instance.

>35 cm/s), suggesting reduced arterial inflow. The end-diastolic velocity was within normal range on the left (2.1 m/s) but was bordering on abnormal on the right (5.3 m/s), indicating possible venous leakage (figure 1).

Invasive percutaneous management

In view of a consistently poor response to initial therapy with all the routinely available treatment modalities and abnormal penile Doppler, and after a very careful discussion and consent process, the patient agreed to undergo a pelvic angiogram. This was carried out via the radial route and demonstrated diffuse distal disease in the right internal pudendal artery (IPA), and a long but discrete segment of severe stenosis in the left IPA (figure 2).

Six weeks later, the patient underwent PPI of his erectile-related artery via the right femoral route. A Cobra catheter and a Terumo wire were initially used to get to the left IPA. A Pilot 50 guide wire traversed the lesion and after predilation, a 2.25×26 Resolute stent was deployed with an excellent angiographic result (figure 2).

Just prior to starting the procedure, while on the table, the patient gave a classical angina history, and on this basis underwent coronary angiography immediately after pudendal artery stent placement. This showed a proximal left anterior descending (LAD) stenosis, which was also satisfactorily treated with a stent, in the standard way (figure 3).

OUTCOME AND FOLLOW-UP

There were no complications associated with the procedures and the patient was discharged home the same day. At clinical follow-up 3 weeks later, a penile Doppler was repeated using a smaller dose of 15 µg of alprostadil. This achieved normal tumescence compared with the previous study, with an EHS of 4/4. The left cavernosal artery PSV normalised (35.7 cm/s) with absent end-diastolic flow. The right cavernosal artery PSV was still reduced but there was a normal veno-occlusive response with reversed diastolic flow (figure 3). The patient's SHIM score improved to 15/25.

DISCUSSION

This case report highlights several important issues relating the management of ED and coronary artery disease (CAD) in routine clinical practice. First, it demonstrates the role of ED as an early marker of CAD. Despite the absence of angina or evidence of exercise-induced cardiac ischaemia at the time of the initial presentation with ED, the patient later developed angina with severe proximal LAD stenosis 18 months later. The recognition of ED is of critical importance in the CV patient. In a recent and very large meta-analysis of nearly 93 000 patients, the significance of ED as an independent predictor of risk for

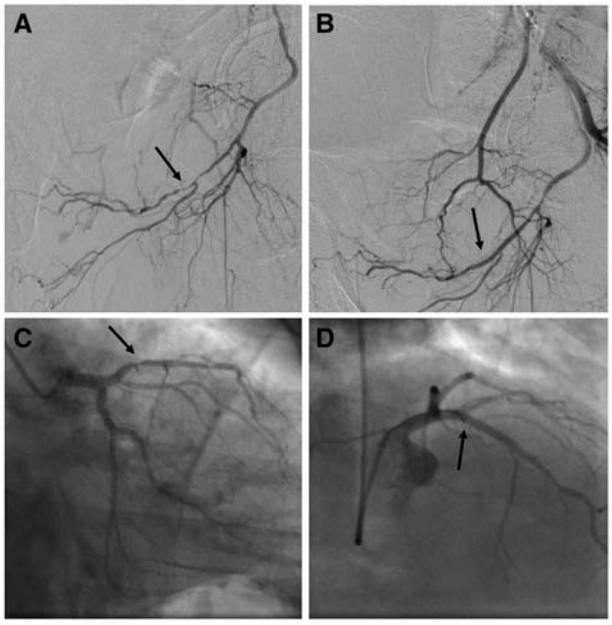

Figure 2 Percutaneous pelvic intervention showing arrowed left internal pudendal artery before (A) and after (B) stenting, and coronary angiography showing proximal left anterior descending before (C) and after stenting (D).

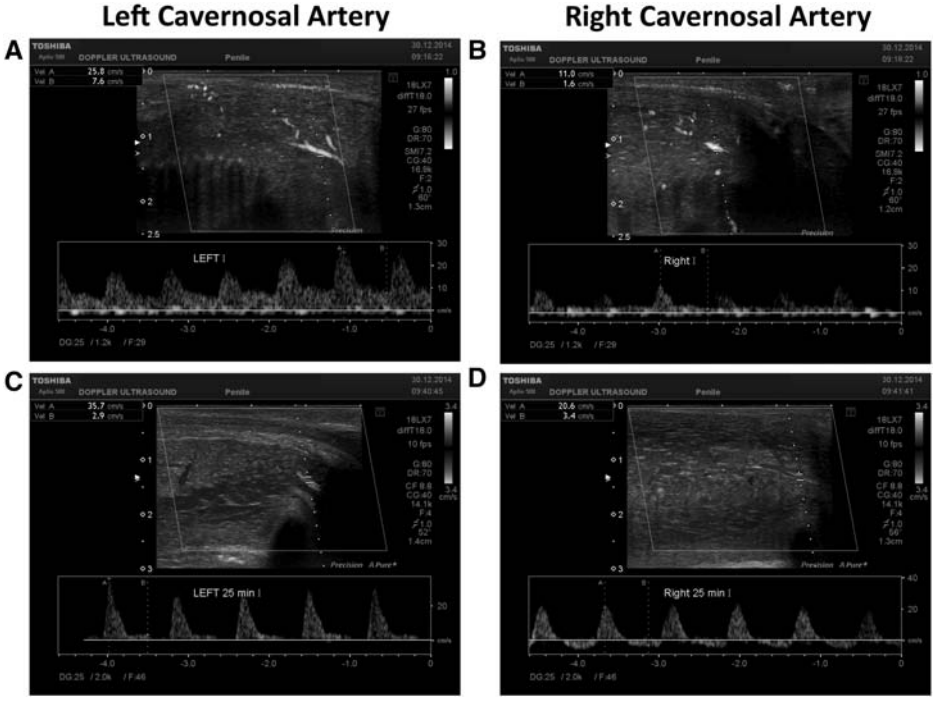

Figure 3 Post-stenting penile Doppler of patient's left and right cavernosal arteries before (A and B), and 25 min after Caverject injections (C and D).

future fatal and non-fatal CV events, CAD, stroke and all-cause mortality was confirmed, with an estimated relative risk of 2.0 over 5–10 years.[5] ED precedes clinically overt CV events by 2–5 years (3 years on average), providing a unique window of opportunity for diagnostic and therapeutic intervention.[5 6]

Second, this report highlights the controversial role of non-invasive testing in the management of patients with ED. Despite a negative ETT, our patient probably had subclinical CAD, which manifested later on, highlighting the low specificity and sensitivity of the test. Previous studies have demonstrated that inducible ischaemia occurs in 22% (5–56%) of patients with ED with ETT.[7] Furthermore, in a prospective angiographic study, 19% of patients with ED had clinically silent obstructive CAD.[8] The role of non-invasive testing and which modality of test to use requires further evaluation. However, due to its ease of access and cost, ETT is likely to remain important in the assessment of these patients. It is likely that more sensitive and specific tests such as myocardial perfusion scanning, pharmacological stress echocardiography, coronary artery calcium scoring or myocardial RI will supersede ETT, but this remains to be further evaluated in this particular clinical setting.

Third, this case is an example of successful treatment of ED in a CV patient with severe erectile-related artery stenosis using PPI. Stenting of the left IPA in our patient was feasible and produced a concomitant increase in penile flow, as demonstrated by a rise of 13 cm/s in PSV in the left IPA. This was associated with an apparent improvement in the veno-occlusive mechanism, as demonstrated by the end diastolic flow reversal. This results from more blood entering the corpora cavernosa, compressing the emissary veins, thereby reducing venous leak. There was also a subjective improvement of erectile function after the procedure, with the SHIM score rising by 10 points after the procedure. Furthermore, there was an objective improvement in EHS at follow-up penile Doppler. Importantly, these improvements were in the scenario of a medically refractory patient, where the response to initial treatment with three PDE-5Is, intracorporal prostaglandin E1 and vacuum pump therapy were either suboptimal or unacceptable.

In the presence of proximal fixed stenosis of the erectile-related arteries, enhancing smooth muscle relaxation using pharmacological therapy may produce a limited response due to a reduction in arterial inflow. PPI offers dual benefit to patients with VED by restoring adequate arterial flow and enhancing the occlusion of the emissary veins, and limiting venous outflow and sustaining the erection. Furthermore, this improvement in cavernosal blood filling may result in a much more favourable response to the initial medical therapy with PDE-5Is and intracavernosal injections of vasoactive agents. According to the current recommendations of the European Association of Urology guidelines for ED, an inadequate treatment outcome in our patient would warrant a consideration of penile prosthesis implantation.[9] However, this is far more invasive and costly, and is frequently not acceptable to many patients and their partners.

PPI of the erectile-related arteries is emerging as a novel therapeutic option for patients. The zotarolimus-eluting peripheral stent system for the treatment of ED in men with suboptimal response to PDE-5Is (ZEN) trial was the first feasibility and safety trial to evaluate the use of a balloon-expandable peripheral drug-eluting stent to treat patients with atherosclerotic ED and IPA stenosis.[10] Stenting of the IPA was technically feasible, safe and associated with meaningful subjective improvement in erectile function in most (69.6%) but not all patients. In addition, the procedure produced an increase in penile flow parameters as demonstrated on duplex ultrasonography at 6 months poststenting. Furthermore, angiographic follow-up demonstrated no stent fractures and reasonable binary patency. The preliminary data from the Incidence of Male Pudendal Artery Stenosis in Suboptimal Erections Study (IMPASSE; NCT01341483) provides further evidence for the use of endovascular stents for the treatment of ED.

It has been previously demonstrated that increased cavernous intimamedia thickness (cIMT) could be a new parameter in addition to PSV, and that this can identify a vascular pathogenesis of ED in an earlier phase.[11] Cavernosal arteries are not currently regarded as a target of endovascular treatment with stents. However, future studies should evaluate if cIMT can be used as

a reliable screening tool to identify patients with VED who can benefit from PPI, as well as assess whether it is a reliable parameter of clinical outcome following endovascular treatment of larger and more proximal erectile-related arteries.

Learning points

- Coronary artery disease is more common in patients with erectile dysfunction (ED) than is generally appreciated, and should be considered in all patients with ED and vice versa.
- In patients with ED with limited response to standard therapies, percutaneous pelvic intervention of the erectile-related arteries is effective at restoring adequate blood flow to the penis, and can produce clinically significant improvement in objective and subjective measures of erectile function.
- Further studies confirming the efficacy and durability of this therapy are essential before widespread adoption of endovascular angioplasty and stenting as a standard therapeutic option for vasculogenic ED.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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