Endovascular treatment for post-thrombotic syndrome. Two case studies and a literature review

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\textbf{Abstract}  The recent application of endovascular treatment techniques to venous pathologies has meant that new therapeutic solutions can be offered to patients suffering from post-thrombotic syndrome. This often-underestimated condition frequently complicates cases of deep vein thrombosis, whether treated or not, leading to a chronic and disabling set of clinical symptoms (oedema, claudication, pain, venous ulcers, etc.) due to the combination of the pathophysiological phenomena of obstructions and reflux. These clinical signs see only minimal improvement when managed with the classic medical treatment, venotonics agents, and venous compression. We report the cases of two patients suffering with chronic post-thrombotic venous obstruction of the lower limbs in whom endovascular treatment brought clear and long-lasting clinical improvement.

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Post-thrombotic syndrome (PTS) is a common complication of deep vein thrombosis in spite of widespread usage of anticoagulants. One patient out of every two or three will develop it after having had deep vein thrombosis (DVT) treated with anticoagulants [1]. Two clinical forms have been described. The first and less serious form presents as venous stasis, with varicose veins, oedema, depigmentation, heavy and "restless" legs; the second and more serious form involves significant pain, chronic oedema and ulcers [2]. PTS has a major impact on patients’ quality of life as well as significant medical, economic and social consequences in terms of care and cessation of work [3]. The clinical symptomatology reported is categorised into seven stages depending on the seriousness

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of the symptoms (Table 1) [4]. The pathophysiology of PTS concerns the combination of two phenomena:

- deterioration of the intima, valve incompetence and compromised calf muscle pump function, leading to chronic reflux;
- persistent chronic proximal venous obstruction (iliac veins, common femoral vein), due to patency of the proximal vein being incompletely re-established [5]. This results in serious cases of PTS [6].

We report here the endovascular technique used and the clinical outcome in two case studies of patients with serious PTS.

**Case 1**

A 50-year-old female was seen for diagnostic and therapeutic management of a chronic oedema of the left lower limb, which had suddenly worsened and become painful. The main feature of her medical history was a left DVT 10 years previously. This chronic thrombosis had caused disabling symptoms but the patient had not acted on them and so her doctor had not had the opportunity to refer her to a specialised centre. This presentation of PTS is classed as C3s, Es, Ad, Po according to the Clinical, etiological, anatomical and pathophysiological (CEAP) classification [4]. Explorations (Doppler ultrasonography, pulmonary and venous CT angiography) revealed a recent thrombosis of the left external iliac vein with a fibrous occlusion of the common iliac vein. The results of coagulation investigations to check for thrombophilia were normal. In spite of 15 days of anticoagulant treatment that the patient adhered to, this painful oedema of the left lower limb persisted (the diameter of the thigh was 36 cm on the right compared to 41.5 cm on the left). A repeat Doppler ultrasound scan was carried out in view of the absence of any favourable clinical progress. This showed that the occlusion persisted in the left common iliac vein. In view of this persistent and hyperalgesic chronic occlusion of the left common iliac vein, endovascular revascularisation was carried out using the technique described below. Firstly, a 5F introducer sheath was placed in the left common femoral vein under ultrasound guidance. Venography performed through the sheath. It confirmed the presence of the left common iliac vein occlusion. And allowed the area and extent of the obstruction to be localised. The venography also showed that thrombi were present (Fig. 1). In order to protect against pulmonary embolism during the recanalisation procedure, a retrievable vena cava filter (ALN™ Implant Chirurgicaux, Ghisonaccia, France) was placed in the inferior vena cava (below the renal veins), by a jugular access. Under effective anti-coagulation (Heparin 2.000 IU), recanalisation of the occlusion was carried out using a straight 0.035” hydrophilic guidewire. This guidewire was manipulated through a 5F vertebral catheter. The occlusion was easily crossed. The angioplasty was conducted using a balloon 8 mm in diameter and 40 mm long. When the balloon was inflated, two focal areas of severe stenosis were revealed, situated in the common iliac and external iliac veins. Repeat venography further to angioplasty showed the venous system to have a striated appearance together with the presence of numerous endoluminal thrombi, and a moderate recoil. Note: BTW in French the current term is “retour élastique” and in English recoil. A 10 mm × 60 mm self-expandable stent was placed over the residual stenoses. Manual thromboaspiration was carried out to extract the remaining thrombi. The final venography confirmed that the veins treated were patent. Straight after the procedure the patient was started on dual anti-platelet aggregation therapy with clopidogrel and aspirin, prescribed for a 1-month duration. Oral anticoagulant therapy was prescribed for a 3-month duration. The vascular medicine team planned to consider whether to prolong anticoagulant therapy after the third month of monitoring. The vena cava filter was removed successfully 2 weeks after the procedure. This time, angiography of the vena cava conducted prior to extraction of the filter confirmed that the iliac and femoral veins were patent without further stenosis (Fig. 2). The clinical symptomatology was seen to resolve within ten days. Six months after the intervention, the symptoms had completely disappeared and a Doppler ultrasound confirmed that the external and common iliac veins and the common femoral vein were patent.

**Case 2**

A 66-year-old male had a 5-year history of recurrent DVT of the right lower limb. During the most recent episode,
right iliopopliteal thrombosis had been complicated by PTS involving significant oedema of the lower limb and venous ulcers. The ulcers took several months to heal, and the oedema persisted. Although the patient was on long-term anticoagulant therapy, as well as class III venous compression, the oedema remained disabling. This presentation of PTS is classed as C5s, Es, Ad, Po according to the CEAP classification [4]. Thrombophilia investigations did not reveal any abnormalities. A Doppler ultrasound scan of the veins showed complete and chronic occlusion of the right external iliac vein, and chronic partial occlusion of the common femoral vein and superficial femoral vein. Venography was carried out via a venous puncture in the back of the right foot and revealed multiple chronic venous occlusions in the right external iliac vein and common iliac vein as well as stenosis of the common femoral vein. Numerous collateral veins anastomosed with the pelvic venous system were draining the right lower leg via the left iliac and common femoral veins (Fig. 3). Retrograde access for the endovascular intervention was gained through the right and left common femoral veins. This allowed catheterisation of the common femoral vein stenosis and, using the crossover technique, the iliac occlusion could be passed. In a the same way as in our first clinical case, an angioplasty was carried out using an 8 mm/40 mm balloon in the common femoral vein, followed by angioplasty using a 9 mm/40 mm balloon for the occlusion of the iliac veins. The recoil of the external iliac and common femoral veins required a 10 mm/60 mm self-expanding stent. The final venography showed the femoral and iliac veins to be fully patent. Furthermore, none of the pelvic collateral veins could now be visualised (Fig. 4). Straight after the procedure the patient was started on dual anti-platelet aggregation therapy (clopidogrel and aspirin), prescribed for a 1-month duration, together with oral anticoagulants. The clinical symptomatology resolved within five days. Six months after the intervention, the oedemas had resolved and the patient did not report that the venous ulcers had returned. A Doppler ultrasound confirmed that all of the recanalised vessels were patent.

**Discussion**

The two clinical cases presented above illustrate the technical feasibility of recanalisation of proximal veins and the
clinical benefits that it can offer patients with PTS. The collateral veins linking to the pelvic system and their subsequent disappearance seen in the second case are evidence that low-pressure venous flow had been restored. This is evidence that the intervention, which offers an instant improvement in symptoms, is haemodynamically effective.

This principle is based on a percutaneous approach to the proximal venous system using common femoral access. The techniques used for recanalisation, angioplasty and stent implantation are the same as those applied in the arterial system.

There are currently no publications that provide level A or B evidence, but a number of studies providing level C evidence. These studies report technical success rates of 90 to 98%. Primary patency after 1 and 4 years ranges from 50 to 83%. Secondary patency after 1 and 5 years is 81 and 93% respectively [7–10]. Complications are rare (< 6%). When they do arise, they usually concern early rethrombosis of the revascularised vessel and minor haematomas at the puncture site. There has been no report of serious haemorrhage in spite of the use of dual anti-platelet aggregation therapy combined with anticoagulants [7–10]. The authors report a strong correlation between patency and resolution of symptoms. The indication for revascularisation applies to patients with stage C3 and higher PTS according to the CEAP classification (Table 1) [11]. However, although the results are remarkable some questions remain unanswered. There has been no published article that satisfactorily studies the possibility of venous reflux arising or worsening after recanalisation.
From a technical point of view, recanalisation may be carried out ipsi- and/or contralaterally. An angioplasty alone is rarely sufficient, because in a system with low pressure and low flow it is essential that a perfect result in terms of morphology is achieved. The slightest vessel wall damage or change in pressure gradient will cause immediate re-obstruction. This is why long self-expansible stents with a large diameter are required to treat these patients. Although there is no consensus on the use of a retrievable vena cava filter to protect against pulmonary embolism during recanalisation of chronically occluded proximal veins. Their use for preventive purposes seems to be justified. O’Sullivan recommends using them in patients with pulmonary hypertension, right ventricle dysfunction, and a recent history of pulmonary embolism or venous thrombosis during procedures to revascularise chronic or acute venous occlusions [12].

Triple anti-thrombotic therapy combining aspirin, clopidogrel and an anticoagulant is usually prescribed in order to prevent rethrombosis [12,13]. Justification for this approach is based only on opinion and analogies with the treatments prescribed after coronary artery stenting. Currently there is no established consensus on the safety and efficacy of this combination of anti-platelet drugs and an anticoagulant in patients who have received a venous stent. This prescription is, however, commonly given for a 3-month period [12,13]. Anti-platelet aggregants have not been proved to be effective in the treatment of DVT. Anticoagulants remain the reference therapy for DVT and pulmonary embolism in the acute phase. Ruiz-Gimenez et al. assessed the risk of complications of haemorrhage due to anticoagulants in the specific context of DVT/PE to be 0.1%, 2.8%, and 6.2%, in low-, medium- and high-risk patients respectively. This triple anti-thrombotic therapy represents a potential risk of haemorrhage, and must be subject to both a rigorous assessment of the risk/benefit balance for patients when they are selected and very close monitoring.

A number of radiological investigations are required in order to propose this indication and consider this revascularisation technique. Doppler ultrasound is the first step for screening patients. It can detect the pathology of reflux and locate the occluded area, identify the direction of venous flow, and the possible routes of derivation. CT angiography and MRI angiography capture morphological information on the localisation and extent of the occlusion. In any case, as soon as the presence of a proximal obstacle is confirmed, lesion anatomy will be confirmed by venography. It is immediately followed by recanalisation. Comparable reports have been made in the management of proximal occlusions of the upper limbs [14].

PTS is caused by the development of venous hypertensive. This is secondary to the existence of chronic venous reflux secondary to the loss of normal valve function. The presence of a proximal venous obstruction is the cause of serious clinical forms of PTS. It is prolonged persistence of hypertension in the deep venous system that causes valve function to deteriorate in the perforating veins, resulting in the direct transmission of venous hypertension (especially on standing and walking) to the superficial venous system. Progressively, there is a resulting increase in endothelial permeability. This excessive permeability means that water, macromolecules and granulocytes can pass from the vascular space to the interstitium. This passage of water causes oedema, the presence of free radicals and proteolytic enzymes, and has been suggested to be the cause of ulcers developing [15–17]. Reflux in the proximal veins is recognised as being a crucial feature for the development of PTS. The presence of severe proximal stenosis or a proximal occlusion is a major aggravating factor [6,18,19]. Proximal DVTs (common femoral and/or iliac veins) are major predictive risk factors for developing PTS [19,20]. Other factors such as a history of ipsilateral DVT, age more than 60 years, obesity, and varicose veins are also predictive for developing PTS [19,21]. If oral anticoagulant therapy prescribed for acute DVT is unsuccessful, this is associated with a high risk of developing PTS [22,23]. Equally, adhering to the anticoagulant treatment regimen and duration reduces the risk of developing PTS [19,21]. Although the cornerstone of symptomatic treatment is elastic venous compression, adherence is difficult [24]. In 2003 Kahn et al. [25] published the results of a satisfaction survey of patients with PTS. It appears that elastic venous compression stockings and physical exercise are effective for the relief of symptoms, but their use is restrictive and uncomfortable and only 20 to 30% of patients follow this treatment [23,24].

The endovascular management of disabling cases of post-thrombotic syndrome is feasible, and remarkably clinically effective. Today, it seems that awareness of this technique and its results needs raised among the clinicians managing these patients as well as among radiologists.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


