Collateral Damage—The Risks of Central Venous Hemodialysis Catheters

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Received 18 December 2019; revised 4 February 2020; accepted 24 February 2020; published online 4 March 2020

Kidney Int Rep (2020) 5, 746–750; https://doi.org/10.1016/j.ekir.2020.02.1029
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INTRODUCTION

Maintenance of definitive vascular access (VA) for patients with end-stage renal disease can be a challenge, particularly in those who have been established on hemodialysis (HD) for many years. The optimal access route for patients on HD has long been thought to be an arteriovenous fistula (AVF), as high blood flow rates and improved clearance can be achieved, furthermore there are reduced risks of long-term complications and often financial benefits compared with other types of long-term VA (e.g., arteriovenous grafts and tunneled HD catheters [THCs]).1–3 Over recent years there has been an increase in the number of patients commencing HD via THC due to the ease and speed by which VA can be obtained using this method.4 UK Renal Registry data suggest that as many as 50% of incident HD patients commenced HD via THC or temporary central venous catheters (CVCs) in 2018. Furthermore, a significant proportion of prevalent patients on HD continue to dialyse via THC at 1 year.5

THCs are considered to be a less desirable form of long-term HD access because of the increased risk of complications and all-cause mortality, when compared with other forms of VA.5–8 Common complications include localized and systemic infections, central venous thromboses (CVTs) and stenosis, and poor blood flow.9,5 The use of AVF for HD, although preferred, also can be associated with complications, including infection, aneurysm, ischemic steal syndrome, venous hypertension, and thrombosis.5,9

We present a case of a patient who presented with chest pain while dialysing through an AVF, after previously starting HD via a left internal jugular THC. Investigation demonstrated a mediastinal hematoma, hemopericardium, and hemothorax from a bleeding mediastinal collateral vessel. To our knowledge, there are no previous reports describing this presentation. It highlights the risks of THC use as well as the importance of, where possible, establishing optimal long-term access in the form of an AVF in all patients before commencing HD.

CASE PRESENTATION

A 40-year-old woman with end-stage renal disease secondary to nephrotic syndrome of unknown cause presented via the emergency department with sudden onset of severe chest pain that developed while on HD. She had been established on HD for just over 3 years, after an initial period of 2.5 years on peritoneal dialysis. When peritoneal dialysis failed, she switched to HD via a left-sided internal jugular THC. This was used for 10 months until a left-sided brachiocephalic AVF was formed. The brachiocephalic AVF achieved pump speeds of 350 ml/min with a urea reduction ratio of 77%. Routine Doppler studies of the AVF, performed several months before presentation, had revealed a patent fistula with peak systolic velocity of 3.9 m/s and flow of 1800 to 2000 ml/min. A left brachiocephalic vein occlusion was identified, with blood flow draining via a large collateral vessel into the internal jugular vein. In spite of this finding, there was no associated elevation in venous pressures, difficulties needling the AVF, or symptoms, including arm swelling.

On initial assessment in the emergency department, the patient reported sharp central chest pain that radiated to the jaw and left arm, was worse on deep inspiration, and eased with opiate analgesia. There were no associated symptoms of cough, shortness of breath, nausea, or palpitations. She had completed her...
usual session of 4 hours of HD, anticoagulated with heparin, with 1.3-l ultrafiltration. She remained hemodynamically stable throughout the dialysis session, with no drop in blood pressure. Regular medications at the time of presentation included amlodipine, bisoprolol, doxazosin, ramipril, alfalcacilidol, atorvastatin, folic acid, Sandocal (calcium carbonate; calcium lactate gluconate) with meals, Venofer (i.v. iron sucrose) 100 mg weekly on HD, and NeoRecormon (epoetin beta) 4000 units twice weekly on HD. On examination in the emergency department, 4 hours after completing HD, patient was hemodynamically stable with a pulse rate of 83 beats per minute, blood pressure 144/86 mm Hg, oxygen saturations 96% on room air, and respiratory rate 18. The chest was clear on auscultation and heart sounds normal. Laboratory investigations at the time of presentation included hemoglobin 120 g/l, platelets $257 \times 10^9$/l, international normalized ratio 1.08, activated partial thromboplastin time ratio 1.40, and troponin I 24 pg/l. Additional laboratory values are shown in Table 1. Electrocardiogram demonstrated longstanding T-wave inversion in lateral leads V4–6, with no evidence of any acute ischemic changes. A plain posteroanterior chest radiograph showed a widened mediastinum when compared with a chest radiograph from 3 months prior (Figure 1).

A computed tomography angiogram (Figure 2) demonstrated the key findings with the presence of a high attenuation (65 Hounsfield units) mediastinal hematoma lying predominantly anterior to the trachea and displacing the superior vena cava and ayzygous veins anterolaterally. There was no evidence of dissection, aneurysm, or active bleeding from the ascending aorta, aortic arch, or thoracic aorta. A short segment of occlusion in the proximal left brachiocephalic vein was identified with numerous superior mediastinal collateral vessels bypassing the occlusion. A moderate pericardial effusion was noted. No pleural effusions were present. These findings were suggestive of a venous bleed with no evidence of active bleeding on computed tomography angiogram. An echocardiogram demonstrated a circumferential pericardial effusion measuring 1.5 cm by the right ventricle and atrium, and 1.1 cm by the left ventricle. No right ventricle/atrial collapse was seen. Normal inferior vena cava size with $>50\%$ collapsibility was noted.

Following admission to the renal ward, the patient underwent heparin-free HD via her AVF using low pump speeds of 250 ml/min. The HD circuit was prevented from clotting with the use of intermittent flushes of 0.9% saline, and the patient remained stable on HD throughout. Repeat blood tests demonstrated only a small drop in hemoglobin from admission 120 g/l to 94 g/l, which subsequently remained stable. The patient was observed to be hemodynamically stable for 72 hours. A repeat computed tomography angiogram then demonstrated stable appearances of the mediastinal hematoma and pericardial effusion, but with new bilateral hemothoraces. These were managed conservatively, and the patient was discharged back to her satellite HD unit without intervention. She was later discussed in the local complex access multidisciplinary meeting. A decision to attempt radiologically guided crossing of the brachiocephalic occlusion $\pm$ dilatation and stenting was made, to relieve pressure in the collateral vessels and prevent further bleeding. At the time of writing, the patient had received a deceased donor renal transplant and remained stable off HD, with excellent renal function. All vascular intervention procedures were therefore cancelled.

### DISCUSSION

The rising incidence of patients commencing HD as unplanned starters has led to THC and temporary CVC being increasingly used as first-line VA in many. CVTs are a common complication of both THC and temporary CVC use. CVTs are classified as intrinsic or extrinsic depending on the location of the thrombosis relative to the catheter lumen. Intrinsinc thromboses are associated with poor or absent blood flow through the catheter lumen. Extrinsic thromboses may present asymptomatically or with difficulty aspirating blood through the catheter lumen, poor blood flows during HD, collateral vessels visible on the chest wall, and venous pressure-related symptoms in the ipsilateral arm. Studies observing the rate of CVT associated with CVC used for all indications, not just HD, demonstrate an incidence ranging from 2% to 67%. The risk of developing a CVT is affected by several factors.

### Table 1. Laboratory values at the time of admission

| Laboratory investigation, Units | Results | Reference range |
|--------------------------------|---------|-----------------|
| Hemoglobin, g/l                | 120     | 115–155         |
| White blood cells, $\times 10^9$/l | 5.54    | 4.00–11.00      |
| Mean corpuscle volume, fl      | 89.3    | 77.0–95.0       |
| Mean corpuscular hemoglobin, pg| 29.4    | 25–34           |
| Mean corpuscular hemoglobin concentration, g/l | 329 | 320–370 |
| % Hypochromic cells            | 3.3     | –               |
| International normalized ratio | 1.08    | 0.9–1.2         |
| Activated partial thromboplastin time ratio | 1.40 | 0.85–1.15 |
| Sodium, mmol/l                 | 140     | 135–145         |
| Potassium, mmol/l              | 4.2     | 3.5–5.0         |
| Urea, mmol/l                   | 3.6     | 3.3–6.7         |
| Creatinine, $\mu$mol/l         | 354     | 45–120          |
| Total protein, g/l             | 80      | 60–80           |
| Albumin, g/l                   | 51      | 35–50           |
| C-reactive protein, mg/l        | 74      | <5              |
| Troponin I, ng/l               | 24      | <16             |

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different factors, including type and size of catheter inserted and site of catheter placement. Patient factors also can increase the risk of developing CVT, and include coagulability state, comorbidities, number of previous catheters, and history of previous thromboses (Table 2). S7, S8

In addition to the symptoms that may result from CVTs, their presence can have superadded consequences, including thromboembolic phenomena, catheter-related infections, catheter dysfunction, post-thrombotic syndrome (edema, pain, and limb swelling) and venous hypertension.9–S11 Many of these complications necessitate dialysis line removal or exchange, which further increases the risks of developing CVT, in addition to an increased risk of failure of subsequent AVF maturation and function in the ipsilateral limb. S11 Ultimately, THCs are associated with an increased risk of long-term vascular compromise.

This case demonstrates a previously undescribed risk associated with medium/long-term THC VA use in patients on HD. Our patient developed a CVT in the left brachiocephalic vein as a consequence of left internal jugular THC placement, despite placement for only 10 months. As with many patients who develop occlusive disease, collateral venous blood vessels developed and matured around this thrombus to permit blood to bypass the occluded segment. S10 These collateral vessels meant that our patient remained asymptomatic for many years in spite of the presence of a CVT.

Figure 1. (a) Baseline posteroanterior (PA) chest radiograph (CXR) 4 months before admission. (b) Admission PA CXR; arrow demonstrates a widened mediastinum.

Figure 2. Computed tomography angiogram demonstrating mediastinal collateral blood vessels and mediastinal hematoma lying anterior to the trachea causing anterolateral displacement of the superior vena cava (SVC).
Collateral blood vessels (collaterals) tend to be of smaller caliber than the main vessel whose function they replace. They often develop from existing vessels to form a new pathway around an occluded vessel segment.\textsuperscript{S12} The pattern of collateral formation often can be predicted according to which major vessel segment is occluded,\textsuperscript{S13} although on rarer occasions form from more unusual pathways.\textsuperscript{S14} Brachiocephalic occlusion often results in collaterals forming between the chest wall and azygous, or internal thoracic veins.\textsuperscript{S13} Unusually, although our patient had an occlusion in her left brachiocephalic vein, collaterals appear to have developed from unnamed mediastinal vessels, which allow blood flow to bypass the occlusion.

Collateral development is stimulated by increased shear stress on the vascular endothelium, following occlusion of a major vessel. This leads to activation of complex pathways that ultimately result in altered growth factor gene expression, and in turn remodelling of the endothelium and smooth muscle cells within collateral vessel walls.\textsuperscript{S12} Studies have shown there to be inherent differences in the nature of endothelial and smooth muscle cells within collateral vessel walls, compared with other vessel walls of similar caliber. It is hypothesized that these differences allow for collaterals to deal with the increased shear stress, wall stress, and altered hemodynamics they encounter.\textsuperscript{S15} Furthermore, genetic factors have been shown to play an essential role in the extent of collateral development, and studies suggest that individuals may differ in their ability to develop collateral networks.\textsuperscript{S15,S16} It may well be that these same, or even unidentified, genetic factors may impact the ability of collateral vessel walls to remodel, and therefore to withstand stress factors.

Most work surrounding collateral vessel development and maturation observes changes in arterioles, following artery occlusion. There are few studies observing the extent of these changes in the venous system, to see if and how the changes that occur within vessel walls may differ. The overall integrity of collateral blood vessel walls in comparison with major blood vessels is not well understood. It is assumed collateral vessels are more fragile than established large-bore vessels, meaning they are at increased risk of damage from minor insults. It is unclear how our patient bled from a collateral vessel, and what might have precipitated this event. One theory is that it could be related to the added stress from the large volume and turbulent flow going through her AVF. More work is required to observe the cellular aspects of venous collaterals to characterize the nature of these vessels, their associated integrity, and how/if blood flow on HD may affect them.

In conclusion, increasing numbers of patients commence HD via suboptimal VA, that is, CVC and THC. Although these methods of obtaining VA are a life-line, they should be avoided where possible to reduce the risk of associated complications. CVTs are an increasingly common complication of HD catheter insertion, which, with proper planning of VA options, could potentially be avoidable in many. (Table 3) We present a patient with a CVT who presented with a mediastinal hematoma resulting from rupture of a venous collateral, a previously undescribed complication of CVT. It remains unclear how and why this vessel bled, but it highlights the importance of obtaining optimal long-term VA for patients on HD.

**Table 3. Teaching points**

- Arteriovenous fistulas are considered to be the most optimal form of long-term VA in patients on HD.
- Increasing numbers of patients are commencing HD via suboptimal forms of VA (temporary CVC or THC).
- THC and CVC are more frequently associated with complications, including CVTs.
- CVTs can result in thromboembolism, post-thrombotic syndrome, collateral blood vessel formation, and, ultimately, loss of VA.
- Where possible, clinicians should aim to ensure patients have optimal VA formed before commencing HD.
- Clinicians should be mindful of the need to establish definitive VA when other methods of renal replacement therapy (including peritoneal dialysis and transplantation) are failing.

CVC, central venous catheter; CVT, central venous thrombosis; HD, hemodialysis; THC, tunneled hemodialysis catheter; VA, vascular access.

**DISCLOSURE**

All the authors declared no competing interests.
ACKNOWLEDGMENT
The authors acknowledge Dr. Hugh Cairns who cared for the patient during her inpatient stay.

AUTHOR CONTRIBUTIONS
TR reviewed the case and wrote the main body of text. MF reviewed and amended subsequent drafts and approved the final version. TA reviewed and provided the radiological images and approved the final version. FDF reviewed and approved the final version.

SUPPLEMENTARY MATERIAL
Supplementary File (PDF)
Supplementary References.

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