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Challenges in The Management of Post-Thrombotic Syndrome in a Low-Resource Setting

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ABSTRACT

Post-thrombotic syndrome (PTS) is the most common long-term complication of deep venous thrombosis (DVT) and occurs in up to 20-50% of proximal DVTs. Patients with PTS present with pain and swelling of the affected limb, edema with pruritus, skin hyperpigmentation, and venous ulcers. Risk factors for PTS include ineffective anticoagulation, obesity, and proximal DVT. The Villalta scale is validated for the diagnosis and severity scoring of PTS. The American Heart Association recommends primary and secondary prevention of PTS as the most effective management strategy since treatment of established PTS is very challenging, especially in resource-limited settings. The latter includes external compression devices, exercise, pharmacotherapy, venous ulcer management, and surgical endovascular procedures in selected patients. PTS leads to frequent hospital visits, reduced productivity, and a low quality of life. In this study, we present the diagnostic and therapeutic challenges in managing a 30-year-old woman with PTS in a rural Kenyan setting. We propose a patient-centered multidisciplinary approach to managing PTS.

INTRODUCTION

Post-thrombotic syndrome (PTS) is a common long-term complication of deep venous thrombosis (DVT) that occurs in up to 20-50% of proximal DVT and may be severe in 5-10% of the cases (Galanaud *et al.*, 2018). It occurs primarily due to impaired and incomplete resolution of the thrombus, persistent obstruction of venous outflow with ambulatory venous hypertension, and secondary valvular incompetence (Cosmi *et al.*, 2022). The main risk factors for PTS include previous and recurrent ipsilateral DVT, proximal DVT (especially iliofemoral), persistent symptoms ≥ 1 month after DVT diagnosis, obesity, and having subtherapeutic INRs while on warfarin for $> 50\%$ of the duration of treatment (Vazquez & Kahn, 2012). Table 1 below summarizes the risk factors for PTS (Wang *et al.*, 2023). The typical symptoms of PTS include heaviness of the affected leg, pain, edema, and pruritus, which tend to worsen in the evenings, and trophic skin changes like hyperpigmentation and venous ulcers in severe cases (Makedonov *et al.*, 2020). There are many challenges in the management of PTS in low-resource settings. Difficulties in the diagnosis of PTS arise from the widespread use of point-of-care diagnostic compression ultrasound (CUS) which is unable to distinguish between acute DVT and PTS. A lack of confirmatory imaging modalities like CT and MRI scans in these clinical settings means that patients with PTS are repeatedly misdiagnosed as acute DVT and put on unnecessary prolonged anticoagulation with either warfarin or direct oral anticoagulants. This is especially true where patients seek treatment from different centers for “non-resolving” DVT symptoms. Though not lethal, PTS leads to a reduced quality of life, increased use of healthcare services through frequent hospital visits, and

decreased productivity (Wang *et al.*, 2023). This case report from a rural Kenyan hospital highlights some of these challenges in the diagnosis and management of PTS and the resulting negative impact in the quality of life for the patient. We call for an increased awareness of the principles of PTS diagnosis and management.

Table 1: Risk factors for development of PTS (Wang *et al.*, 2023).

Risk factors at baseline	Risk factors during follow-up
Proximal DVT (especially iliofemoral)	Subtherapeutic INR
Recurrent DVT history	Ipsilateral recurrent DVT
Obesity	Residual thrombus
Pre-existing venous insufficiency	Venous reflux
Higher severity of symptoms at diagnosis	
Older age	

Key: PTS, post-thrombotic syndrome; DVT, deep vein thrombosis; INR, international normalized ratio.

LITERATURE REVIEW

The diagnosis of PTS is based on the risk factor profile and clinical symptomatology. There is considerable overlap in the symptoms of PTS, acute DVT, and primary venous insufficiency. Many low-resource clinical settings rely on compression ultrasound (CUS) for the diagnosis of acute DVT. CUS may not distinguish acute DVT from a chronic thrombus (PTS), especially where previous imaging is unavailable for comparisons. This situation

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is common in low-resource settings when patients seek treatment from different health centers that often lack central integrated electronic medical records (Gautam *et al.*, 2020). There are no biomarkers that are validated for diagnosing DVT or predicting acute DVT patients who will develop PTS later. Due to these diagnostic challenges, the Villalta scale has been validated for use in both clinical practice and research to standardize the diagnosis and estimate the severity of PTS (Kahn *et al.*, 2014). Table 2 below, adapted from Guanella (Guanella & Kahn, 2012), shows the Villalta scale.

Table 2: The Villalta Scale (Guanella & Kahn, 2012).

	None	Mild	Moderate	Severe
Symptoms				
Pain	0	1	2	3
Cramps	0	1	2	3
Heaviness	0	1	2	3
Paresthesia	0	1	2	3
Pruritus	0	1	2	3
Clinical Signs				
Pretibial edema	0	1	2	3
Skin induration	0	1	2	3
Redness	0	1	2	3
Hyperpigmentation	0	1	2	3
Venous stasis	0	1	2	3
Pain in calf compression	0	1	2	3
Venous ulcer	Absent			Present

Key: Total score of 0 to 4 indicates no post-thrombotic syndrome (PTS); score of ≥ 5 indicates PTS. PTS severity: total score of 5 to 9, mild PTS; score of 10 to 14, moderate PTS; and score of ≥ 15 or venous ulcer present, severe PTS.

The treatment of established PTS is challenging. The American Heart Association (AHA) recommendations for treating established PTS include i) compression-based therapies like graduated external compression stockings (ECS) and intermittent compression devices, ii) pharmacotherapy with rutosides, defibrotide, and hidrosmin, iii) exercise training programs, iv) venous ulcer management, and v) surgical and/or endovascular procedure interventions for selected patients, including bypass procedures, stents, and complex reconstruction surgeries (Kahn *et al.*, 2014). Given these challenges in treating established PTS, the AHA recommends both primary and secondary prevention as the mainstay of management. These strategies include i) primary prevention of DVT using pharmacological and mechanical thromboprophylaxis in high-risk patients and ii) secondary prevention strategies such as optimal and effective anticoagulation for DVT treatment, use of elastic compression stockings, and thrombolysis/endovascular therapies for selected patients (Kahn *et al.*, 2014). There is no reported case of PTS from a Kenyan hospital in

the literature as at the writing of this case study. The Kenya Ministry of Health guidelines on the diagnosis and management of venous thromboembolism does not include any information on PTS (Division of Non-Communicable Diseases, 2018). Therefore, this study aims to expose the presence of PTS in a rural Kenyan setting and highlight the challenges in the diagnosis and management of PTS in a low-resource clinical setting.

MATERIALS AND METHODS

Patient History and Physical Examination

A 30-year-old married mother of 7, a business lady from Tanzania but living in Nakuru, Kenya, first presented to us at the medical clinic in April 2022, with persistent left leg pain, swelling, and numbness over the preceding 18 months. She had been first diagnosed with left leg common femoral vein (CFV) deep venous thrombosis (DVT) on Doppler ultrasound in February 2021, following a cesarean section. She was treated with warfarin for 8 months (by the 6th month, she reportedly still had significant pain and swelling of the left leg, hence the decision to continue warfarin beyond 6 months). Notably, her INR remained subtherapeutic between 1.2 and 1.8 during the 8 months of treatment. She stopped breastfeeding after 8 months. The next month, she was put on 20 mg of rivaroxaban daily for another month in another facility when a repeat Doppler ultrasound showed DVT in the left CFV. In the 10th month, she was switched back to warfarin plus aspirin for another month in yet a different facility in which the left CFV still had DVT. From the 11th month, she was put on rivaroxaban in a different facility following a Doppler scan showing left CFV DVT. She was on rivaroxaban (20 mg daily) when she came to us. She was visibly frustrated with the diagnosis of persistent left CFV DVT by multiple doctors who “failed to listen to her and were in a hurry to prescribe anticoagulants” and the possibility of lifelong anticoagulation without much symptomatic improvement.

She was hemodynamically stable, obese with a weight of 98 kg and a BMI of 32.4 kg/m², and limping on the left leg. The left leg was swollen and moderately hyperpigmented from the mid-leg to the foot and tender on the entire medial aspect from the foot to the groin, with no lymphadenopathy, no venous ulcers, and no features of varicose veins. See figure 1 below. The rest of the systemic examination was unremarkable. A repeat Doppler scan showed DVT in the left CFV. Her baseline metabolic workup was unremarkable.

RESULTS AND DISCUSSION

Diagnosis, Management, and Follow-up

We made a diagnosis of severe post-thrombotic syndrome (given the fact that the DVT in the left CFV had not changed since 2021) based on the Villalta scale with a score of 27. We proposed to stop the anticoagulation, manage pain with non-steroidal anti-inflammatory drugs, elevate the left leg while in bed, use external compression



Figure 1: Swollen left leg with hyperpigmented skin from the mid-leg to the foot. There were no venous ulcers or varicose veins.

stockings, undergo physiotherapy, and that she actively lose weight in a structured nutritional support system. We also referred her for psychological counseling. Two physiotherapy centers near her home declined her physiotherapy following their evaluation of the left leg over fears of possibly dislodging the clot and precipitating a pulmonary embolism. The surgical team added Daflon (diosmin and hesperidin) to her treatment and requested a CT venogram, which confirmed an organized clot in the left CFV with resultant significant luminal narrowing. She was referred to vascular surgeons at the national teaching and referral hospitals for a possible endovascular recanalization procedure. At 2 vascular surgical clinics in different towns, she was seen by different doctors who restarted the rivaroxaban 20 mg daily at different times for left CFV DVT based on repeat Doppler scans in each of these clinics. She returned to us 20 months after the referral and has had multiple clinic visits with us due to persistent pain and left leg swelling, with frustrations about the persistent symptoms. She has since cut down weight to 92 kg (lost 6 kg over 3 years). We stopped the rivaroxaban again and have been implementing the original management plan, including physiotherapy at our hospital. She went into depression and was seen by a psychiatrist and put on antidepressants. Notwithstanding these interventions, she reports minimal improvement related to better pain control. We consulted a vascular surgeon in a private hospital, who will do a stenting procedure in December 2025. Presently, she is under a multidisciplinary care team while the family is seeking financial resources to actualize the planned surgery.

DISCUSSION

Our patient had severe PTS based on a Villalta score of 27 (Guanella & Kahn, 2012). Her risk factors for PTS included obesity, proximal DVT (left common femoral vein), subtherapeutic INR during the index anticoagulation, persistent symptoms at 6 months of anticoagulation, and residual thrombus (Wang *et al.*, 2023). Achieving and maintaining a target INR of 2 to

3 with warfarin effectively prevents PTS by stopping thrombus propagation and promoting early thrombus resolution (Makedonov *et al.*, 2022). Use of direct oral anticoagulants (DOACs) has been shown to be superior to warfarin in many studies to prevent PTS (Kahn *et al.*, 2014). Our patient has been seen in several different health facilities in which she was repeatedly (mis)diagnosed with persistent/new/recurrent DVT by means of compression Doppler ultrasound (CUS). The symptoms of PTS closely mimic those of acute DVT, and CUS may not distinguish acute from chronic thrombus, especially where previous imaging is unavailable for comparisons (Gautam *et al.*, 2020). This sort of mistake is common where patients are seen in different health institutions, as was with our patient. It is therefore understandable that the various facilities she visited opted to treat her as a case of acute DVT with anticoagulation. At our hospital, we determined from at least 9 different CUS reports that the left CFV was involved in all the reports, making it more likely that the index left CFV DVT had persisted and become organized all this time rather than being a new clot. This finding was confirmed by a CT venogram. Magnetic resonance imaging (MRI) is more accurate than CUS and CT scans in diagnosing recurrent DVT but obviously more expensive (Müller *et al.*, 2023). Ideally, the vascular clinics she was referred to should have put her on management strategies for established PTS since the referral letter had the diagnosis of PTS established clinically and with the attached CT venogram report. The AHA guidelines for the management of established PTS are both class I and II recommendations, with mixed outcomes in several studies due to the heterogeneity of the study participants (Kahn *et al.*, 2014). There is no therapeutic value in prolonged anticoagulation of patients with PTS.

Our patient has responded, albeit suboptimally, to the management strategy, including weight reduction, external compression stockings, physiotherapy and exercise, analgesics, and psychological counselling. The diagnosis of PTS has markedly affected her quality of life negatively due to frustrations about the non-resolution of the PTS despite multiple clinic visits with the attendant financial expenditures. Our multidisciplinary approach has alleviated most of her pain and psychosocial aspects of the PTS diagnosis. Based on the AHA recommendations, she is a potential candidate for a combined operative and endovenous procedure (Kahn *et al.*, 2014), which she is scheduled for in December 2025.

CONCLUSIONS

PTS is a common complication of proximal DVT due to incomplete resolution of the index thrombus resulting in venous obstruction and secondary valvular incompetence. The main risk factors for PTS include proximal DVT, obesity, ineffective anticoagulation, and persistent DVT symptoms. The Villalta scale is validated for the diagnosis and severity of PTS. The AHA recommends both primary and secondary prevention of

PTS as the most effective management. Established PTS may respond to ECS, pharmacotherapy, exercise, venous ulcer management, and surgical endovascular procedures in selected cases. Clinicians ought to have a high index of suspicion for the diagnosis of PTS in patients with a compatible risk factor profile who present with “persistent” DVT in the same leg. These patients should be managed in a patient-centered multidisciplinary team that includes psychosocial care. There is no therapeutic value to prolonged anticoagulation in patients with PTS.

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