CASE REPORT

Isolated portal vein thrombosis as a rare complication of minimal change disease in nephrotic syndrome

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SUMMARY

Minimal change disease (MCD) accounts for the majority of idiopathic nephrotic syndrome, distinguished by significant proteinuria, oedema, and hypoalbuminemia. Although rare, thromboembolic complications like portal vein thrombosis (PVT) pose life-threatening risks owing to the hypercoagulable state of nephrotic syndrome. This report details a case of a 28-year-old man with histologically proven MCD who developed PVT during treatment. The patient reported symptoms of frothy urine while experiencing lower limb swelling on both sides and difficulty breathing. Both laboratory results and clinical assessments confirmed a full-blown relapsing nephrotic syndrome and hepatitis. Doppler ultrasound confirmed the presence of partial portal vein thrombosis. The combination treatment using both corticosteroids and anticoagulants led to complete remission of MCD and the resolution of PVT. This case aims to discuss the underdiagnosis of PVT as a thrombotic sequela of MCD while reviewing the best management approaches.

INTRODUCTION

Minimal change disease (MCD) represents approximately 10-15% of idiopathic nephrotic syndrome cases in adults and is diagnosed based on the classic triad of heavy proteinuria, hypoalbuminemia and generalised oedema. While MCD appears benign on light microscopy – with negative immunofluorescence and diffuse effacement of podocyte foot processes on electron microscopy – and offers an excellent renal prognosis (>90% initial corticosteroid responses), it causes substantial morbidity from the nephrotic syndrome and its treatment regimen. Key complications include:

1. Thromboembolic complications: Venous thromboembolism is common, often as pulmonary embolism or deep vein thrombosis, with risk increasing at serum albumin <20g/L, due to losses of antithrombin III and protein C/S, plus increased procoagulant synthesis.
2. Infections: Urinary immunoglobulin G (IgG) loss increased susceptibility to encapsulated bacteria (pneumococcus, Haemophilus influenzae), spontaneous bacterial peritonitis (SBP), and cellulitis.
3. Acute kidney injury: Usually reversible, arising from prerenal factors or interstitial oedema.
4. Steroid-related morbidity: Osteoporosis, glucose intolerance, cushingoid features and psychiatric disturbances, which are particularly burdensome for the 30-50% who experience frequent relapsing or steroid dependence.

Among these, PVT is exceedingly rare and diagnostically challenging, as abdominal symptoms are often subtle and misattributed to steroid side effects or nephrotic ascites. This case report describes a patient with relapsed MCD complicated by PVT successfully treated with corticosteroids and anticoagulant therapy.

CASE PRESENTATION

A 28-year-old man presented in June 2024 with a one-week history of frothy urine, bilateral lower limb swelling, and shortness of breath. He had a history of MCD diagnosed in 2023 via renal biopsy and had achieved complete remission in May 2024. He denied fever, haematuria, or recent infections. No history of any prior thrombotic events, liver disease, malignancy, or use of prothrombotic medications. He was a non-smoker with no family history of coagulation disorder. He was haemodynamically stable with 3+ pitting oedema in the lower extremities. Laboratory results showed severe hypoalbuminemia (8 g/L), proteinuria (protein 4+ and urine protein creatinine ratio {UPCR} 1001mg/mmol), hyperlipidaemia (total cholesterol 11.8 mmol/L), and mild impairment of renal function (creatinine 108 µmol/L). Coagulation studies were unremarkable, with an international normalized ratio of 1.02. Liver function tests were normal (ALP 79 U/L, ALT 7 U/L). Prednisolone 50mg once daily (1mg/kg/day) was initiated, and he was discharged with a one-week clinic appointment.

During his clinic review in early July 2024, he complained of progressive bilateral lower limb oedema and frothy urine, associated with abdominal distension and shortness of breath. Physical examination revealed ascites and a tender right hypochondriac region. Laboratory evaluation revealed albumin of 9 g/L, UFEME protein 3+, blood negative, a UPCR of 663.88 mg/mmol, serum creatinine of 89 µmol/L, normal liver function tests, leucocytosis (white cell count 16.8 x 109/L) and raised CRP of 107.3 mg/L. Diagnostic peritoneal tapping yielded a transudative ascites with a serum ascites albumin gradient (SAAG) of <1.1. Both peritoneal Gram stain and AFB were negative, and cytology was benign in findings. Given the elevated infective markers, empirical intravenous ceftriaxone and metronidazole were administered for 7 days to cover for possible spontaneous bacterial peritonitis.

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Table I

	June 2024	Early July 2024	End July 2024	Mid August 2024	End August 2024	Oct 2024	Nov 2024	Jan 2025
Haemoglobin (12-15 g/dL)			15.7					
White cell count (x109/L)		16.8	14.6					
Platelet (x 109/L)			248					
Creatinine (62-115µmol)	108	89		75		85	76	76
Albumin (32-48 g/L)	8	9	13	24	32	36	41	43
AST (U/L)	7		154	113	161			
ALT (U/L)		8	311	333	131	64	31	23
ALP (U/L)	79	93	274	175	114	81	76	86
Total Cholesterol (<5.2 mmol/L)	11.8		11.2				5.62	4.6
Urine PCR (mg/mmol)	1001	663.88	1021.84	256.9				5.82
R factor			4.9					
D-dimer (< 0.5 µg/mL)			7.61					
Anti-B2GP1 IgM			positive					

Table II

Re	Age (yr)	Sex	Onset	Clinical Presentation	Thrombosis location	Serum albumin (g/L)	Proteinuria	Serum cholesterol (mmol/L)	Renal biopsy
Varghese J et al [6]	45	M	At diagnosis	Abdominal pain, distension	Portal vein	16	24hr UP: 5.5 g/day	12.7	MCD
Kim G et al [7]	26	M	At relapse	Abdominal pain, nausea, vomiting, ascites	Portal vein	17	24hr UP: 25.3g/day	12.21	MCD
Our patient	28	M	At relapse	Abdominal pain, distension	Portal vein	13	25.3g/day UPCR 1021.84 mg/mmol	11.22	MCD

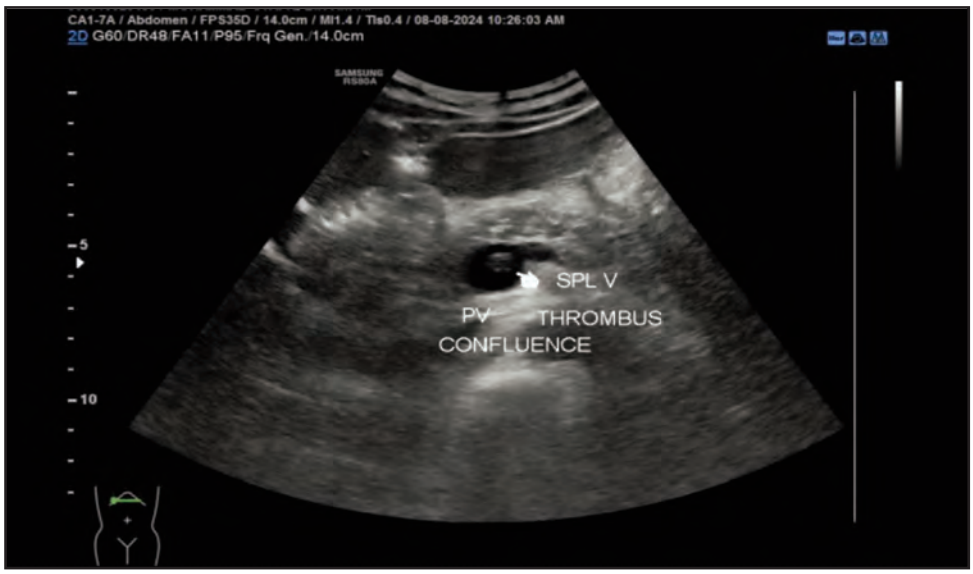

Fig. 1: There echogenic thrombus seen at the portosplenic confluence causing partial thrombosis of the vein

Diuresis was achieved with furosemide. Following clinical improvement with resolution of ascites and lower limb oedema, he was subsequently discharged with prednisolone 50mg once a day.

Upon his next visit at the end of July 2024, his bilateral lower limb swelling and frothy urine persisted even though he was compliant with medications. Clinically, his vitals were stable, no ascites, but gross pitting oedema in the lower extremities were noted. Laboratory investigations (Table I) now showed deranged liver profile with R factor of 4.9 (mixed pattern), hypoalbuminemia, hyperlipidaemia, proteinuria and normal renal profile. Full blood count and coagulation profile were unremarkable while D-dimer was elevated. Hepatitis screening and autoimmune hepatitis panel were both negative. Given the abrupt-onset hepatitis with ALT

predominance and raised D-dimer, abdominal ultrasound with Doppler was performed, revealing partial main portal vein thrombosis extending to the porto-splenic confluence (Fig.1). A limited thrombophilia screen showed positive anti-β2GP1 IgM with negative anticardiolipin IgM/IgG and lupus anticoagulant.

The patient was started on subcutaneous enoxaparin (1mg/kg twice daily) with warfarin. In addition, high-dose prednisolone 1mg/kg/day was slowly tapered down. Follow-up in the clinic showed a significant reduction in his urine protein creatinine index - 5.89mg/mmol, and LFT showed improvement with each follow-up. Warfarin was continued for 6 months until clinical stability was confirmed. He has remained in remission without recurrence of thrombosis.

DISCUSSION

Thromboembolic complications are noted to affect up to 25% of patients with nephrotic syndrome (NS) as it is a well-established prothrombotic condition.[1] MCD results in severe proteinuria with concomitant hypoalbuminemia and urinary loss of proteins, including anticoagulants such as antithrombin III and protein S, thus disturbing the coagulation equilibrium and raising the risk of thrombosis formation. Additionally, overactivity of procoagulant factors, corresponding to fibrinogen, and increased platelet activation further propels thrombus formation. This constellation of factors gives rise to a prothrombotic state, making patients susceptible to venous thromboembolism, particularly PVT.[1-4] In PVT, thrombus forms in the portal vein with resultant obstruction of hepatic blood flow, which may cause portal hypertension, varices or ischaemic liver damage.

Isolated PVT as a complication of nephrotic syndrome is quite rare due to the unique haemodynamic and anatomic features of the portal venous system. The MCD hypercoagulable state might predispose to thrombosis more easily in high-flow venous systems such as the renal veins where stasis and endothelial damage are more marked. Furthermore, the low flow state of the portal vein is rare and needs additional stimuli for thrombosis (e.g., endothelial damage or stasis due to cirrhosis) that are less commonly present in MCD.[2,5]

Few case reports described PVT in patients with MCD, and out of the cases documented, there were only two cases involving isolated portal vein thrombosis (Table II).

Since PVT can manifest in a subtle manner, clinical vigilance is warranted among patients who exhibit new-onset abdominal symptoms, ascites, deranged liver profiles, or signs of intestinal ischemia. The deranged liver enzymes could be explained by either congestive hepatitis from the ascites or ischaemic hepatitis from the vein thrombosis itself. Ultrasound with Doppler is the primary imaging modality on account of its availability and sensitivity (80-100% for ruling out PVT).[8] Contrast-enhanced CT or magnetic resonance imaging is more specific to determine thrombus extent, but since the earlier performed ultrasound doppler done already showed partial main portal vein thrombosis extending to the porto-splenic confluence, this was not done. Thrombophilia testing is indicated to exclude both inherited and acquired coagulation abnormalities in young patients with no apparent trigger.

Treatment of PVT in MCD requires control of the underlying nephrotic syndrome and of the thrombus itself. Immunosuppressive therapy, such as corticosteroids, is essential to minimize hypercoagulability by reducing proteinuria and normalizing the levels of anticoagulant proteins. The preferred class of choice at an initial stage is low-molecular-weight heparin (eg enoxaparin) because of its quick onset and reversibility, followed by warfarin for maintenance. While direct oral anticoagulants (DOACs) like apixaban or edoxaban have shown some benefit in nephrotic syndrome-associated thrombosis, data on PVT remain very limited.[9] There are no specific guidelines in terms of optimal duration of anticoagulation, and oftentimes it is to be continued until the remission of nephrotic syndrome or thrombus, typically 3–6 months.[3] For this patient, warfarin was continued for up to 6 months due to complete thrombus resolution as evidenced by normalisation of liver profile and remission of MCD.

The 2021 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [10] recommend prophylactic anticoagulation for patients with membranous nephropathy and NS who have:

- Serum albumin <20–25 g/L

Additional risk factors for thrombosis include:

- Proteinuria >10 g/day
- Body mass index (BMI) >35 kg/m²
- Genetic predisposition to VTE (e.g., factor V Leiden)
- Prolonged immobilization
- Recent abdominal or orthopaedic surgery
- New York Heart Association (NYHA) Class III–IV heart failure

For other glomerular diseases such as MCD and FSGS, the decision for prophylactic anticoagulant is less clear but may be considered in the presence of severe hypoalbuminemia (<20 g/L) and additional risk factors. Using tools like the HAS-BLED score, the KDIGO guidelines highlighted the need to balance thrombotic with bleeding risk. PVT outcomes in MCD are primarily dependent on prompt diagnosis, efficient anticoagulant treatment, and strict nephrotic syndrome management. Fatal outcomes can arise from complications like bowel ischaemia or portal hypertension if timely intervention is delayed. The favourable outcome of this case (complete remission in the form of normalization of liver profile and MCD remission) supports the combined therapy. Yet, the low incidence of PVT in MCD hampers large studies and makes management mainly based on case reports and expert opinion.

CONCLUSION

Driven by a hypercoagulable state of nephrotic syndrome, portal vein thrombosis is a rare but major complication of minimal change disease. This case highlighted the need for a high index of suspicion for thrombotic events in patients with MCD presenting with abdominal pain and raised liver enzymes. Combining anticoagulation and

immunosuppressive treatment with prompt diagnosis using ultrasonography and/or CT will produce good results. Clinicians should remain alert for thromboembolic complications in MCD and modify treatment to target the underlying disease as well as the thrombus.

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CONFLICT OF INTEREST

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