Low-Molecular-Weight Heparin Successfully Used to Treat a Nephrotic Patient Complicated by Superior Mesenteric Vein Thrombosis and Portal Vein Thrombosis

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\textbf{Abstract}

\textbf{Objectives:} To report the success of treatment with low-molecular-weight heparins (LMWHs) in a case of nephrotic syndrome complicated by mesenteric vein thrombosis (MVT) and portal vein thrombosis (PVT).

\textbf{Clinical Presentation and Intervention:} A 53-year-old man with nephrotic syndrome developed persistent mild abdominal pain for 3 days. Hepatic-portal venous system thrombosis of nephrotic syndrome was suspected due to new-onset superficial vein engorgement of the abdomen without liver cirrhosis. Abdominal computed tomography revealed MVT concomitant with PVT. He was successfully treated with LMWH without thrombolytic therapy. After discharge on day 9, he received continuous anticoagulation by LWMH on an outpatient basis at the nephrology clinic. Venous thromboembolic events or proteinuria did not recur within the 6-month follow-up. \textbf{Conclusion:} This report showed a case of MVT concomitant with PVT, a critical complication of nephrotic syndrome that was diagnosed in time and successfully treated with LMWH. A high index of clinical suspicion and timely management are crucial to tackle thrombotic complications in nephrotic syndrome.

\textbf{Introduction}

Patients with nephrotic syndrome may suffer from various types of thromboembolic events [1]. Portal vein thrombosis (PVT) concomitant with mesenteric vein thrombosis (MVT) has rarely been reported. A diagnosis for PVT with MVT is usually delayed because of its nonspecific presentations. Mortality is very high among these cases because mesenteric vein thrombosis could lead to ischemia of the bowel and septic shock [2]. Treatment by surgical thrombectomy or thrombolytic therapy might be risky, and the effectiveness is varied [2, 3]. Herein, we describe a nephrotic syndrome patient who presented with abdominal pain and new-onset superficial vein engorgement of the abdomen.
Clinical Presentation and Intervention

A 53-year-old man with nephrotic syndrome was known to have proteinuria since childhood. No liver or heart disease was noted. Mild tenderness was observed in the whole abdominal area without rebounding pain. A hemogram revealed the following: hemoglobin level, 17.3 g/dl; hematocrit level, 49.9%; platelet count, 232 × 10^3/mm^3; white blood cell count, 13,300/mm^3; prothrombin time international normalized ratio, 0.95, and activated partial thromboplastin time, 32.7 s (normal, 25–34 s). The results of biochemical analyses were as follows: serum albumin, 2.1 g/dl; blood urea nitrogen, 8 mg/dl; creatinine, 0.7 mg/dl; sodium, 139 mEq/l; potassium, 4.1 mEq/l; aspartate aminotransferase, 39 U/l; amylase, 73 U/l; and lipase, 26 U/l. Spotted urinalysis revealed a protein content of 500 mg/dl and a red blood cell content of 3/high-power field. A serological study revealed a low antithrombin III level of 16% (normal, 75–127%), a normal protein C level of 100% (normal, 75–107%) and a normal protein S level of 130% (normal, 70–130%). The total protein content in a 24-hour urine sample was 5.29 g/day. Due to his history of nephrotic syndrome and superficial vein engorgement of the abdomen without liver cirrhosis, thrombosis of the hepatic portal venous system was suspected. Computed tomography (CT) was performed, which revealed the presence of PVT along with superior MVT without renal vein thrombosis (fig. 1). Therefore, anticoagulant therapy with low-molecular-weight heparin (LMWH) (enoxaparin 1 mg/kg every 12 h s.c.) and warfarin (5 mg/day) was initiated immediately. In addition, prednisolone (30 mg/day) and irbesartan (150 mg/day) were administered. His abdominal pain gradually subsided within 2 days, and the proteinuria was improved. On day 5, abdominal magnetic resonance imaging (MRI) revealed a regression of the thrombosis. Therefore, he was discharged on day 9 of admission. He received continuous anticoagulant treatment with LMWH on an outpatient basis at the Nephrology Clinic. An MRI scan obtained on day 45 did not show any thrombosis in the mesenteric vein or portal vein, and LMWH was discontinued on day 51. A renal biopsy performed on day 78 revealed minimal-change disease. Warfarin was also discontinued on day 100. Follow-up MRI on day 165 showed that the portal vein and superior mesenteric vein continued to be free of thrombi (fig. 2). During the 6-month follow-up period, venous thromboembolic events did not recur. No further proteinuria was detected by urinalysis.

Discussion

A well-recognized complication in patients with nephrotic syndrome is various types of thromboembolic events. PVT with concomitant MVT has rarely been reported and carries nonspecific clinical presentations. Patients with PVT might experience nausea, vomiting, anorexia, diarrhea or distension. Acute abdominal pain might occur when the thrombosis also extends to the mesenteric vessels as in our patient. Due to diverse symptoms or signs, it is a great challenge to accurately diagnose PVT with MVT in patients with nephrotic syndrome. A high index of suspicion of venous thrombosis of nephrotic syndrome is the key to early detection.

Superficial vein engorgement of the abdomen is an important finding in nephrotic syndrome patients.
There has been a controversy regarding various therapeutic modalities for thromboembolic events in nephrotic syndrome. Surgical thrombectomy is invasive and risky. Thrombolytic therapy may be effective to some extent but is associated with a high risk of hemorrhage. Once hemorrhage occurs, incomplete thrombolysis or anticoagulation could result in ischemia of the bowel or severe sepsis. Although anticoagulation therapy with unfractionated heparin is reported to be the mainstay therapy for venous thromboembolism, it requires the use of an inpatient monitor and is disadvantageous due to the risk of thrombocytopenia and osteoporosis [5]. LMWH might have equal effectiveness and safety compared to unfractionated heparin treatment on an outpatient basis [6]. Besides, LMWHs produce a more predictable anticoagulant response, have a better bioavailability at low doses, undergo dose-independent clearance and exhibit a longer half-life [5]. These benefits result in a more predictable treatment efficiency and make outpatient treatment possible. LMWH therapy has been suggested as a safe and effective modality for various types of venous thromboembolic events such as renal vein thrombosis [7]. For these reasons, we decided to use LMWHs for the treatment of MVT concomitant with PVT. On the other hand, serious adverse events might occur in patients with renal insufficiency when administered LMWHs [8]. Therefore, LMWH may require cautious dose reduction or increased monitoring for bleeding in patients with renal impairment [9].

In patients with nephrotic syndrome who have low serum albumin and antithrombin III levels, heavy proteinuria, a high fibrinogen level and hypovolemia are significantly associated with an increased risk of thromboembolic complications [10]. Therefore, correcting the risk factors for thrombosis in nephrotic syndrome is another important issue. At the same time, this patient received corticosteroid therapy coupled with angiotension receptor blocker treatment. His nephrotic syndrome and clinical status were gradually improved during the ensuing outpatient treatment.

**Conclusion**

This report showed a case of PVT concomitant with MVT, a critical complication of nephrotic syndrome that was diagnosed in time and successfully treated with LMWH. A high index of clinical suspicion and timely management are crucial to tackle thrombotic complications in nephrotic syndrome.
References


