Thrombocytopenia Associated with Portal Vein Thrombosis as a Presenting Sign of Adult Nephrotic Syndrome: A Case Report

Yetişkin Nefrotik Sendromun İlk Bulgusu Olarak Portal Ven Trombozu ile İlişkili Trombositopeni: Olgu Sunumu

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ABSTRACT

The nephrotic syndrome is a risk factor for venous thromboembolism. This is strikingly apparent in young adults. Portal vein thrombosis as an initial sign of nephrotic syndrome is extremely rare. A 49-year-old male was admitted to our center with complaints of severe abdominal distension, generalized edema, and oliguria for one week. On admission, serum creatinine was 2.1 mg/dl, proteinuria was 3.2 g/dl, serum albumin was 1.8 g/dl, and platelet count was 13.000/ml. Microscopic hematuria, acute kidney injury, and nephrotic range proteinuria were present. Portal vein thrombosis, massive ascites, and mild splenomegaly were detected by Doppler ultrasound and dynamic magnetic resonance imaging. We present here a case with rapidly progressive glomerulonephritis who developed acute portal vein thrombosis.

KEY WORDS: Nephrotic syndrome, Portal vein thrombosis, Thrombocytopenia

ÖZ

Nefrotik sendrom venöz tromboembolizm gelişimi açısından bir risk faktörüdür. Daha çok genç hastalarda görülmesi ilgi çekicidir. Portal ven trombozunun nefrotik sendrom başlangıç bulgusu olarak ortaya çıkması oldukça nadirdir. 49 yaşında erkek hasta kliniğimize 1 haftadır karında şişkinlik hissi, yaygın ödem ve idrar çıkımında azalma nedeniyle kabul edildi. Hastaneye yatışı esnasında serum creatinin 2,1 mg/dl, proteinuria 3,2 g/dl, serum albümin 1,8 g/dl, ve trombosit sayısı 13.000/ml idi. Mikroscopik hematuri ve nefrotik düzeyde proteinüri mevcuttu. Doppler ultrasound ve dinamik magnetik resonans görüntülemesinde portal ven thrombozu, yaygın assit ve orta derecede splenomegali tespit edildi. Bu olguda biz, hızlı ilerleyen progresif glomerülonefritin başlangıç bulgusu olarak portal ven trombozunu yayınlamayı amaçladık.

ANAHTAR SÖZCÜKLER: Nefrotik sendrom, Portal ven trombozu, Trombositopeni

INTRODUCTION

Venous thromboembolism (VTE) is a well-known complication of nephrotic syndrome (NS) (1). Relative to those who did not have proteinuria, patients who tested positive for protein had a 3.4-fold increased risk of VTE (2). Urinalysis should be done in all patients with VTE. Acute portal vein thrombosis (PVT) as the presenting sign of NS is extremely rare. PVT is a serious and life-threatening condition (3). We report an unusual case who was admitted with acute portal vein thrombosis, splenomegaly, and severe thrombocytopenia as the presenting signs of newly diagnosed NS.

CASE REPORT

A 49-year-old male presented with severe abdominal distension, massive ascites, generalized edema, and oliguria for one week. Physical examination on admission revealed a blood pressure of 100/60 mmHg, pulse 96/min., body temperature, 38°C and respiratory rate, 18/min. Cardiovascular examination was normal. Generalized edema, massive ascites, and reduced breathing sounds with bilaterally crackles at the lower lung fields were found. Petechial hemorrhages and severe pitting edema were found on bilateral lower extremity.

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Laboratory tests revealed as follows; hemoglobin was 14.3 g/dl; leucocyte, 14.240, and platelet count, 13.000/mm3. Biochemical results were as follows; serum albumin, 1.8 g/dl; serum creatinine, 2.1 mg/dl; serum low density lipoprotein (LDL) 240 mg/dl. Liver enzymes were slightly elevated on admission. After two days of admission all the liver enzyme returned to normal levels. Erythrocyte sedimentation rate was 18 mm/hour (0-10). The coagulation profile test results were as follows: prothrombin time, 19.6 s; activated partial thromboplastin time, 42.5 s; thrombin time, 16.5 s; serum fibrinogen level, 48 mg/dL (175-400); Factor V, % 14,3 (% 50-150); factor VIII, % 8.1 (% 50-150); protein C, % 87 (% 55-125); protein S, % 260 (% 55-160); antithrombin III, % 49 (% 83-118). Factor V Leiden mutation was not detected. Urinalysis revealed a protein level of 500 mg/dl, 145 red blood cells per high power field, 5–6 white blood cells per high-power field. Proteinuria level was 3200 mg/24 h. Serum samples were negative for hepatitis markers, p-ANCA, c-ANCA and antinuclear antibody, IgG and IgM anticardiolipin antibodies, anti-double-stranded DNA antibodies. Peripheral blood smear was compatible with thrombocytopenia. Bone marrow aspiration was normal other than megakaryocytosis. Budd-Chiari syndrome, abdominal neoplasia, sepsis, thrombotic microangiopathies, heparin-induced thrombocytopenia, intravascular hemolysis, and disseminated intravascular coagulation were excluded. Diagnostic paracentesis revealed no diagnostic findings for infection or neoplastic disease.

All cultures except for urine culture were normal. Urine culture revealed *Klebsiella pneumoniae*, on admission. Appropriate antibiotherapy was administered. The body temperature returned to normal levels after one day.

Cavernous transformation and tubular vascular formation in the portal region were found on Doppler ultrasound and dynamic magnetic resonance imagines (DMRA) examinations (Figure 1). Hepatic veins and inferior vena cava were normal. There was no evidence of splenorenal shunt or renal vein thrombosis. Hepatic vein and the inferior vena cava were also normal. Upper gastrointestinal endoscopy was normal. The diagnosis of NS complicated by isolated PVT was established on the basis of these results.

During hospital stay, the patient's renal function was found to deteriorate rapidly over one week. Renal biopsy was not performed because of severe thrombocytopenia. Because of the clinical presentation highly suggestive of rapidly progressive crescentic glomerulonephritis or rapidly progressive membranoproliferative glomerulonephritis, empirical pulse methylprednisolone therapy was started at a dose of 1 gr/d over 3 days. Thereafter, oral prednisolone was administered at a dose of 1 mg/kg/d. After 10 days of treatment, his 24-hour urine volume gradually increased to 2.000 ml/d. Proteinuria, hypoalbuminemia, and renal function gradually improved over one month.

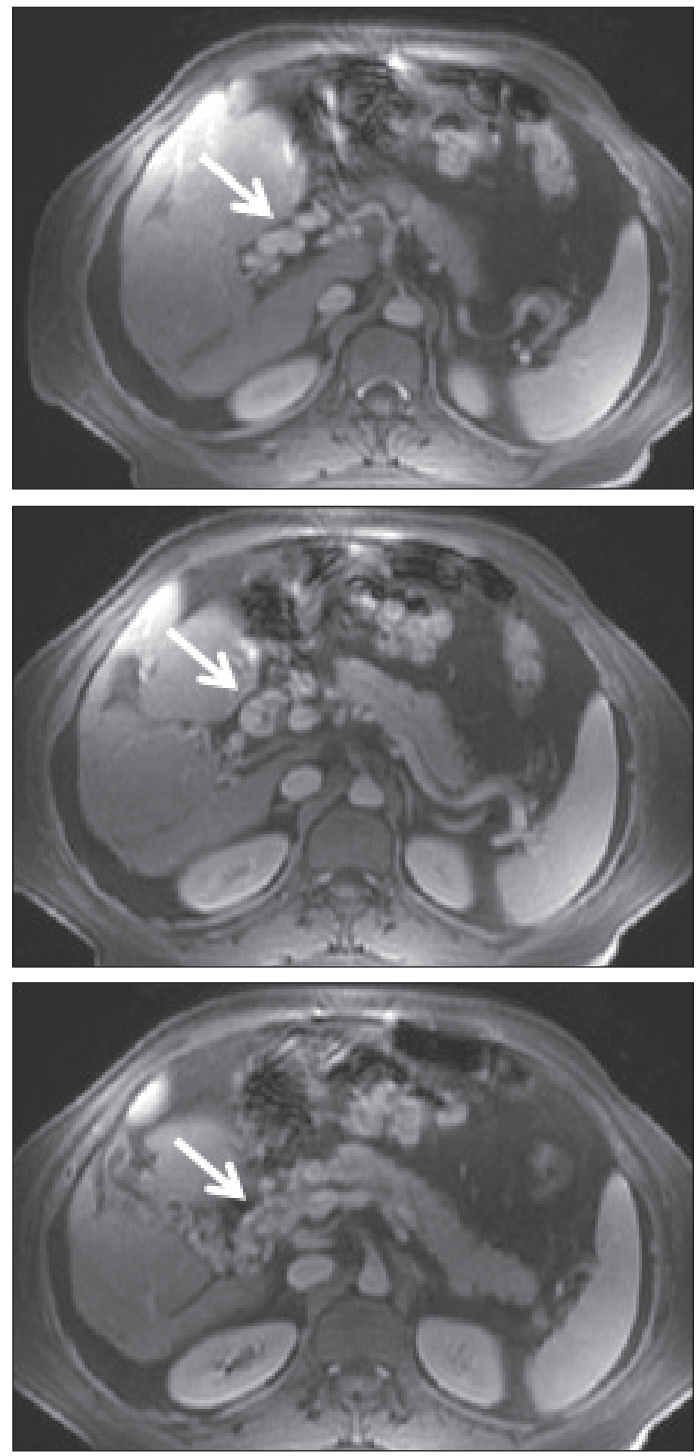

Figure 1: *After the application of I.V Gd,, while T1-weighted MRI at portal phase reveals abnormal configuration, diameter and signal aspects of portal vein, varicose formations which are harmonious with portal cavernous transformation are seen at the level of the liver hilus.*

Because of severe thrombocytopenia and suspected low-grade gastrointestinal hemorrhage, we could not administer heparin or antiaggregant therapy. After two months of outpatient follow up, complete remission of NS was obtained, but repeated Doppler ultrasound showed no complete recanalization of the portal vein. After complete remission of the NS, all abdominal complaints of the patient and ascites completely resolved, but platelet level increased modestly. Four months after initial presentation, the patient was healthy. Unfortunately, nephrotic syndrome recurred six months later. 24-hour proteinuria increased to 3.5 g/day; serum albumin level decreased to 2.1 g/dl.

DISCUSSION

The association between NS and VTE is well known in adults. VTE has been described in various veins including deep veins of the lower limbs, renal veins, inferior vena cava, and mesenteric veins in nephrotic adult patients (4). While arterial thrombosis and intracardiac thrombosis may also develop in these patients, PVT is very rare, particularly as an initial sign.

The prevalence of VTE is high among several renal disease including primary glomerular diseases, particularly membranoproliferative glomerulonephritis and minimal change disease however, the VTE appears to be more prevalent in patient with membranous glomerulonephritis (5,6). The exact mechanism of thrombophilia in NS is poorly understood. VTE in NS may arise from various abnormalities including loss of anticoagulant factors and proteins, increased synthesis of factors promoting thrombosis, platelet abnormalities, decreased fibrinolytic system, venous stasis, and hemoconcentration. Several studies have demonstrated an association between severe hypoalbuminemia and VTE. However, serum albumin levels in patients with and without VTE are not significantly different (5). It has been shown that the ratio of proteinuria to serum albumin was significant predictor of NS. Mahmoodi et al. suggested that it is a reliable reflector of the severity of NS than serum albumin levels or the degree of proteinuria alone (6). Risk of VTE is particularly high within the first 6 months of NS, as was seen in our patient.

PVT has been reported anecdotally in a few of patients with NS (7). In a large retrospective cohort study, Mahmoodi et al did not report PVT in nephrotic patients with VTE (6). One of the most common consequences of PVT is the clinical syndrome of hypersplenism characterized by splenomegaly and the associated destruction of one or more cell lines in the peripheral blood (8). Consumption coagulopathy as well as hypersplenism may also have contributed to the thrombocytopenia in our patient. Other disease and disorders that associated with hypersplenism were not found in our patient. However, Sun and Xu did not report thrombocytopenia in their nephrotic patient with PVT (7).

Asymptomatic patients with portal vein thrombosis can remain untreated. All patients with clinical symptoms should be treated. For the mild to moderate cases, treatment with low molecular heparin may be considered, although more-severe cases require thrombolysis and/or thrombectomy (6). Thrombectomy was not indicated in our patient, as his symptoms had already been present for 2 weeks. Because of severe thrombocytopenia and suspected low-grade gastrointestinal hemorrhage, we could not administer heparin or antiaggregant therapy. The patient remained untreated for PVT. Interestingly, after the complete remission of the NS, all abdominal complaints and ascites completely resolved, but the platelet level increased modestly.

CONCLUSION

Portal vein thrombosis as the presenting sign of NS in adults is a severe clinical condition, and when complicating with severe thrombocytopenia histopathological diagnosis of glomerular disease is not possible as was seen in our patient. Empirical immunosuppressive treatment can be use to treat of selected patients with progressive glomerular disease as in our patient.

REFERENCES

1. Cameron JS: The nephrotic syndrome and its complications. Am J Kidney Dis 1987; 10: 157-171
2. Kato S, Chernyavsky S, Tokita JE, Shimada YJ, Homel P, Rosen H, Winchester JF: Relationship between proteinuria and venous thromboembolism. J Thromb Thrombolysis 2010; 30(3): 281-285
3. Gupta A, Al Fulaij R, Gupta RK, Gupta G, Marouf R: Development of paroxysmal nocturnal haemoglobinuria in systemic lupus erythematosus: An unusual cause of portal vein thrombosis. Lupus 2009; 18: 743-746
4. Yang GF, Schoepf UJ, Zhu H, Lu GM, Gray JC, Zhang LJ: Thromboembolic complications in nephrotic syndrome: Imaging Spectrum. Acta Radiol 2012; 53(10): 1186-1194
5. Singhal R, Brimble KS: Thromboembolic complications in the nephrotic syndrome: Pathophysiology and clinical management. Thromb Res 2006; 118(3): 397-407
6. Mahmoodi BK, Ten Kate MK, Waanders F, Veeger NJ, Brouwer JL, Vogt L, Navis G, Van der Meer J: High absolute risks and predictors of venous and arterial thromboembolic events in patients with nephrotic syndrome: Results from a large retrospective cohort study. Circulation 2008; 117(2): 224-230
7. Sun L, Xu C: Portal vein thrombosis as the first sign of nephrotic syndrome. Nat Clin Pract Nephrol 2008; 46: 342-345
8. Peck-Radosavljevic M: Review article: Coagulation disorders in chronic liver disease. Aliment Pharmacol Ther 2007; 26: 21-28