

## A Case of Proteinuria Developing Secondary to Solitary Renal Vein Thrombosis Due to Oral Contraceptive Use

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### ABSTRACT

Renal vein thrombosis (RVT) is the presence of thrombi in major renal veins or their branches and is a rare clinical entity. RVT is one of the common thrombotic complications of nephrotic syndrome or renal cell carcinoma. Hormonal contraception can also rarely cause this complication. Herein, we presented a case of renal vein thrombosis accompanied by subnephrotic proteinuria after oral contraception.

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**Keywords:** Renal vein thrombosis, proteinuria, nephrotic syndrome, oral contraception, thrombolytic therapy.

### Introduction

Common symptoms of renal vein thrombosis (RVT) are flank pain, hematuria, and acute kidney injury. The leading causes of RVT are nephrotic syndrome, renal cell carcinoma, trauma, kidney transplantation, hypovolemia, and hereditary procoagulant defects.<sup>1</sup> Recently, cases of COVID-19-related RVT have also been reported in the pandemic. Oral contraception is one of the rare causes of RVT.<sup>2</sup> Usually, RVT may occur due to hypercoagulation during the nephrotic syndrome, generally bilateral. We presented a case of renal vein thrombosis with subnephrotic proteinuria after oral contraception use.

### Case Report

A 29-year-old female patient presented with complaints of left flank pain and nausea-vomiting for two days. She had a previous diagnosis of trigeminal neuralgia and history of nonsteroidal anti-inflammatory drug use. Her physical examination revealed left costovertebral angle tenderness and bilateral pretibial oedema (+/+). We learned that the patient was using oral contraceptives. The examination of urine sediment revealed 38 erythrocytes and 15 leukocytes per HPF. In urine, proteinuria was positive (++) . Protein excretion in 24-hour urine was 2,562 mg. In the biochemistry tests, creatinine was 0.92 mg/dL, urea 10 mg/dL, albumin 31 g/L, D-dimer



13 mg/L, LDH 351 U/L, and triglyceride 334 mg/dL. Contrast-enhanced computed tomography reported that a thrombus causing total occlusion in the left renal vein extended from the left renal vein to the inferior vena cava. We diagnosed acute RVT, and the interventional radiology unit performed thrombolytic therapy, thrombectomy and balloon angioplasty. After the procedure, they coded flow in both renal veins in the control doppler ultrasonography. ANA, ANA profile, anticardiolipin IgM and IgG, beta-2 glycoprotein IgM and IgG antibodies were negative. Heterozygous MTHFR mutations were positive in the thrombophilia panel. PAI 4g/5g, MTHFR c.1298A>C, FXIII p.V34L, prothrombin g.20210G>A, and FV Leiden c.11691G>A was normal. We thought that RVT developed secondary to oral contraceptive use in the patient. We followed up the patient with anticoagulant therapy after the procedure. She had no complaints at the outpatient polyclinic control five months after, and urinary proteinuria (150 mg/24 hours) and kidney function tests were within normal ranges.

## Discussion

Renal veins are rarely thrombosed, and the cause is usually almost always clear. The use of oral contraceptive drugs is known among the risk factors for RVT.<sup>3,4</sup> The relationship between the use of oral contraceptives and the risk of venous thrombosis was investigated in women aged 15-49 years without a history of cardiovascular or malignant disease in Denmark between 1995 and 2005.<sup>5</sup> In this cohort, out of a total of 4,213 venous thrombotic events, 2,045 were observed in current oral contraceptive users. The overall absolute risk of venous thrombosis per 10 000 women-years was 3.01 in non-users and 6.29 in current users of oral contraceptives.<sup>5</sup>

Pregnancy-postpartum, surgery and trauma can often trigger thrombotic events even in the general population. Clinicians should also look for the presence of a prothrombotic disorder if there are no obvious risk factors in oral contraceptive users who develop venous thrombosis. These conditions can cause acute renal vein thrombosis in the presence of a trigger such as oral contraceptive medication. Several case series in the literature

have reported patients with RVT associated with hyperhomocysteinemia, elevated factor VIII levels, congenital disabilities of clotting inhibitors such as potential heterozygous true deficiencies of antithrombin III (low ATIII antigen and activity), a decreased protein C antigen to factor X antigen ratio, a heparin cofactor II deficiency, and a type I protein S deficiency after oral contraceptive use.<sup>6-9</sup> In our case, heterozygous MTHFR c.677C>T mutation was positive. This heterozygous mutation generally increases the susceptibility to arterial thrombosis.

A previously healthy 15-year-old female patient was taking oral contraceptives admitted with isolated, unilateral renal vein thrombosis. This patient had mild proteinuria (760 mg/24 hours).<sup>10</sup> Nephrologists often encounter RVT as a complication of nephrotic syndrome. However, we should be aware that RVT can lead to mild or nephritic proteinuria. Rapid diagnosis and intervention with radiological imaging are essential in patients with RVT. In some cases, thrombosis has been effectively treated with streptokinase.<sup>11</sup> After early diagnosis, we treated the present case with RVT with successful intervention and thrombolytic agents.

## Conclusions

When patients use oral contraceptives with flank pain and hematuria, one of the differential diagnoses should be acute renal vein thrombosis. The treatment can change depending on the patient's prognosis and clinic. Patients without acute kidney injury can generally follow up with anticoagulant therapy. Thrombolytic treatment and thrombectomy should be considered primarily in patients with the presence of acute kidney injury, transplanted kidneys, and bilateral RVT or unilateral patients with a high thrombus load.

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### **Conflict of interest**

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### **Authors' Contribution**

Study Conception: MS, AG; Study Design: MS, AG, AE; Supervision: MS, AG, AE; Materials: MS, AG; Data Collection and/or Processing: MS, AG; Statistical Analysis and/or Data Interpretation: MS, AG, AY; Literature Review: MS, AG, AY; Manuscript Preparation: MS, AG; Critical Review: MS, AG.

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