

➤ **Case Report** ◀

Renal Vein Thrombosis Occurring in Association with Oral Contraceptives: A Case Report

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Peripheral venous thromboembolism is a well-known complication of hormonal contraception, but reports on its association with visceral vein thrombosis is limited. We report the case of left renal vein thrombosis (RVT) associated with oral contraceptives (OCs) and concurrent smoking. The clinical presentation of this patient was acute left flank pain. Computed tomography revealed left RVT. The OC was discontinued, and we initiated anticoagulation with heparin and switched to edoxaban. Computed tomography 6 months later showed complete resolution of the thrombosis. This report alerts us regarding the importance of OCs as a risk factor for RVT.

Keywords: renal vein thrombosis, oral contraceptives, anticoagulation

Introduction

Renal vein thrombosis (RVT) is a common thrombotic complication of renal cell carcinoma or nephrotic syndrome; however, this visceral vein thrombosis is a rare complication of hormonal contraception.¹ Previous studies have reported an increased risk of venous thrombosis with the use of oral contraceptives (OCs)^{1–3}; however, reports on its association with solitary RVT is limited.^{4–6} Cases of solitary RVT is rare in Japan⁶ since the incidence of venous thromboembolism (VTE) is relatively low in Asian population.⁷ We report a case of solitary RVT in

association with OCs.


Case Report

A 36-year-old woman who was on OC visited our hospital with a chief complaint of acute-onset severe left flank pain, followed by nausea. She did not have any significant medical history. She was a smoker and concurrently ingested OCs 2 weeks prior to admission.

The patient was with a height of 168 cm and weight of 64 kg, which had been constant in the past few years. The patient was conscious without shortness of breath. Her blood pressure, pulse rate, respiration, percutaneous oxygen saturation, and body temperature were 128/88 mmHg, 64 beats per minute, 24 breaths per minute, 99%, and 36.8°C, respectively. Abdominal examination showed spontaneous dull pain in the left dorsal area and slight tenderness in the left flank area without obvious rebound and muscular defense. Knocking pain was induced by light percussion at the left costovertebral angle. Other physical examinations, as well as the chest, abdominal, and pelvic radiographs, were normal. Renal ultrasound revealed a low-echoic defect in the left renal vein and a swollen left kidney. Contrast-enhanced computed tomography (CT) revealed left RVT and an enlarged left kidney (Figs. 1A and 1B) but other visceral VTEs, including pulmonary thromboembolism, were not detected. There were no other masses or apparent compression of the renal vein, suggestive of nutcracker syndrome. Ultrasonography did not reveal deep vein thrombosis of the lower extremities. Blood tests showed that the routine hematological tests, liver function tests, and C-reactive protein levels were within the normal range. The blood urea level (13.1 mg/dl) was also normal while both serum creatinine level (1.01 mg/dl) and D-dimer level (4.00 µg/dl) were slightly elevated. Urinalysis revealed hematuria (3+), and urine sediment showed 1–5 neutrophils, 31–40 red cells, and 1–5 squamous epithelial cells per high-powered field, without bacteria or casts. Nephrotic syndrome was excluded since both repeat urinalysis and serum albumin levels were normal. There were no abnormalities in the level of protein C, protein S, antithrombin-III, and immu-

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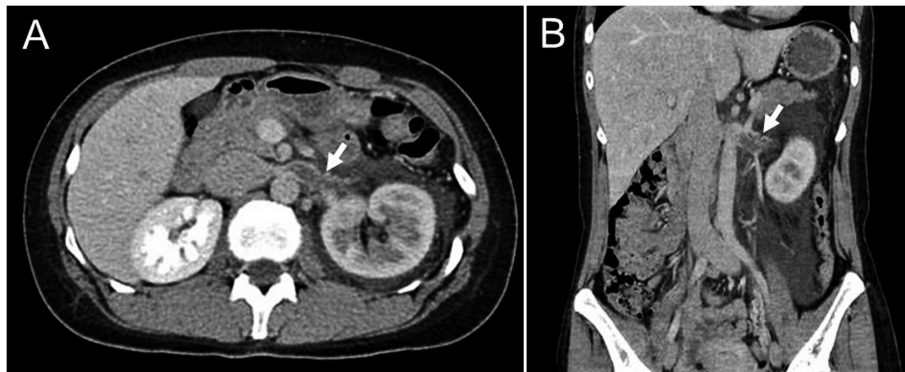


Fig. 1 Radiological examination at the onset. (A) Axial image of abdominal computed tomography (CT) scan with contrast showed a large thrombus in the left renal vein (arrow) and an enlarged left kidney with perirenal stranding. (B) Coronal image of abdominal CT scan with contrast showed a large thrombus in the left renal vein (arrow).

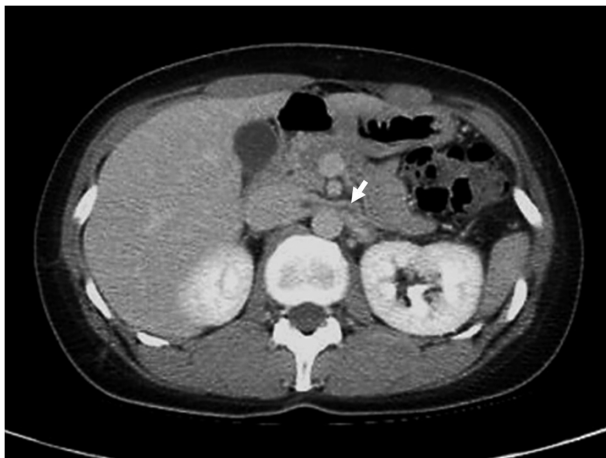


Fig. 2 Repeat contrast-enhanced computed tomography scan 1 week postanticoagulation, showed a residual thrombus in the left renal vein.



Fig. 3 Repeat computed tomography scan with contrast 6 months after anticoagulation showed patent renal vein and complete resolution of the thrombus.

nologic analysis for anticardiolipin antibodies and lupus anticoagulant.

The OC was discontinued and heparin administration was initiated on the day of admission. The patient was relieved from the flank pain 2 days later, and heparin was replaced with edoxaban, a direct oral anticoagulant (DOAC). The patient was discharged on the 10th day of hospitalization. Subsequently, the administration of edoxaban was continued for 6 months. Residual thrombosis was immediately detected in the CT image before discharge (Fig. 2). The thrombosis in the left renal vein was completely dissolved in the repeat CT 6 months later (Fig. 3). The anticoagulation with DOAC was discontinued after 6 months administration. The patient quit smoking and ingesting OCs. Thus, RVT was nonrecurrent 2 years after the onset.

Discussion

In 1840, Rayner initially reported the association between nephrotic syndrome and RVT.⁸⁾ RVT is considered a complication secondary to nephrotic syndrome. Other predisposing conditions include neoplastic diseases, blunt trauma, renal transplantation, and use of drugs, such as diuretics and steroids.

Renal vein is occluded in the main renal vein and in larger intrarenal veins in most RVT cases, followed by the development of collateral vessels. Thus, patients commonly present with nausea and progressive flank or back pain. Patients may appear asymptomatic if the development of collateral vessels is adequate. Conversely, acute RVT is a rare condition usually associated with renal transplantation or blunt abdominal injury. Acute RVT usually have an acute-onset flank pain, hematuria, and dysfunction of the involved kidney. Involving the bilateral kidneys with RVT can result to oliguria and acute renal failure.

Color-flow Doppler ultrasonography aids in the early diagnosis of RVT since it may demonstrate intravenous thrombus, kidney enlargement, and diminished venous blood flow. Contrast-enhanced CT scan is also useful in accurately diagnosing and excluding other causes of acute abdomen.

The treatment choices for RVT depend on clinical manifestation and prognosis. Generally, anticoagulation therapy using conventional heparin, low-molecular-weight heparin or warfarin is considered the first-line treatment for RVT. Anticoagulation therapy is commonly used to treat VTE to prevent the disease progression by reducing additional thrombus formation and promoting the recanalization of occluded vessels. Heparin is administered in the acute phase and then switched to warfarin or DOACs. Shimada et al. reported that edoxaban was effective for recurrent pulmonary embolism associated with RVT after anticoagulation using warfarin.⁹⁾ Treatment with systemic or catheter-directed thrombolysis is considered for the management of acute RVT. Thrombectomy with catheter and intravenous stenting is considered for the direct treatment for thrombi.

There is strong evidence that the incidence of venous thrombosis is significantly lower in Asians than that in other ethnicities in the European countries and North America.⁷⁾ RVT occurs in only 0.8% of all VTE cases due to hormonal contraception.¹⁾ Thus, solitary RVT associated with hormonal contraception is rare in Japan.⁶⁾ OCs predispose the user to thrombophilia. Previous studies have shown a threefold increased risk of thromboembolism in women using OCs,^{1,2)} and these studies have generally suggested a higher risk during the first year of OC use. We note that the shorter duration of OC intake in this present case compared with the previous cases was due to the presence of coexisting factors such as smoking and dehydration.

Although the evidence regarding the relationship between venous thrombotic disease and smoking is limited, some studies have reported 3.3-fold increased relative risk of VTE in smokers.¹⁰⁾ Epidemiologic studies showed the synergistic effect of smoking and OC use on cardiovascular and cerebrovascular incident. Therefore, the World Health Organization has suggested that OC should not be taken by women over 35 years of age who smoke >15 cigarettes per day.

RVT is also caused by extrinsic compression due to an anatomical variation, known as nutcracker syndrome. The diagnostic criteria for nutcracker syndrome is the <5-mm distance between the aorta and superior mesenteric artery at the level of left renal vein (nutcracker distance). Because this distance was 10-mm at the onset and 8-mm after thrombus dissolution in the present case, the extrinsic compression was considered to have little relation with

the occurrence of this RVT.

This report shows that OCs is a precipitating risk factor for RVT, which should be regarded as differential diagnosis for acute abdominal pain in patients who take OCs. In addition to radiological examination, including CT scan, a detailed medical and social history taking with regard to OC use and smoking would help us to diagnose and treat RVT.

Conclusion

We report a case of a solitary RVT in a patient taking OCs and smoking. Although RVT, a rare complication in the Asian population, occurred in association with OCs, our experience shows that OCs is a precipitating factor for RVT. Smoking cessation should be strongly recommended for OC users. Further study regarding VTE and RVT is warranted.

Disclosure Statement

All authors declare no conflict of interest.

Additional Note

Appropriate written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Author Contributions

Study conception: TM, MO (M. Ogiwara)

Data collection: TM, YN

Analysis: TM, YN

Investigation: TM, YN

Manuscript preparation: TM

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