The use of rivaroxaban in deep venous thrombosis associated with vena cava inferior agenesis

Vena kava inferior agenezisi ile iliskili derin ven trombozunda rivaroksaban kullanımı

Ali Ahmet Arıkan1, Selçuk Emre2, Bayraktar Fatih Avni2

ABSTRACT

Inferior vena cava agenesis (IVCA) is a rare anomaly which may result in deep vein thrombosis (DVT). Its prevalence ranges from 0.0005 to 1% among the general population.[1] In the literature, there is no clear scientific evidence for the most effective therapeutic management, optimal duration, or the choice of anticoagulant therapy. [2-5] Herein, we report a young male case with DVT associated with IVCA who was prescribed rivaroxaban as a lifelong anticoagulation treatment for symptoms of venous stasis and the presence of heterozygotic thrombophilic mutations. Keywords: Inferior, rivaroxaban, thrombophilia, vascular malformation, vein thrombosis, vena cava.

CASE REPORT

A 17-year-old male presented to the emergency department with complaints of pelvic pain, swelling and pain in his legs, which started after a vigorous exercise session. His medical history revealed that he was a smoker without drug use or no history of chronic disease, surgery or immobilization and no familial history of thromboembolic events. Blood tests revealed leukocytosis and elevated D-dimer, lactate dehydrogenase, creatinine, kinase, and C-reactive protein levels. A venous Doppler ultrasound scan showed thrombosis in the
right iliac vein and bilateral DVT in the femoral, popliteal, and crural veins. Computed tomography revealed the absence of inferior vena cava (IVC) and dilated collateral venous circulation (Figure 1). Echocardiography revealed no abnormalities of the cardiac chambers or cardiac functions. The hepatic veins were entering directly into the right atrium without IVC. Thoracic magnetic resonance imaging (MRI) showed IVCA, hepatic veins opening directly to the right atrium, dilated azygos/hemiazygos veins, tortuous collateral veins, and an aberrant right subclavian artery in combination with a common trunk of the right and left common carotid arteries. The dilated azygos vein was draining to the superior vena cava in the form of an arch. Heterozygotic mutations were detected in plasminogen-activator inhibitor 1 (PAI-1) 4G/5G, β-Fibrinogen 455G/A, and GPIIIa L33P genes.

Conventional treatment with subcutaneous enoxaparin and warfarin was started. Pain and edema resolved after 10 days. In first three months of outpatient follow-up, he was re-admitted to the hospital, once following epistaxis with an international normalized ratio (INR) of 10 and two times due to subtherapeutic INR values. Warfarin dose was regulated to achieve an INR between 2 and 3 before discharge. Recurrent bilateral DVT in the femoral, popliteal, and crural veins was detected by Doppler ultrasound during his last hospitalization with an INR of 1.8. Based on these findings, we decided to switch the anticoagulant regimen to rivaroxaban (15 mg bid for the first 21 days, followed by 20 mg once daily). Following the six months of rivaroxaban therapy, complaints of tenderness over dilated veins on the abdominal wall and symptoms of mild post-phlebitic syndrome were noted. Repeated Doppler ultrasound showed no venous thrombosis of the lower extremities. Despite the absence of a sign of recurrent thrombosis on imaging studies and laboratory testing, dilatation of the collateral circulation of the abdominal wall and mild pretibial edema were considered as a result of stasis. Considering also the heterozygous mutations for thrombophilia, we decided to administer lifelong prophylaxis with rivaroxaban. Compression stockings were recommended. The patient had no recurrence after a 48-month follow-up without any adverse event related to rivaroxaban therapy.

**DISCUSSION**

Inferior vena cava agenesis, a rare anomaly which may cause significant morbidity, is associated with cardiac, vascular, pulmonary, or gastrointestinal malformations. In our case, a thoracic MRI with a contrast agent showed an aberrant right subclavian artery in combination with a common trunk of the right and left common carotid arteries.

In the literature, the use of anticoagulation for short durations as three months in IVCA and DVT has been reported. However, recurrent DVT after discontinuation of anticoagulation is also frequent. It has been shown that IVCA may lead to dilatation of azygos/hemiazygos veins, ascending lumbar veins, the paravertebral venous plexus, and epigastric veins in the abdominal wall to maintain the circulation of the lower extremities. An inadequate blood return through collaterals may result in stasis and increases

![Figure 1.](image-url)
the venous blood pressure in the leg veins, thereby, facilitating DVT.\cite{1,7} Our case had heterozygotic mutations in PAI-1 4G/5G gene, which increases the risk for venous thromboembolism in patients with other thrombophilic disorders.\cite{8} Considering the signs of venous hypertension on physical examination and the presence of thrombophilic abnormalities, indefinite anticoagulation was recommended to our case.

Therapy with vitamin K antagonists is used in 99\% of patients with IVCA and DVT.\cite{4} Despite being used safely for DVT, there is a limited number of data on the use of rivaroxaban for DVT in IVCA. In a large review of Tufano et al.\cite{9} including 175 cases of IVCA, only four cases were treated with rivaroxaban. One of these cases was switched from rivaroxaban therapy (20 mg/day) to vitamin K antagonists due to hemorrhage and another case (dose not reported) due to recurrent thrombosis. The remaining two cases were treated with pharmacomechanical thrombolysis followed by heparin and oral rivaroxaban therapy without complications or recurrence. Aday et al.\cite{10} also presented a case with IVCA and DVT treated with pharmacomechanical thrombolysis, followed by an indefinite administration period of rivaroxaban at a dose of 20 mg daily. Khalafallah et al.\cite{3} reported a case in which rivaroxaban at a dose of 15 mg orally twice daily was initiated after DVT recurrent, despite the use of vitamin K antagonists. Pharmacomechanical thrombolysis as described by Aday et al.\cite{10} and open venous thrombectomy with surgical veno-venous or veno-atrial bypass procedures as described by Sagban et al.\cite{11} can be considered in the treatment of DVT in IVCA, although effective anticoagulation is the cornerstone of all therapeutic options. In our case, anticoagulation with rivaroxaban is used with freedom of recurrent DVT and without worsening of post-phlebitic symptoms.

In conclusion, inferior vena cava agenesis should be considered in young patients with bilateral deep vein thrombosis. Patients should be investigated for other cardiovascular and hematological abnormalities. Uncommon genetic mutations related to hypercoagulability and signs of venous stasis are recognized as the major risk factors for deep vein thrombosis. In our case, long-term anticoagulation with rivaroxaban is recommended and used safely without any recurrent deep vein thrombosis.

### Declaration of conflicting interests
The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

### Funding
The authors received no financial support for the research and/or authorship of this article.

### REFERENCES