

# [Factor v leiden case study](https://assignbuster.com/factor-v-leiden-case-study/)

Factor V Leiden Case Study

Abstract

Factor V Leiden is a common hereditary thrombophilia associated with an increased risk of thrombotic events such as deep venous thrombosis or pulmonary embolism. Characterized by Factor V resistance to activated protein C, Factor V Leiden is an autosomal dominant disorder. This case study explores the case of a college-age female athlete who experienced a pulmonary embolism and was diagnosed with Factor V Leiden.

Case Presentation

A 19-year-old female collegiate soccer athlete experienced a cough, fatigue, and progressive decrease in exercise tolerance over the course of several days but was otherwise healthy with no significant preexisting conditions. Attributing the symptoms to stress, lack of sleep and a recent illness, she and her trainer dismissed the symptoms initially, however on the evening of the third day after a competition, the patient’s symptoms worsened. At the emergency department, she presented with dyspnea and lower left pleuritic pain. She was unaware of any family history of pulmonary embolism, deep venous thrombosis (DVT) or any genetic risk factors for thrombophilia. No medications were taken, other than an oral contraceptive for treatment of endometriosis.

Clinical Laboratory Testing

The patient proceeded to undergo testing including an echocardiogram, chest x-rays, CBC and chemistry panel, in addition to a physical examination where her vitals were taken. All results were unremarkable with no abnormalities. When tested, her prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR) were all within range, however her D-dimer concentration was elevated to 16. 45mg/L (normal range = 0. 43-1. 10mg/L).

Diagnosis/Treatment/Prognosis

After a computed tomography (CT) scan, the patient was diagnosed with bilateral pulmonary emboli. Further genetic testing indicated that she was heterozygous for Factor V Leiden (FVL) and activated protein C resistance (APCR). The patient’s treatment included intravenous heparin therapy and anticoagulant therapy for 12 months following discharge from the hospital. Because of the risk of increased bleeding time, the patient was instructed to limit conditioning drills and avoid contact within her soccer activities.

FACTOR V LEIDEN

History

The disorder known as Factor V Leiden (FVL) thrombophilia was discovered by Swedish researchers in 1993. 1 Researchers proposed a new mechanism for familial thrombophilia which highlighted an inherited resistance to activated protein C (APC). It has been shown that around 90% of cases involving activated protein C resistance are a result of Factor V Leiden. 5, 8

Etiology

Factor V Leiden is a relatively common inherited thrombophilia following an autosomal dominant pattern of inheritance. 1 The mutation in FVL occurs in the F5 gene, which lies on the long arm of chromosome 1, position 24. 2. 3 This gene encodes Factor V (FV), a coagulation factor produced in the liver. When activated, Factor V is responsible for interacting with Factor X, and forming a complex that converts prothrombin to thrombin, ultimately facilitating the conversion of fibrinogen to fibrin. Normally, Factor V also interacts with activated protein C, which cleaves Factor Va (and Factor VIIIa) at specific sites by way of negative feedback inhibition, preventing the forming clot from growing too large. A missense mutation in the F5 gene causes the substitution of guanine to adenine at nucleotide 1691, exon 10. 8 The replacement of arginine with glutamine at codon 506 results in an abnormal Factor V molecule known as Factor V Leiden . 5, 7, 8

The mutation causing Factor V Leiden alters the cleavage site where activated protein C binds, reducing the efficacy of APC in its role of inactivating Factor Va. 5, 8 As a result, the coagulation cascade continues to produce fibrin for longer than usual, because APC cannot degrade the mutated Factor V Leiden ­ ­ as quickly. This results in a condition referred to as activated protein C resistance (APCR). 2 The extended duration of clot formation leaves affected individuals susceptible to developing abnormal blood clots. As such, FVL is the most common hereditary predisposition to venous thrombosis including deep venous thrombosis (DVT) with or without pulmonary embolism (PE). 8

Epidemiology

Cases of Factor V Leiden account for around 40% of all cases of hereditary thrombophilia. 5 FVL is most common in Caucasians, with minimal incidence in other ethnic groups, such as Africans, Asians, Australians and Native Americans. 5, 8 The prevalence of a heterozygous FVL mutation is up to 15% in Caucasian populations. 2, 3, 5 Homozygous FVL mutations occur at a rate of about 1 in 5, 000. 3, 8 Individuals who are homozygous for FVL are at an increased thrombotic risk. Risk is increased 3- to 7- fold in heterozygotes and 80-fold in homozygotes. 8 Considering cases of patients who do experience episodes of venous thrombosis, 10-25% of all cases have the FVL mutation present in either its homozygous or heterozygous form. 5

Clinical Laboratory Testing

Laboratory testing for Factor V Leiden includes a variety of clot-based functional screening tests, confirmed by molecular DNA assay. One method of APCR screening tests involves an activated partial thromboplastin time (aPTT) and modified aPTT test with the addition of purified APC. 8 Typically, an aPTT test is performed to measure the intrinsic and common pathways of the coagulation cascade by measuring the length of time that it takes for a clot to form after reagents are added to patient plasma.

In the aPTT-based method, the addition of APC should prolong the duration of the test in patients unaffected by FVL due to the successful inactivation of FVa by APC, and subsequent regulation of fibrin formation. APCR is determined if the addition of APC fails to extend the duration of the aPTT, meaning that FVa is unable to be inactivated by APC and fibrin formation continues uninhibited. Once the aPTT and modified APCR aPTT have been performed, a ratio of the two clotting times is calculated and expressed as APC sensitivity – a low ratio being indicative of APCR. 5, 8 Patients found to have low APC sensitivity must then undergo further molecular analysis via PCR in order to be diagnosed with FVL.

Although it has been a common screening test method for determining APCR, the aPTT-based version of the APCR screening test is subject to interference from other disorders causing elevated aPTT, such as the presence of a lupus anticoagulant, and discrepancies have been discovered between APCR and FVL testing. 6 Newer assays, such as the Russell Viper Venom-based test, have been found to produce a higher specificity, sensitivity and positive predictive value when compared to the aPTT-based screening test. 4 This particular assay incorporates activating reagents, plus the venom from a Russell Viper and other snakes. The Russell Viper venom acts to directly activate Factor V, and venom from other snakes, such as the Southern Copperhead or Australian Tiger Snake, directly activates Protein C. 4 Similar to the aPTT-based method, clotting times with and without APC are measured to determine the ratio and APC sensitivity is expressed as a ratio. For patients with a low APC sensitivity as a result of the Russell Viper Venom-based assay, molecular testing should be pursued to confirm diagnosis with FVL mutation.

Diagnosis/Differential Diagnosis

Diagnosis of Factor V Leiden typically requires both an APCR screening test and a molecular assay to determine the molecular defect. Patient history is important in diagnosing FVL, as it is an inherited disorder. Patients with FVL are usually asymptomatic, however may experience abnormal bleeding. Often, patients are unaware that they may have the disorder, until they experience a thrombotic event, such as a DVT or PE. When considering the differential diagnosis, other hypercoagulability disorders must be considered, such as Antithrombin deficiency, Protein C deficiency, Protein S deficiency or Prothrombin 20210. 2, 5

Treatment

Treatment of Factor V Leiden may potentially include prophylactic anticoagulant therapy if patients have reoccurring thrombotic events or are exposed to increased thrombotic risk. 5 Lifelong anticoagulant therapy is not usually prescribed. 6 Woman with FVL have an increased risk of developing a DVT during pregnancy and may require anticoagulant therapy throughout their pregnancy. 6 Risk factors for developing thrombosis include age, obesity, cancer, immobility, trauma/surgery, pregnancy, oral contraceptive use, smoking, hospitalization and air travel. 2, 3, 5, 6 Special considerations for women include the use of oral contraceptives or hormone replacement therapy, as both hormonal therapies can increase risk for thrombotic event. 6

Conclusion

To conclude, Factor V Leiden is a common hereditary thrombophilia resulting in a mutation in the gene responsible for encoding Factor V. The affected gene results in the abnormal clotting protein, Factor V Leiden . Activated protein C, typically responsible for regulation of the formation of fibrin through the inhibition of Factor V, is unable to bind the mutated Factor V Leiden protein, allowing for fibrin formation to continue mostly unregulated. Because of the excessive production of fibrin, patients who are diagnosed with FVL experience increased risk of DVT or PE. Overall, FVL is a relatively manageable condition that is only life-threatening in the occurrence of a thrombotic event.

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