Blood Clots within the Body and the Effects of Having Factor V Leiden

November 15, 2011
Abstract

Deep vein thrombosis and pulmonary embolisms are blood clots that are not only harmful to the physiology of the human body, but can be deadly to a patient if not treated correctly. Often times where the vein thrombosis and the pulmonary emboli come from are similar but the effects they can have on the body are different. Factor V Leiden is a common blood disorder that affects the existence of these clots. It can be diagnosed using radiologic methods followed by blood tests. While Factor V Leiden can be detrimental for a patient, a normal life can be achieved if a patient and their physicians keep careful evaluation and observation while carrying out the suitable treatment.
Blood Clots within the Body and the Effects of Having Factor V Leiden

In the human body normal physiology entails having blood travel and function within blood vessels that are unobstructed. This is referred to as hemostasis. Coagulation processes however do start when an injury occurs. During coagulation blood patches form on the vessel walls and the anticoagulant system keeps blood moving fluidly. If at any time this hemostasis of the blood vessels is compromised the body can experience serious effects (Kang, Ren, Sharma & Peiper, 2009).

Deep Vein Thrombosis and Pulmonary Embolisms

Deep vein thrombosis (DVT) describes a blood clot within the blood vessels. DVTs are caused by multiple issues in the body including venostasis, vessel wall damage, and hypercoagulability or a combination of the three (Yasuoka & Kubota, 2011). (See Fig. 1) Many incidents of DVT come from trauma or stress put on the body such as motor vehicle accidents, surgery, or injury to a specific part of the body (Shahir, Goodman, Tali, Thorsen & Hellman, 2010). Travel has also been a key culprit in the creation of DVTs. Because of the positioning and lack of movement during travel, the blood vessels experience cut off and the blood in turn has a tendency to pool.

Fig 1 A illustration showing the appearance of a DVT.

and clot. Symptoms of DVTs include swelling, warmth of the skin, and aching at the sight of the clot.

Pulmonary embolisms (PE) are also clots but are found in the lungs versus extremities. Often times DVTs if unnoticed can lead to PEs. According to Stralen et al. (2008), “both autopsy and clinical studies have shown that approximately 90% of the PE’s arise from thrombi in the deep veins of the lower limbs” (p. 1872). (See Fig. 2) Risk factors that can cause both DVTs and PEs can include long term treatment of prophylaxis drugs, oral contraceptives, and hormone replacement therapies (Laberge, Psaty, Hindorff, & Burke, 2009). While DVTs can be extremely harmful if not treated quickly and properly, PEs can be deadly even when treated. In one study evaluating 50 patients with severe PEs, it was recorded that within the 30 day follow up period 1 patient died and 11 other patients suffered additional clinical effects. Within this group of 11 patients, some required endotracheal intubation while others required thrombolysis, vasopressors, and cardiopulmonary resuscitation. In addition, during the next nine months of follow ups 4 patients past away due to complications arising from the initial PE (Kang, Ramos-Duran et al., 2009). Kang & Ramos-Duran et al. also describe the severity of PEs and what they do anatomically to cause death. They state:

Acute pulmonary embolism (PE) is a common disease with a 3-month mortality rate of up to 17.4%. Even if PE is properly treated with anticoagulation, the mortality rate in
hemodynamically stable patients varies from 8.1% to 15.1%. Death is usually caused by acute right heart failure. Acute PE increases the pressure of the pulmonary arterial system and right ventricle (RV) resulting in RV dysfunction, which may progress to right heart failure and circulatory collapse. Patients with RV dysfunction have a higher mortality rate than those without, even if they are initially hemodynamically stable. Thus, the presence of RV dysfunction is a marker for adverse clinical outcome with patients with acute PE (p.1500).

**Factor V Leiden**

While many blood clots whether in the extremities or lungs can be spontaneous or caused by specific traumas, clots in others may be the result of a blood clotting disorder. (See Fig. 3) Factor V Leiden (FVL) is an abnormality in one of the clotting factors found in blood. It is a hereditary blood coagulation disorder and it is found in 5% of Caucasians and 1.2% of African Americans (Kang, Ren et al., 2009). FVL can be described as activated protein C (APC) resistant and is the most common among the coagulation disorders in the United States (US). Factor V (FV) is the essential factor that the mutation pertains to. Activated FV is necessary in order for the blood patches to form on the vessel walls as previously discussed during an injury or trauma. While initially activated, FV needs to be

<table>
<thead>
<tr>
<th>Location</th>
<th>FVL</th>
<th>Total</th>
<th>Percentage FVL* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal thrombosis‡</td>
<td>318</td>
<td>1559</td>
<td>20% (18–22)</td>
</tr>
<tr>
<td>Isolated inferior vena cava</td>
<td>1</td>
<td>7</td>
<td>14% (9–14–42)</td>
</tr>
<tr>
<td>Isolated iliac vein</td>
<td>6</td>
<td>48</td>
<td>12% (4–29)</td>
</tr>
<tr>
<td>Iliofemoral vein</td>
<td>12</td>
<td>61</td>
<td>20% (11–30)</td>
</tr>
<tr>
<td>Isolated femoral vein</td>
<td>40</td>
<td>170</td>
<td>24% (17–30)</td>
</tr>
<tr>
<td>Popliteal-iliofemoral vein</td>
<td>11</td>
<td>58</td>
<td>19% (9–29)</td>
</tr>
<tr>
<td>Popliteal-femoral vein</td>
<td>79</td>
<td>358</td>
<td>22% (18–27)</td>
</tr>
<tr>
<td>Isolated popliteal vein</td>
<td>109</td>
<td>858</td>
<td>20% (17–22)</td>
</tr>
<tr>
<td>Distal thromboembolism</td>
<td>53</td>
<td>323</td>
<td>16% (12–20)</td>
</tr>
<tr>
<td>Isolated calf veins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of affected veins:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One vein</td>
<td>276</td>
<td>1208</td>
<td>18% (16–20)</td>
</tr>
<tr>
<td>≥2 veins</td>
<td>175</td>
<td>750</td>
<td>22% (20–26)</td>
</tr>
</tbody>
</table>

*Fig. 3* A chart showing the number of clots and the % of those clots that actually occurred in people with FVL mutation.

inactivated by APC in order to prevent clotting. This is where the mutation has occurred. One amino acid mutation causes FV to become FVL. When APC enters to inactivate FV, FVL is resistant to it. After five minutes FV is inactivated, however FVL can still have up to 50% vitality after those five minutes. It is possible that 10-20% FVL activity is still occurring after 60 minutes. It is this mutation of FVL and its resistance to APC that causes thrombosis (Kang, Ren et al., 2009).

With the FVL mutation DVTs are almost guaranteed if proper treatment is not administered; PEs however are rarities. “Factor V Leiden is only a mild risk factor for isolated PE, whereas the risk of DVT is substantially increased by this mutation” (Stralen et al., 2008, p. 1875). Stralen et al. further explains some of the effects FVL has on clots by describing a study that showed FVL to affect the location of the DVT as well as the number of veins affected and the growing speed of the clot. The presence of FVL showed to increase the risk of the more dangerous proximal vein clots as opposed to the distal veins. Laberge et al. (2009) suggests that FVL may also cause affects in other areas and play a role in arterial thrombosis as well. They also document its effect on pre-eclampsia, placental abruption, and intrauterine growth retardation.

**Diagnosing Clots and FVL**

Diagnosis of FVL too often begins with the diagnosis of a clot. DVTs come with symptoms that a patient is able to recognize including swelling, warmth, and aching at the sight of the DVT. Discoloration and tenderness may increase the longer
the clot is present in the extremity. Once approached clinically there are a few different tests to help in the diagnosis of a DVT. One of these tests is the Homan’s sign. (See Fig. 4) To perform Homan’s sign, the examiner will force the patient’s ankle into a dorsiflex position. If there is pain in the popliteal region and the calf is elicited as the foot is dorsiflexed this often indicates a positive sign (Rasavong, 2009). While a positive indication may not mean a sure DVT, it is a good indicator as to whether further testing should be performed.

A D-Dimer test is a blood test used to detect both DVTs and PEs alike. It tests the breakdown product of fibrin and is used to measure clotting easily and inexpensively when compared to radiology based exams. A normal D-Dimer result is anything less than .72 ug/ml. Some patients with pulmonary embolisms can reach upwards of 50 to 60 ug/ml (Yasuoka & Kubota, 2011). The D-Dimer exam has been a great aid in early detection. While the D-Dimer test was reportedly used up through 2007, it was not a routine test available and was not used productively as it has been the last few years (Shahir et al., 2010). There is however a disadvantage to using the D-Dimer test. Yasuoka and Kubota (2011) suggest that its results may not be specific and that levels of the tested element could potentially be elevated not due to a clot, but due to pneumonia, recent history or surgery, traumatic injury, and even cancer.

There are multiple radiologic exams that can be done to check for DVTs or PEs. A Doppler ultrasound can be performed to check for DVT on any extremity (See Fig.5). High probability

![Fig. 5](image) Doppler ultrasound and how a clot may appear on such a scan. This scan is of a 19 year old female patient.
ventilation perfusion (VQ) scan and spiral computerized tomography (CT) or angiography (CTA) can be done to scan for PEs (Stralen et al., 2008). (See Fig. 6) Diagnosing using CTAs will show the emboli but in addition will offer useful information regarding the status of the right portion of heart. Despite which exam type is employed, detection is becoming more proactive. Shahir et al. (2010) tells of increases in the detection rate because of the availability of different ways to diagnose. They say that because of newer methods, that in one study- “The number of nuclear examinations has increased from 31 to 49 per year and the number of CT pulmonary angiographic examinations has increased from 0 to 116 per year” (p. 214).

All of these tests for clots, usually lead to an investigation for FVL mutation if the clot appeared spontaneously without reason. Tests for the FVL mutation include multiple DNA tests. Testing for FVL without the presence of a clot usually occurs when a patient has obtained genome based information that may need to be explored for the purpose of improving their health or simply to develop treatment or preventative plans (Laberge et al., 2009). While the DNA testing is accurate in showcasing the FVL mutation, it is costly and takes substantial amounts of time. Blood drawn in a rural hospital may have to be sent away for this special testing and results may not be available for up to two weeks. A new rapid test is being researched now that is both accurate and cost effective. This test is the immune fiber-optic biosensing system. In short, it works by targeting specific amino acids and thus differentiating between FV and FVL (Kang, Ren et al., 2009).
Treatment for Clots and FVL

Treatment for clots and FVL coincide. After an initial clot, “on average patients with DVT were treated for 4 months with anticoagulant therapy, whereas patients with a PE were treated for 6 months” (Stralen et al., 2008, p. 1876). Treatment for FVL patients consists of the same but with further observation. Treatment may include inferior vena cava filters, heparin therapy, a warfarin/Coumadin treatment, or an aspirin regiment (Yasuoka & Kubota, 2011).

Living with FVL

Just as is true with any other disease process the earlier the detection and treatment the better the outcome and the greater reduction in risk of embolization. PEs can be potentially fatal and knowledge is power. Research has been done concerning whether or not the immune system is affected by blood clotting disorder such as FVL. According to Benfield et al., (2010) FVL does indeed have an effect on long term survival and rehabilitation after serious illness. (See Fig. 7) Acute lower respiratory tract infections and urinary tract infections especially have been associated with vascular events including that of thromboembolisms. Any acute inflammation can affect the integrity of vascular health. Illness is commonly accompanied by rest and bed ridden tendencies and therefore allows FVL to manifest itself in the form of DVTs.

Fig. 7 A chart illustrating the log survival rates of those with FVL disorder versus those without.

FACTOR V LEIDEN

While clotting is stereotypically allotted to the older generations, children and young adults have dangers associated with FVL. FVL has significantly been associated with ischemic strokes in this much younger generation (Hamedani, Cole, Mitchell, & Kittner, 2011).

**FVL and Pregnancy**

A predominant concern of female patients with FVL is that of pregnancy. As mentioned before, FVL can play a significant role in pre-eclampsia, placental abruption, and intrauterine growth retardation. However, physicians reassure each patient that while treatment is imperative during pregnancy, it is possible to deliver healthy babies while staying healthy as the carrier as well. Diagnosis and careful constant evaluation of the baby and its blood supply is done using the well-established ultrasound. When pregnant the pulmonary artery opacification is assumed to be lower and this may be due to the increased circulatory volume as well as the altered cardiac output. This change in the circulatory system creates a vulnerable opening for a mutation like FVL to cause damage (Shahir et al., 2010).

While the physicians reassure women with FVL of the possibility of successful pregnancy it doesn’t come without its risks. Having a baby becomes a trial and error game at the start. “The odds of pregnancy loss in women with FVL appears to be 52% higher as compared with women without FVL” (Rodger et al., 2010, p. 7). If or when pregnancy does occur and a successful birth follows the risk is not yet over for the mother or the child. FVL is a hereditary disorder therefore making it possible for the child to have the blood disorder as well. Careful evaluation of the baby will need to be fulfilled. According to James (2009) the changes occurring in the circulatory system may take up to 8 weeks to return to normal. It is even suggested that half of the risk of venous thromboembolism events exist during the pregnancy and the other half exists post-partum. While anticoagulants may seem the best option for all women
prone to clotting, risk of bleeding complications may cause reconsideration. Women with FVL however are guaranteed anticoagulant therapy for the deration of her pregnancy.

**Conclusion**

A blood clot despite its location in the body can be detrimental to human physiology. Pulmonary embolisms especially can be extremely harmful to the heart and can cause death. FVL is one of many inherited thrombophilic diseases that can lead to different complications. Individuals and their families can be greatly burdened by such disorders. Proper diagnosis and the active use of radiologic tools to discover and diagnosis the symptoms of these disorders are imperative. Furthermore, treatment of these disorders must be structured and constantly observed. Living with FVL whether in children, young adults, or the elderly alike will take constant proactive supervision of the body. Patients can live their life as planned whether that includes pregnancy or other intentions as long as proper treatment and continuous monitoring takes place. FVL can have deadly life threatening occurrences, but with the right tools and knowledge it is a blood disorder that can be successfully managed.
References


