Inherited thrombophilia: A genetic counselor's personal journey

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I clearly remember that Saturday morning in 2000, the year I began training as a genetic counselor, when my physician called to tell me I am heterozygous for Factor V Leiden (FVL), a genetic mutation associated with increased risk of venous thromboembolism (VTE). She had ordered the test because my mother and grandfather both suffered from recurrent thrombophlebitis, the formation of blood clots in the veins, and my mother had tested heterozygous for FVL. She was also concerned because I was on oral contraceptives, known to increase the risk of developing a blood clot. Based on my test result, my physician instructed me to stop taking oral contraceptives immediately. Many critical clinical decisions informed by this test result were to follow, as my healthcare team and I worked through three successful pregnancies, and as I became a champion and advocate for myself and for all who are affected by inherited thrombophilia.

A public health problem

Venous thromboembolism (VTE) most commonly manifests as deep vein thrombosis (DVT) in the leg, or pulmonary embolism (PE), when a portion of the DVT clot breaks loose and travels to the heart or lungs, often resulting in chronic shortness of breath and heart failure or even sudden death. VTE affects hundreds of thousands of Americans each year, at a significant cost to the healthcare system.1,2 Age is a risk factor, as are obesity, recent trauma, surgery, smoking, cancer, pregnancy, and hormone therapy. Perhaps the most significant risk factor is genetics—more than one-third of VTE patients have hereditary thrombophilia. Caucasians tend to have the greatest genetic risk.

Genetic risk factors

Discovered in 1994, FVL is a single point mutation of the human Factor V gene found in an estimated 15% to 20% of VTE patients. The mutation results in a modified Factor V protein that is partially resistant to activated protein C, which prevents blood clots from growing too large by inactivating Factor V protein. As a result, the clotting process continues longer than normal. Another mutation, Factor II Prothrombin, is found in 6% of VTE patients and leads to a 3-fold increase in risk of thrombosis. Other genetic mutations that result in deficiencies in protein C, its cofactor protein S, and antithrombin are also risk factors, though they are less prevalent compared with FVL and Factor II Prothrombin.

Managing thrombophilia

In my case, stopping oral contraceptives had ramifications beyond birth control, as they were originally prescribed also to help regulate my menstrual cycles. Eventually, I went through in vitro fertilization (IVF). Since IVF stimulates estrogen production, a VTE risk factor, the reproductive endocrinologist prescribed Lovenox (enoxaparin), an anticoagulant, when IVF was initiated. My obstetrician/gynecologist kept me on Lovenox throughout my pregnancy and 6 weeks post-partum. About 30 weeks into my first pregnancy, I experienced preterm labor and was put on bed rest for the remaining 7 weeks, until the baby was born. Compression stockings and related devices were added to my regimen during bed rest. This combination of clinical management and personal vigilance enabled me to enjoy three successful pregnancies. Throughout, my healthcare team and I kept in mind the multiple risk factors—elevated estrogen, pregnancy, immobility from bed rest—with FVL tipping the scale. Even with the prophylactic use of anticoagulants, I am always conscious of my inherited risk and am diligent with preventive measures such as walking around during airplane travel.

To test or not to test

When it comes to the need for genetic testing, there is no consensus and guidelines are equivocal.2,3,4 In my own case, knowledge of my FVL heterozygous status as a patient has made all the difference in receiving treatment and elevating my own vigilance and adherence. Based on my observation, while healthcare providers take note of family history, they respond more definitively to a genetic test result that clearly delineates a risk factor. An often-cited reason for exercising caution in recommending testing is the fear of increasing a patient's anxiety and the potential harm of unnecessary prophylactic interventions. As a genetic counselor, I believe this is where the healthcare professional can play an important role in educating patients to help them put test results in context and, importantly, understand how they can manage some of the lifestyle risk factors (e.g., obesity, immobility) or avoidable circumstantial risk factors such oral contraceptives, hormone replacement, and travel.5 And this education begins with the healthcare professionals—clinical labs that respond to physician queries about testing, physicians who identify patients who could benefit from testing and/or genetic counseling, and genetic counselors who can help the patient and family navigate through the information on inherited and acquired risk factors and effective interventions to prevent VTE.

Awareness is key

The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism1 cites case studies where a lack of awareness of the symptoms of VTE, compounded with undiagnosed hereditary thrombophilia, resulted in suffering and untimely death. Most healthcare professionals, like myself, have firsthand experience of such incidents. That same Call to Action cited a telephone survey that found that only 25% of respondents had heard of DVT, fewer than 1 in 10 had knowledge of its symptoms or risk factors, and only 1 in 17 knew that DVT can be prevented. This was compared with 93% awareness of diabetes and allergies, and 91% of stroke.

Improving outcomes

Since the risk of VTE is life-long, there are advantages to the identification of individuals at increased risk in order to provide counseling regarding overall thrombotic risk and advice on risk reduction strategies (such as maintaining a healthy weight, abstaining from smoking, avoiding immobility, and maintaining hydration). Furthermore, since the signs and symptoms of VTE are often not well recognized by the general population, and delayed diagnosis of VTE can increase morbidity and mortality, increased awareness will ensure that prompt attention is sought should symptoms arise. In my view, one senseless death from a VTE that could have been prevented is one too many, and the public health problem of VTE is far too large to ignore.

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References

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