Genetic hypercoagulability: screening should be an informed choice

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Recently, I received an e-mail from a frantic woman in another state. She had just learned that her husband’s brother had a thrombosis associated with an inherited tendency to hypercoagulability. Her 12-year-old daughter was about to undergo hernia surgery. She asked whether the operation should be canceled and her daughter have genetic testing.

The brother-in-law was heterozygous for the prothrombin gene mutation (prothrombin G20210A). This mutation occurs in up to 3% of Caucasian Americans. The simplest response to the woman’s query would be to suggest postponement of the surgery and to have the daughter tested. If the test were positive, a visit to a hematology consultant would be recommended. Although this is the simplest course, I do not believe it is the right approach.

Proponents of screening observe that knowledge of the presence of a gene mutation may enable affected individuals to better protect themselves against thromboembolism by taking various measures. These measures might include avoiding known risk factors such as prolonged sitting or standing during travel, as well as not using oral contraceptive agents or other drugs considered thrombogenic. In addition, these persons may educate themselves about the signs and symptoms of venous thromboembolism so that earlier recognition of an event might occur. Furthermore, they might inform their healthcare providers about the presence of the mutation, which might lead to more intensive thromboprophylaxis during periods when the person is at risk and to earlier diagnosis of thromboembolic events. However, identifying a specific mutation is not required for introducing these measures. Simply knowing that a relative has a thrombotic disorder may give sufficient warning that there is a potential risk of thrombosis. Family members could communicate this information to their healthcare providers and inform themselves about the risks of thrombosis.

What is the downside of screening? Yan et al listed a number of reasons for caution. First, they noted that identification of a gene mutation may lead to insurance and employment discrimination as well as loss of privacy. Second, testing in the absence of effective interventions raises ethical concerns; analogy is made to screening for sickle cell trait. Affected individuals with thrombophilic mutations are at risk for thrombosis and there is no simple intervention that changes that fact. Third, the mutations are usually associated with a late onset of symptoms. Thrombosis in childhood is rare; factor V Leiden, prothrombin 20210 mutation, and heterozygosity for mutations in the protein C, protein S, and antithrombin genes are almost never the only cause. When clinical events occur in persons with these mutations, they are usually after puberty and in association with other risk factors. Fourth, learning of the presence of a mutation may provoke considerable anxiety and may affect important life decisions. For example, female family members found to have thrombophilia genes would probably be unable to obtain prescriptions for oral contraceptives or estrogens. If the gene mutation was not explicitly recognized, a woman’s physician might conclude that, in her specific case, the benefit of hormonal use outweighed the risk of thrombosis (3.3 in the case of carriers of factor V Leiden). Finally, because of technologic problems, testing may be incomplete or inaccurate.

Ultimately, decisions about screening for mutations should be made by family members and their physicians. Persons for whom testing is contemplated should be informed about the risks and benefits of screening. They should be told that, even if a mutation is discovered, no more than 5% of persons with the most common mutations, those involving factor V and prothrombin, will ever experience an event. In addition, no major effect of factor V Leiden on life expectancy may be anticipated. There would appear to be very few instances in which it is justified to screen children; such testing should be deferred until the child is past puberty and better able to decide whether the benefits of testing outweigh the risks. For other family members, thorough counseling is required so that each person can make a fully informed choice.

References

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