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EDITORIAL COMMENT



The basic science of this article is likely beyond the scope of the average practicing urologist, but nevertheless raises interesting genetic and clinical issues.

It is not entirely clear that the disordered genes of RAF-1 and MEK/ERK are the cause of the torsions and cryptorchidism in this family or merely coincidental. And even if this genetic testing was unfailingly specific and sensitive, it is unlikely to be available for use in the acute setting of scrotal pain. It seems to me the main utility of this genetic testing would be to get this test in infancy or even in utero and educate males who test positive of the risk of torsion in the future. And if the tests were found to be exceedingly predictive of testis torsion, would there be a role for prophylactic orchidopexy to prevent later torsion, or (and this suggestion would surely be controversial) earlier delivery to prevent neonatal torsion?

The authors would hopefully continue this line of investigation by testing for abnormalities of RAF-1 and MEK/ERK in the larger populations of controls versus patients with cryptorchidism and testis torsion.

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AUTHOR REPLY



We identified a novel nonsynonymous mutation in RAF1 in a Caucasian family whose father experienced cryptorchidism while both sons had bilateral testicular torsion shortly after birth. Testing our hypothesis that RAF1 is part of the MEK/ERK pathway, we demonstrated in testicular tissue sample that decreased expression of RAF/MEK/ERK proteins. A limitation to all familial genetic studies is that causal relationships cannot be established rather only associations can be reported; however, the screening of nonaffected individuals and tissue analysis further strengthens these associations.

Although our study may not have immediate clinical application at this time, we expect our findings can add to the growing body of literature describing the molecular pathway for testicular descent. Several studies have suggested that cryptorchidism and testicular torsion are on a continuum of impaired testicular descent.^{1,2} Understanding the pathway involved in testicular descent may aid in identifying those males who have a dysfunctional gene required for normal descent. While genetic screening during a testicular torsion presentation would be impractical, genetic screening may be useful in cases of cryptorchidism to help decide whether natural descent of the testis would occur with age. Taken together, this familial genetic study provides further evidence that impaired testicular descent may result in testicular torsion or cryptorchidism phenotypes.

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