Comment on: Screening for Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer) among Endometrial Cancer Patients

To the Editor:

This correspondence is an addendum to our recent report (1) about the prevalence of Lynch syndrome among all newly diagnosed endometrial cancer patients. Two additional deleterious MSH6 gene mutations were found on completion of molecular analysis in the last 19 patients. In addition, RNA studies have allowed the reclassification of one of the presumptive missense mutations c.1304T>C (p.Leu435Pro) from the original report as a deleterious frameshift mutation. As a result, the prevalence of Lynch syndrome in our cohort of Columbus, OH area endometrial cancer patients has increased from 1.8% to 2.3% (95% confidence interval, 1.3–4.0%). This is an important update as many institutions and policy groups are considering whether to implement screening for Lynch syndrome among endometrial cancer patients.

We reported 10 Lynch syndrome cases out of 543 patients with completed molecular analysis and a total of 564 patients on study. Two patients have since been removed from study for insufficient tumor material, leaving 562 patients on study. Molecular analysis has now been performed in the 19 patients who did not have testing completed at the time of publication. Two of the 19 patients were found to have nonsense mutations in MSH6. Case 18 is a Caucasian female with mixed endometrioid and clear cell carcinoma diagnosed at age 58 years whose family history meets the Bethesda guidelines (2). Her tumor was microsatellite instability (MSI) high, immunohistochemistry was absent for MSH6 only, and she was found to have a c.3768T>G (p.Tyr1256X) mutation. Case 1079 is an African-American patient diagnosed with endometrioid carcinoma at age 51 years whose family history does not meet any published Lynch syndrome criteria. Her tumor failed MSI testing; however, immunohistochemistry staining indicated the absence only of MSH6 so sequencing of the MSH6 gene was performed. She was found to have a c.220G>T (p.Gly74X) mutation. Overall, with these additions, 8 of the 13 (61.5%) cases were diagnosed at age 50 years or later, 8 did not meet any of the published family history criteria for the diagnosis of Lynch syndrome, and 2 would have been missed by MSI testing (1 negative and 1 failed).

References
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Heather Hampel, Jenny Panescu, Janet Lockman, et al.


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