Update: New Recommendations for Lynch Syndrome Testing

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Those of you who frequently read the genetics articles in this newsletter have read much about Lynch syndrome (also known as Hereditary Non-Polyposis Colorectal Cancer, or HNPCC). You may recall articles where we described the different ways in which one can screen for Lynch syndrome (LS), including germline testing (gene test via blood for mutations in the mismatch repair genes: MLH1, MSH2, MSH6 and PMS2) or screening the colorectal cancer (CRC) itself via microsatellite instability (MSI) and/or immunohistochemical (IHC) staining for the mismatch repair gene products known to be implicated in LS. Typically, MSI/IHC screening is warranted for anyone with CRC diagnosed under age 50 via the Bethesda criteria.

The May issue of Gastroenterology contained several articles on different aspects of Lynch syndrome. The topics included a review of microsatellite instability (MSI) testing on CRC, a review of Lynch syndrome and familial colon cancers, and a summary of recommendations and proceedings from a recent meeting of international LS experts. In Fall 2009, international LS experts convened in Jerusalem to develop consensus for optimal management of LS, as well as to identify areas in need of research for LS. From this meeting, a new expert recommendation for when to screen CRCs via MSI/IHC staining was developed.

Known as the Jerusalem criteria, MSI/IHC is now recommended to be routinely performed on all CRCs diagnosed at age 70 or younger. This is in contrast to the Bethesda criteria as discussed previously. It is understood that 3% of all CRCs and 2.5% of all endometrial cancers are due to Lynch syndrome, so the frequency is high enough to justify a broader approach to screening. Also, colorectal and endometrial cancers in LS families where MSH6 or PMS2 are mutated tend to be older age at onset, and these would be missed by the current Bethesda criteria. Given the ability to predict cancer risk for individuals in LS-affected families and the prevention that can be achieved starting at younger ages, mortality in these families can be significantly decreased if management recommendations are utilized. Individuals in these families who are proven to be unaffected do not have to undergo the rigorous screening and/or surgical recommendations that they might have been subjected to previously.

Another topic discussed at the Jerusalem meeting was adjuvant chemotherapy use in stage II or III CRC with either MSI or abnormal IHC. There have been several data sets in the literature that show adjuvant chemotherapy does not benefit stage II or III CRC patients with MSI. The consensus from Jerusalem was that more data from prospectively designed studies are needed to resolve the issue.

Surveillance recommendations for LS-related cancers were also discussed. Previously, routine clinical management recommendations for LS-affected patients included colonoscopy every other year starting at age 20-25 and annual colonoscopy at age 40, upper endoscopy with brush biopsy every 1-3 years to monitor for gastric, biliary/pancreatic and duodenal cancers, endometrial and ovarian cancer
screening starting at age 25-30 annually (no proven benefit) until age 35-40 when total abdominal hysterectomy with bilateral salpingo oophorectomy (TAHBSO) should be considered, and urine cytology with possible abdominal ultrasound every 2-3 years (particularly for LS families with a higher rate of urinary tract cancers or MSH2-affected families).

In contrast, LS experts are now saying that routine endoscopy for gastric cancer is not recommended, and urinary cytology is insensitive and nonspecific for urinary tract cancers. Improved screening techniques for endometrial, ovarian and urinary tract tumors were identified as major areas in need of research. The importance of annual colonoscopy for LS-affected patients was reiterated since interval cancers are common when longer surveillance intervals are used; unfortunately, Medicare has recently changed their coverage benefit to only cover colonoscopy every other year for LS-affected patients.

Finally, another topic discussed was chemoprevention options for LS patients. The published randomized CAPP2 trial used 600 mg of aspirin and 30 g of resistant starch given to LS patients to see if adenoma recurrence would decrease. After 4 years, no benefit was seen in these patients, but analysis of data after 10 years of use showed a significant reduction in CRC and endometrial cancer incidence in the treated cohort. Chemoprevention and “nutraceutical” approaches continue to be an active area of research in LS.

As always, please feel free to call your local friendly genetic counselor with any questions at 817-838-4871.

Reference: