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Editorial

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The gate-keeping role of surgeons with regard to endometrial cancers in Lynch syndrome

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After the discovery of Lynch syndrome in the 1960s [1], its definition started from hereditary nonpolyposis colorectal cancer (HNPCC) specifically focusing affected organs. However, affected organs include nearly the whole body the endometrium, ovary, ureter, stomach, pancreas, biliary system, small bowel, brain, and skin. The past several decades have shifted our focus from organs to genes. In the case of Lynch syndrome, mismatch repair genes (MLH1, MSH2, MSH6, and PMS2) and EPCAM play a role. Before gene discovery, several screening methods including family history, immunohistochemistry (IHC), microsatellite instability (MSI) and other criteria (Amsterdam [2] and Bethesda [3]) were developed to diagnose Lynch syndrome efficiently; some of these tools remain popular despite the development of gene based diagnostic tools.

An understanding of the concept of Lynch syndrome and the history of gene discovery is a prerequisite for adapting Lynch syndrome to daily clinical practice and patient education. Cancer prevention has great advantage with finding of Lynch syndrome about secondary cancer and affected family member mutation carrier. Risk reducing surgery [4], chemoprevention, and screening methods have been reported sufficiently. A cost-effective way of identifying candidates must take several factors into account, like ethnicity and insurance.

Pecorino et al. [5] screened 41 patients <50 years of age for endometrial cancer from 2007 to 2014 via IHC (MLH1, MSH2, MSH6, and PMS2) and MSI testing. The screening tests used included Novocastra (Leica Biosystem, Wetzlar, Germany) monoclonal murine liquid primary antibodies and mononucleotide repetitions (BAT25, BAT26, NR27) using the QIAxcel system (Qiagen, Venlo, the Netherlands). Their results showed that 46% (19/41) of samples were IHC-negative, while 42% (8/19) of IHC-negative patients exhibited abnormal MSI results. Six patients were MSI-L and two patients were MSI-H. Although these authors did not perform final confirmative gene sequencing tests, they showed a relatively high percentage of abnormal IHC and MSI results among endometrial cancer patients under 50 years of age. IHC has variables to control reliability and a certain degree of subjectivity aspect when it is evaluated by a pathologist; MSI is more objective than IHC although processing evaluation process. MSI has another kit produced by private company since MSI was approved by National Cancer Institute (NCI) [6].

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Lynch syndrome associated germ line mutation is estimated to occur in 5% of endometrial cancer patients [7]. Although the preventive role of risk reducing surgery in sequential mutation-positive cancers and in primary cancers of mutation-positive family members has been established, prospective enrollment, and recruitment has not reached 50%. This suggests that surgeons act as an initial gate-keeper in detecting and preventing Lynch syndrome-associated endometrial cancer.

Are we waiting for a cheaper gene era or not ready to be an active preventer of cancer?

In conclusion, gynecologic oncologists are responsible for initial diagnosis of endometrial cancer and should take responsibility for prevention of sequential cancers and patient education in these cases. Educating young gynecologic oncologists about the prevention of cancers associated with Lynch syndrome and risk-reducing options is equally important for comprehensive cancer care including active treatment and supportive care.

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