Histology of colorectal cancers in Lynch syndrome

This case study is an illustration of how tumor histology can be a clue to an underlying diagnosis of Lynch syndrome.

Case: 65-year-old male presents to his gastroenterologist for 5-year screening colonoscopy.

Personal history:
- Resection of sigmoid colon cancer at age 57; negative colonoscopies at ages 58 and 60

Family history:
- Mother alive and well at age 86; no contact with father for past 40 years
- No children
- 55 y/o paternal half-sister alive and well, with 4 children in their 20s

Review of pathology:
- Microscopic description includes “mucinous adenocarcinoma”
- MSI (microsatellite instability) testing not performed

Hereditary cancer risk assessment:
- The mucinous description of the tumor suggests the possibility of Lynch syndrome. The patient meets revised Bethesda criteria, which include colorectal cancer < age 60 with MSI-high histology.
  o MSI-high histology is identified by the presence of any one of the following: tumor infiltrating lymphocytes; Crohn’s-like lymphocytic reaction; mucinous or signet-ring differentiation; or medullary growth pattern.
  o Jenkins et al. found that each of these characteristics was independently associated with a 30-40% likelihood of an MSI-high tumor in patients under 60. Assuming a conservative 20% incidence of Lynch syndrome with MSI-high tumors, this would equate to roughly a 6-8% chance of a Lynch mutation when any one of the above histologic features is seen in a tumor under the age of 60 (similar to the chance of Lynch for a colorectal tumor under age 50).
- The proximal location of this patient’s colon tumor raises further suspicion for Lynch syndrome. Approximately two thirds of colorectal tumors in Lynch syndrome are proximal compared to less than one half in the general population.
- This patient’s family history is not fully informative due to the lack of information about the father and that side of the family.

Testing:
A saliva sample was submitted for germline testing for the Lynch syndrome genes (COLARIS®), and the patient was confirmed to have a deleterious mutation in the MLH1 gene. The gastroenterologist chose this direct approach because he did not have access to the old tumor sample and many institutions do not routinely perform tumor testing for Lynch syndrome. NCCN guidelines support proceeding directly to germline testing when a tumor sample is not readily available, and cost effectiveness has been demonstrated when there is at least a 5% chance of a positive result.

Benefit of results:
The patient is now known to have a greatly elevated risk for additional cancers, including a second colon cancer. According to guidelines, the patient’s colonoscopy schedule was changed to annual. His half-sister underwent “single site” testing for the specific MLH1 mutation. No mutation was found, providing reassurance for routine surveillance according to general population guidelines for her and her 4 children.
REFERENCES:


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