For Colon Cancer Awareness month, a case is presented which describes a relatively common dilemma: distinguishing between Lynch syndrome (hereditary nonpolyposis colorectal cancer) and the polyposis syndromes.

**Case:** A 54-year-old female presents with colon cancer. Her personal history is notable for multiple colon polyps over the past 4 years. Her family history includes:
- Father: colon cancer age 71
- Paternal aunt: duodenal cancer at age 48
- Brother: multiple colon polyps

**What type of test, if any, would be appropriate for this patient, Lynch or polyposis?** Although this patient meets Amsterdam criteria for Lynch syndrome (three family members with Lynch syndrome cancers, two generations affected, one under the age of 50), there is also reason to suspect a polyposis syndrome. An estimated 2-4% of all colorectal cancers are due to Lynch syndrome. Familial adenomatous polyposis (FAP) and attenuated familial adenomatous polyposis (AFAP) account for about 1%, as does MYH-associated polyposis (MAP).

**Asking a few more questions may clarify which test would be most appropriate.**

**Are the polyps adenomas?** Yes, all of the polyps are adenomas in the patient and her brother. Adenomatous polyps are associated with both Lynch syndrome and the polyposis syndromes. If possible, review the patient’s pathology report. If that is not possible, patients often report adenomas as “precancerous” polyps. Asking about their follow-up care may provide additional clues. If a patient has multiple hamartomatous, hyperplastic or juvenile polyps, a different, less common hereditary syndrome might be suspected, and the patient might benefit from a genetic evaluation.

**How many polyps and at what age?** The patient had 9 and her brother 18 adenomatous polyps. The brother’s history is significant because a polyposis syndrome should be considered in individuals with more than 10 cumulative polyps. Although the patient had only 9, the number of adenomas in individuals with AFAP or MAP can vary greatly, from less than 10, to hundreds. Furthermore, patients with Lynch syndrome are unlikely to have more than 2 adenomas by age 30 or more than 5 by 50.

**Has there been tumor testing (immunohistochemistry or microsatellite instability)?** Tumor testing was not performed in this family. Lynch syndrome would be more likely with abnormal tumor IHC or MSI results; however, testing adenomas has limited sensitivity. Although uncommon, microsatellite instability has also been reported with polyposis syndromes. For more information on tumor testing, see the February 2012 listserv posting.

**Does anyone in the family have a history of additional cancers?** Yes, the patient’s aunt had duodenal cancer. Additional family members with Lynch syndrome related cancers* or other findings seen with polyposis syndromes** can provide additional clues. Patients do not always think this information is relevant. It is helpful to ask about all cancers and major or unusual health conditions among 1st, 2nd and 3rd degree relatives. Although associated with both syndromes, duodenal cancer is more indicative of a polyposis syndrome.

**Outcome:** Germline testing was ordered for polyposis genes with reflex to Lynch syndrome genes if negative. A deleterious mutation found in the APC gene confirmed a diagnosis of AFAP. A medical management plan was established for the patient, and her family members were offered single site testing for the mutation.
Lynch related cancers include: endometrial, gastric, ovarian, ureter/renal pelvis, biliary tract, small bowel, pancreas, brain, and sebaceous adenoma.

** AFAP and FAP associated cancers include: duodenal/periampullary, thyroid, gastric, pancreatic, adrenal, CNS (generally medulloblastoma), and hepatoblastoma; additional findings may include polyps of the gastric fundus and duodenum, osteomas, dental anomalies, congenital hypertrophy of the retinal pigment epithelium (CHRPE), soft tissue tumors, desmoid tumors.

*** Children, parents, siblings, aunts, uncles, nieces, nephews, grandparents, great aunts/uncles and first cousins

REFERENCES:

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