NCCN Guidelines for Reflex Testing of Newly Diagnosed Colorectal Cancer: A Quality Improvement Audit

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Introduction:

- *Study purpose*: To investigate the compliance of NCCN guidelines for reflex genetic testing in colorectal cancer in a community hospital.
- *Background*: Lynch syndrome remains the most common hereditary form of colorectal cancer.
- It makes up 2-4% of all new colorectal cancer diagnoses with a prevalence rate of 0.5%.
- Patients with Lynch syndrome develop colorectal cancer at younger ages, making detection so important.
- A reflex testing strategy as recommended by the NCCN is one of the best tools we have for detection, treatment and prevention for both the patient and their families.

Methods:

- A one-year retrospective analysis was performed for reflex testing of colorectal cancer tumors to evaluate for Lynch syndrome at a community hospital.
- Colorectal tumors were investigated using immunohistochemical (IHC) analysis for the presence of microsatellite instability (MSI) demonstrating a germline mutation for DNA mismatched repair (MMR) genes.
- Secondary testing of positive specimens with loss of MLH1 gene for BRAF mutation or hyper methylation was performed to rule out a sporadic mutation.
- Analysis of data was performed with respect to compliance with the NCCN guidelines. Compliance was analyzed based on initial reflex testing, secondary testing to exclude sporadic tumors and referral to genetic counseling for patients younger than age 50 and/or positive testing for MSI.

Results:

- 88 cases of newly diagnosed colorectal cancer were reviewed for reflex testing between 2019 and 2020.
- 74/88 (84%) of patients had the recommended reflex testing for Lynch syndrome.
- 61/74 (82%) patients had normal IHC testing.
- Of those patients, 13 were under age 50 and 1 had a positive family history resulting in 14 (23%) genetic referrals.
- 13/74 (18%) patients were found to be IHC positive for MSI.
- Three patients had gene mutations in MSH2/MSH6/PMS2, appropriate for referral.
- 5/10 (50%) patients went on to additional testing for BRAF/hyper methylation testing to exclude a sporadic mutation.
- Of those 5 patients, only 1 was BRAF negative and appropriate for genetic referral.
- Two additional referrals were made for genetic testing based on age at diagnosis and family history alone.

Conclusion:

- This audit highlights improvement opportunities for compliance with NCCN guidelines for genetic testing in colorectal cancer tumors.
- Infrastructure improvement with reflex testing and increased awareness of guidelines among physicians may increase genetic counseling referrals and therefore, improved detection, treatment and prevention.