Natural Sciences Engineering & Technology Journal (NASET Journal)

Journal Homepage: https://nasetjournal.com/index.php/nasetjournal

Genetics in Colorectal Cancer: A Narrative Literature Review

Billy Peter Manawan[1*]

[1]Department of Surgery, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Alcohol
Colorectal cancer
Genetic
Lynch syndrome
Polyposis

***Corresponding author:**
Billy Peter Manawan

E-mail address:
manawanbilly@gmail.com

The author has reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/nasetjournal.v1i1.4

A B S T R A C T

Colorectal cancer (CRC) is the third most commonly diagnosed form of cancer globally, which is about 11% of all cancer diagnoses. Obesity, together with kind of sedentary lifestyle, red meat consumption, tobacco, and alcohol consumption are considered as predisposing factors of progression of CRC. This literature review was aimed to describe genetic aspect in colorectal cancer. In the development of colorectal cancer, genetic factors having a role in its incidence. The hereditary type of colorectal cancer was divided into two types is polyposis and Lynch syndrome which have each and different mechanism and genetic pattern. Lynch syndrome contributes to 3–5% of CRC cases and is caused by a germline mutation in one of four genes associated with the DNA mismatch repair (MMR) system; MLH1, MSH2, MSH6, or PMS2. In polyposis, there are some types such as familial adenomatous polyposis (FAP) which is mostly caused by APC mutation, MYH-associated polyposis, and the rare hamartomatous polyposis syndromes. In conclusion, genetic testing and better family history documentation can enable those with a hereditary predisposition for the neoplasm to take preventive measures.

1. Introduction

Colorectal cancer is a type of cancer that starts in the colon or rectum, which are parts of the digestive system.[1] Colorectal cancer (CRC) is one of the mortality causes of cancer in some developed countries, especially. CRC together are the third most commonly diagnosed form of cancer globally, which about 11% of all cancer diagnoses.[2] Obesity and a sedentary lifestyle, red meat, tobacco, and alcohol consumption are considered predisposing factors for the progression of CRC. Genetic is considered an interaction factor besides environmental and individual ones. So genetic testing and good family history documentation can enable those with a hereditary predisposition for the neoplasm to take preventive measures.

New cases are expected to increase significantly. About 1,096,000 new cases of colon cancer are estimated to be diagnosed in 2018, while about 704,000 in rectal cancer.[3,4] From this estimation, both colon and rectal cancer will increase by 1.8 million new cases. Males have a higher prevalence than females and 3-4 times more common in developed than in developing countries. Genetic contribution of CRC is considered when the patient has one or more of these factors following; a family history of CRC and or polyps; multiple primary cancers; the existence of other cancers, such as endometrial cancer; and earlier onset at CRC diagnosis.[5] This literature review aimed to describe the genetic aspect of colorectal cancer.

Gene affected in colorectal cancer types

In polyposis, there are some types such as familial adenomatous polyposis (FAP), MYH-associated

polyposis, and the rare hamartomatous polyposis syndromes. In familial adenomatous polyposis (FAP), APC is an affected gene which considered the leading cause of disease. From this disease, clinical features mostly come from gastrointestinal problems such as gastric fundic gland polyps and duodenal and ampullary adenomas/adenocarcinomas. Other features are non-gastrointestinal cancers (thyroid, hepatoblastoma, medulloblastoma), CHRPE, epidermoid cysts, osteoma jaw and skull, desmoid tumors, and supernumerary/impacted teeth. Another colorectal cancer type affected by APC is attenuated familial adenomatous polyposis (AFAP) which has featured duodenal and ampullary adenomas/adenocarcinomas.[6]

In MYH-associated polyposis, MYH plays a role in developing a disease with a feature of duodenal adenomas/adenocarcinomas. Juvenile polyposis is another type of polyposis in colorectal cancer. SMAD4 BMPR1A is considered a gene that has a role in the disease. There are some differences from the other because gastrointestinal features are cancer in the pancreas, stomach, and small bowel. Other features are mucocutaneous telangiectasis and congenital cardiopulmonary defects.[7]

Lynch syndrome (LS) contributes to 3–5% of CRC cases and is caused by a germline mutation in one of four genes associated with the DNA mismatch repair (MMR) system: MLH1, MSH2, MSH6, or PMS2. CRC in Lynch syndrome has an early onset with a mean of 45 years of age, and multiple synchronous CRCs are not uncommon. CRC has specific histologic features, including poor differentiation, a mucinous component, and an intense Crohns-like lymphocytic reaction, and has a predilection for the proximal colon. Among women, endometrial cancer is the second most common cancer associated with Lynch syndrome, with an estimated lifetime risk of 40 to 60%. The spectrum of Lynch syndrome-associated malignancies also includes cancers of the stomach, small intestine, pancreas, biliary tract, and urothelial carcinoma of the renal pelvis and ureter. Sebaceous neoplasms of the skin are seen in the Lynch syndrome variant, Muir-Torre syndrome, and Turcot syndrome is associated with brain tumors, including glioblastomas and astrocytomas.[7,8]

Genetic counseling in colorectal cancer

Genetic counseling is a must for a patient who has a high risk of colorectal cancer. A previous study stated a high-yield point on how to identify individuals with a high-risk personal and family history of cancer. The criteria are colon cancer diagnosed at <50 years of age, multiple colonic malignancies present, either synchronous or metachronous. Multiple primary cancers diagnosed, either colonic or extracolonic; over a lifetime, ≥ 10 adenomas present or ≥ 2 histologically characteristic hamartomatous polyps; colon cancer in >1 generation of individual's family, and clustering of extracolonic cancer in family members.[8-10]

Genetic evaluation referral for hereditary CRC syndromes is mostly underused. We mostly knew that Lynch syndrome is the most common inherited predisposition CRC. Genetic counseling is performed when there were individuals with CRC for the absence of DNA MMR protein expression or MSI, known as "universal testing," which has been shown to maximize sensitivity for identifying individuals with LS compared with selection based on clinical criteria.[9,11]

Microsatellite instability (MSI) is considered to be a feasible and informative option in evaluating a family suspected of HNPCC. Patients with colorectal cancer whose tumors are found to manifest MSI should be considered for further germline mutation analysis, particularly if the family history and the value of risk assessment for family members is warranted. Other promising new research suggests that immunohistochemistry (IHC) for MLH1 and MSH2 expression is an inexpensive first screen of CRC tumors to evaluate whether MSI and/or germline testing is indicated. The lack of expression of either MSH2 or MLH1 by IHC in tumors is correlated with MSI in the tumor. Sensitivity and specificity are about 85%.[12-14]

DNA sequencing is another approach that can be used in HNPCC mutation. Affected individuals in

families with greater ≥3 cases of colon or uterine cancer; if prior MSI tumor assay is done, probability of germline mutation is low if the tumor was microsatellite stable are the indication for this test. It is used for MSH2 and ML1 testing. Sensitivity and specificity are about 50% and 99%, respectively.

2. Conclusion

Some genetic testing can be used in hereditary colorectal cancer, such as MSI, IHC, and DNA sequencing. Genetic counseling is a crucial and important component of genetic risk assessment. Informed consent for genetic testing is an integral part of the process, and a clear understanding by the patient can only be arrived at by careful counseling.

3. References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer J Clin. 2018; 68(6): 394- 424.
2. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Prz Gastroenterol. 2019; 14(2): 89-103.
3. Mastalier B. Genetics of colorectal cancer. J Med Life. 2014; 7(4): 507-11.
4. Stigliano V, Sanchez-Mete L, Martayan A, Anti M. Early-onset colorectal cancer: A sporadic or inherited. World J Gastroenterol. 2014; 20: 12420–30.
5. Abou-Zeid AA, Khafagy W, Marzouk DM, Alaa A, Mostafa I, Ela MA. Colorectal cancer in Egypt. Dis Colon Rectum. 2002; 45: 1255–60.
6. Mansoor I, Zahrani IH, Aziz SA. Colorectal cancers in Saudi Arabia. Saudi Med J. 2002; 23: 322-7.
7. Kaw LL, Punzalan CK, Crisostomo AC, Bowyer MW, Wherry DC. Surgical pathology of colorectal cancer in Filipinos: implications for clinical practice. J Am Coll Surg. 2002; 195: 188–95.
8. Dolatkhah R, Somi MH, Bonyadi MJ, Asvadi Kermani I, Farassati F, et al. Colorectal cancer in Iran: molecular epidemiology and screening strategies. J Cancer Epidemiol. 2015; 2015: 643020
9. Kastrinos F, Syngal S. Inherited colorectal cancer syndromes. Cancer J. 2011; 17(6): 405-15.
10. Lynch HT, de la Chapelle A. Hereditary colorectal cancer. N Engl J Med. 2003; 348: 919–32.
11. Stoffel E, Mukherjee B, Raymond VM. Calculation of risk of colorectal and endometrial cancer among patients with Lynch Syndrome. Gastroenterology. 2009; 137: 1621-27.
12. Ballester V, Cruz-Correa M. How and when to consider genetic testing for colon cancer? Gastroenterology. 2018.
13. Idos G, Gupta S. When should patients undergo genetic testing for hereditary colon cancer syndromes? Clin Gastroenterol Hepatol. 2018; 16: 181–3.
14. Yan H, Papadopoulos N, Marra G, Perrera C, Jiricny J, et al. Conversion of diploidy to haploidy. Nature. 2000; 403: 723-4.