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Genetic Testing for Hereditary Colorectal Cancer Syndromes: Its Role in Diseases Management

De Rosa M[1]*, Duraturo F[1] and Pace U[2]

[1]Department of Molecular Medicine and Medical Biotechnology, University of Naples 'Federico II', Italy
[2]Colorectal Surgical Oncology-Abdominal Oncology Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, 'Fondazione Giovanni Pascale' IRCCS, Italy

*Corresponding author: Marina De Rosa, Department of Molecular Medicine and Medical Biotechnology, University of Naples 'Federico II', I-80131 Naples, Italy, Email: marina.derosa@unina.it

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Introduction

Colorectal cancer (CRC) is the principal cause of cancer deaths and the third most frequent cancer worldwide, with about 30% of hereditary or familial cases [1]. There are several different causes involved in CRC incidence. Sporadic colorectal cancers arise following somatic mutations, and these account for about 75% of all CRCs. Germline-inactivating mutations in oncogenes or tumor suppressor genes cause hereditary CRC, while minor variant and/or single nucleotide polymorphisms in the same genes are responsible for familial CRCs. First-degree relatives of patients with CRC have three-fold greater risk of CRC than that of individuals without familial predisposition [2,3].

Hereditary nonpolyposis CRC (HNPCC), or Lynch syndrome (LS), is an autosomal dominant disease that is caused by a germline mutation in one of the DNA mismatch repair (MMR) genes, such as MLH1, MSH2, MSH6 and PMS2. LS is the most common form of hereditary CRC and it accounts for 1% to 6% of all colorectal malignancies [4]. Familial adenomatous polyposis, MUTYH-associated polyposis and hamartomatous polyposis are inherited syndromes that account to 2-5% of all colon cancer. The mutated genes responsible for the vast majority of these disorders, are now known (APC, MYH, LKB1, SMAD4, BMPR1A, and PTEN) and specific mutations have been identified. Molecular characterization of inherited CRCs allows pre-symptomatic diagnosis identifying at-risk individuals and improving cancer surveillance. Adenomatous polyposis include familial adenomatous polyposis (FAP), attenuated FAP (AFAP), and MUTYH-associated polyposis (MAP). Hamartomatous polyposis include Peutz-Jeghers syndrome (PJS), juvenile polyposis syndrome (JPS) and "PTEN hamartoma tumour syndrome" (PHTS). MAP is an autosomal recessive condition, while all others disorders are inherited in autosomal dominant manner.

Differential diagnosis could be very difficult among Colorectal cancer syndromes because of their phenotypic variability. Attenuated FAP, MAP and Lynch syndrome could be all associated with few numbers of adenomas (3-10 polyps), nevertheless, each syndrome has distinct cancer risks, characteristic clinical features, and separate genetic etiologies. However, differential diagnosis between CRC syndromes is essential for management and cancer prevention of affected individuals, because of each syndrome has its own distinctive organ-specific manifestation and each requires a different surveillance strategy.

LS patients should undergo colectomy with ileorectal anastomosis; patients carrier of a mutation in the MMR genes should undergo colonoscopy every 1 to 2 years from the age of 20 to 25 years, while, for woman, pelvic evaluation should be followed by the age of 25 years to 35 years. All relatives of LS patients should be also tested for MMR gene mutations [5].

FAP patients have high risk of developing gastrointestinal such as extraintestinal neoplasms thus, colonoscopy every 1-2 years, from the age of 10-12 years, is recommended for patients carrying APC mutations. Annual endoscopic follow-up is required when patient already presents gastrointestinal adenomatous polyps. Colectomy is needed when polyps coldn't endoscopically treated [5].

Characterization of a causative mutation in leukocyte DNA is essential for the differential diagnosis among the various hereditary CRC syndromes and for the assessment of cancer recurrence risk and familial cancer risk (based on gene-specific cancer associations). It also allows the predictive testing of asymptomatic at risk individuals. The role of molecular genetic findings in treatment decisions, on the other hand, is limited because identification of a germline mutation can not allow accurate estimation of the likely course of the disease. According to international literature data, we suggest that next-generation sequencing is today the better and more efficient technique for molecular diagnosis of hereditary colorectal polyposis syndrome, hereditary colorectal cancer and familial colorectal cancer. Indeed, it allow to consider a number of different genes associated with colon cancer for differential diagnosis. This approach could consent to detect previously unidentified low frequency allelic variants including a novel candidate locus. Moreover, even if no mutation is found, at-risk patient for hereditary colorectal cancer syndrome still needs to be treated appropriately and clinical follow up should be initiated even before mutation testing is complete [6].

References

1. Ferlay J, Shin H, Bray F, Forman D, Mathers C, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010; 127: 2893–2917.
2. Duraturo F, Liccardo R, Cavallo A, De Rosa M, Grosso M, et al. Association of low-risk MSH3 and MSH2 variant alleles with Lynch syndrome: Probability of synergistic effects. Int J Cancer. 2011; 129: 1643–1650.
3. De Rosa M, Pace U, Rega D, Costabile V, Duraturo F, et al. Genetics, diagnosis and management of colorectal cancer (Review). Oncol Rep. 2015; 34: 1087–1096.
4. Liccardo R, De Rosa M, Izzo P, Duraturo F. Novel Implications in Molecular Diagnosis of Lynch Syndrome. Gastroenterol Res Pract. 2017; 2017: 2595098.
5. De Rosa M, Rega D, Costabile V, Duraturo F, Niglio A, et al. The biological complexity of colorectal cancer: insights into biomarkers for early detection and personalized care. Therap Adv Gastroenterol. 2016; 9: 861-886.
6. De Rosa M, Duraturo F, Liccardo R, Izzo P. Hereditary gastrointestinal polyposis: Diagnosis, genetic test and risk assessment. Open Journal of Genetics. 2013; 3: 50-58.