

Molecular Oncology of Colorectal Cancers Prognosis and Prediction, Radiation Oncologist Perspective

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Abstract

Colorectal cancers (CRC) are a common cancer globally. The commonest symptoms were rectal bleeding (57%), pain (44%), and altered bowel habits (26%). 13 percent of the patients of colorectal cancer found signet ring tumor Histopathology which shows poor outcome of this very tumor, The CEA (Carcinoembryonic antigen) level estimation in patient serum commonly perform, surgery is a backbone of treatment unless until contraindicating factors are present after surgery tissue specimen required to send for not only histopathological studies rather also to look for tumor Immunohistochemistry studies in order to plan colorectal cancer very well directed chemotherapy according to its receptor as well as genetic or epigenetic alterations in BRAF, K-RAS, MMR, Most patients had localized or locally advanced disease. Twenty-eight percent of the patients had metastatic disease with liver being the commonest site of metastases (14%) followed by peritoneum and lung. More than half of the patients received treatment with a curative intent. Colorectal cancer in India differs from data than what we have found in data from western countries, In India we had more young patients, higher proportion of signet ring carcinomas, and more patients presenting with an advanced stage.

Keyword

Colorectal cancers; Immunohistochemistry; BRAF; K-RAS; MMR

Introduction

Colorectal cancers divided on basis of immunohistochemistry reports in three molecular subtypes on expression levels of EMT (Epithelial, Mesenchymal transition) these three molecular subtypes are, Epithelial subtype, Mesenchymal subtype, and Hybrid subtype [1-4].

The epithelial subtype of colorectal cancers are E cadherine positive , Nuclear enzyme β Catenin positive but negative for vimentin these subtypes of colorectal cancers are having less propensity for regional lymphnode involvement as well as these tumor subtypes having low mitotic rate in view of these features these subtypes of colorectal cancers having good prognosis, However contrary to that Mesenchymal subtypes of colorectal cancers are negative for Ecadharin, negative for β catenin but are positive for vimentin they shows higher rate of mitosis higher N/C ratio along higher propensity for regional lymphnode involvement henceforth shows poor prognosis.

On Immunohistochemistry examination and studies we looks for these common genetic and epigenetic alterations these are MMR, BRAF, K-RAS mutations, MMR (Mismatch repair) proteins is a nuclear enzyme which participates in repair of base–base mismatch that occurs during DNA replications (among 9 to 10 percent colorectal cancer cases) refer to given below figure A during tumor cells proliferations. MMR genetic mutations can occurs as result of DNA hypermethylation, germline mutations (most common), or by somatic mutations and unknown reasons in very few case (Figure 1) [5-7].

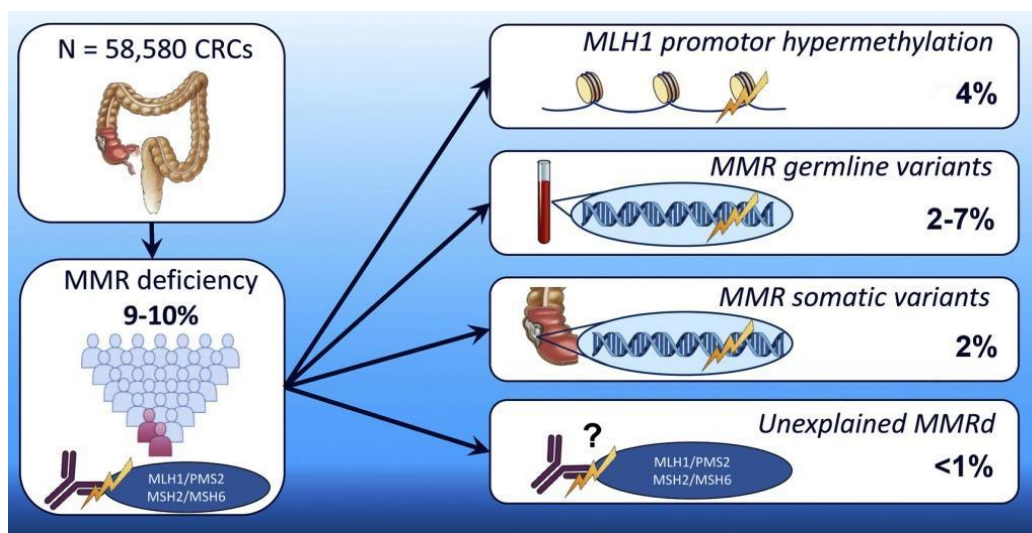


Figure 1: MMR genetic alteration in colorectal cancers.

BRAF mutations explain very poor prognosis of colorectal cancer patients median survival just limited up to one years of these colorectal cancer patients, BRAF is basically Proto-oncogene BRAF mutations have been found among 7 to 10 percent's of colorectal cancers furthermore noticed BRAF mutations more commonly associated with right side of colonic cancers and less common with left side descending colonic cancers along with they exhibits higher rate of mitosis, higher N/C ratio, higher grade of

histology, higher content of mucin in tumor along more commonly associated with peritoneal metastasis in view of all above features, makes the prognosis of BRAF mutant colorectal patients very poor outcome of disease.

RAS, there are three Isoform of this gene in human out three K-RAS is being most commonly associated with many cancers in human K-RAS mutation found 17 to 25 percent among different cancers but in case of Colorectal cancers K-RAS mutations with altered genes found in 30 to 40 percent cases, K-RAS mutation in colorectal cancers have been associated with poor survival and increased tumor aggressiveness.

Adjuvant chemotherapy as per molecular profile of colorectal cancer

Patient those having KRAS positive and having left sided colonic cancer ESMO suggests FOLFOX plus ANTI EGFR (Cetuximab) provides good results, however if patients is KRAS positive but having right side of colonic cancer ESMO suggests FOLFIRI plus ANTI VEGF (Bevasuzimab) for good results, for metastatic colorectal cancer with KRAS positive wild type recommended chemotherapy is Cetuximab plus FOLFOX chemotherapy, BRAF Mutant patients recommended treatment is FOLFIRI plus ANTI VEGF [8-10].

Conclusion

The last half decade of CRC research has produced an important amount of results. In order to personalize the treatment for CRC patients it is necessary to understand its natural history and malignant genesis mechanisms that help the disease progress. Unique biological signature of CRC can be distinguished by identifying biomarkers expression. Several markers have shown potential, Individualized approach studies based on particular disease characteristics will pave the way for personalized medicine. For each disease stage apart, therapeutic management based on biomarkers testing results will allow better use of health care resources and may relieve the patient of unworthy procedures.

Conflict of Interests

The authors declare that they have no conflict of interests.

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