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Review paper

Genetics and current treatment strategy of colorectal cancer

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Abstract

This review aims to sketch a current scenario of colorectal cancer (CRC). Findings say that males are the most susceptible to CRC than the females. BRAF and RAS mutations are known as common causes of CRC. Not only targeted therapy but also a combination of radio- and chemotherapy is very useful in CRC.

Keywords: *Colorectal Cancer; Present Scenario; Medical Science.*

1. Introduction

Colorectal cancer (CRC) is also known as colon, rectal or bowel cancer. CRC is the third most common cancer worldwide (WHO 2015). In this context, males (44.8%) are more susceptible than females (34.1%). Included signs and symptoms are blood in the stool, changes in bowel movements, weight loss, and tiredness. Major risks associated with CRC are familial adenomatous polyposis, hereditary nonpolyposis, inflammatory bowel disorder (e.g.- Crohn's disease and ulcerative colitis), polyps (any types), rectal bleeding/iron anemia deficiency anemia or with known genetic mutations. Some other risk factors include diet (e.g.- red and processed meat, alcohol), obesity, smoking, lack of physical activity (NCI 2014; World Cancer Report 2014;).

Commonly used diagnosis methods of CRC are colonoscopy, computed tomography (CT) colonography, guaiac fecal occult blood test (gFOBT), immunochemical fecal occult blood test (iFOBT) or blood-based biomarker (e.g.- circulating tumor cells, and mutated plasma DNA and RNA, protein-based markers, methylated septin 9, and different kinds of circulating miRNAs) analysis, CRC liver metastases (CRCLM), flexible sigmoidoscopy (FS), barium enema (BE), digital rectal exam (DRE), fecal deoxyribonucleic acid (DNA) and other identified tests (Adam et al. 2015; Fitzpatrick-Lewis et al. 2016; Yörüker et al. 2016). To be noted that vaginal metastases from CRC may be linked with vaginal bleeding or sensation of a vaginal swelling. Therefore, a thorough gynaecological assessment should be done in such presentation (Ng and Aly 2013).

Aim of this review is to note down current circumstances on CRC.

2. Genetics in CRC

BRAF and RAS mutations, including both KRAS and NRAS genemutations, have been reported in about 30-50% of primary CRC. In addition, APC, TP53, SMAD4, PIK3CA and MET mutations are also reported in CRC. An association CRC is also found with the mutations in MMR genes (MLH1, MSH2, MSH6 and PMS2). A significant outcome has drawn with RAS-mutated CRC patients receiving chemotherapy plus anti-EGFR MoAbs (Passiglia et al. 2016; Sinicrope et al. 2016; Siravegna and Bardelli 2016). BRAF mutations have been described in about 10% of primary CRC, representing a well-known negative prognostic factor, associated with worse survival outcomes, regardless of any treatment received (Ahn et al. 2014).

3. Treatment strategy

Radio-, chemo- and targeted therapies are the commonly used therapeutic modes in CRC (NCI 2014). Physical exercise and increasing the consumption of whole grains, fruits and vegetables, and reducing the intake of red meat are important strategies in CRC management (Doyle et al. 2007). Aspirin, celecoxib and vitamin D intake are associated with lower risk of CRC (Cooper et al. 2010; Ma et al. 2011; Yin et al. 2011). CRC at very early stage can be removed by an open laparotomy or sometimes laparoscopically (Cunningham et al. 2010). In the metastatic setting, doublet systemic chemotherapy regimens such as FOLFOX (fluorouracil, leucovorin, oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, irinotecan), and/or Ramucirumab (target: VEGFR-2) (MAbs) and Aflibercept (targets: VEGF-A, VEGF-B and PIGF), or doublets plus anti epidermal growth factor receptors (EGFR) are the mainstay of standard first-line chemotherapy for metastatic CRC in patients suitable for intensive therapy.

Moreover, other antibodies targeting vascular endothelial growth factor (VEGF; bevacizumab) or its receptor (aflibercept) or EGFR (panitumumab/cetuximab) are now standard of care when combined with FOLFOX or FOLFIRI in stage IV patients. Cytoreductive surgery may be seen as a tool to maximizeresponse to intraperitoneal chemotherapy, because locally delivered drugs penetrate in tumor tissue not more than 2-3 mm. Perioperative intraperitoneal chemotherapy is also an effective treatment in CRC (Sunakawa et al. 2016; Serrablo et al. 2016; Baratti et al. 2016; Giampieri et al. 2016; Sinicrope et al. 2016). A combination of radio- and chemotherapy is very useful in CRC (Cunningham et al. 2010). Moreover, genotyping processed blood (plasma and serum) contains free (non-cell-bound) circulating DNA (ctDNA) in blood samples can be used to identify the molecular profile of CRC (Siravegna and Bardelli 2016).

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