

History of Colorectal Cancer: A Short Review on Timeline Basis

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Abstract

Extensive research has been conducted so far on colorectal cancer, especially on the genes responsible for its instigation; and the signal transduction pathways involved in the development of colorectal cancer have been well studied. Indeed, the history of the affected individuals by colorectal cancers crossed over 100 years. But the implementation of researches surrounding colorectal cancer is crucial to the understanding of the growth of metastatic tumors. With the advancement of science, specifically the research on colorectal cancer, various treatment options evolved from time to time based on the genetic and biochemical knowledge gained. Current review briefly discussed based on the information achieved from the previous reports, a simple scheme of the stages of the cancer development has been elucidated in the current review for laymen understanding of cancer progression in the rectum layers; and the historical evolution of the remedies against this dreadful cancer has been placed on a time scale basis of the last 40 years.

Key words: Colorectal cancer; stages of the cancer development; treatment options.

Background: Growth of colorectal cancer inside the human body

The idea of the multi-step cascade of events for the development of colorectal cancers (CRCs) associated with a range of mutations in specific genes and the signal transduction pathways is already widely [1]. As widely known, colorectal cancer starts its growth mostly in the inner lining of the colon, this small growth is known as polyps [2-4]. These polyps may or may not change into cancer over time. This probability depends largely on the type of polyp. If cancer forms in that growth in the mucosa, the polyp can later grow into the wall of the colon over many years as shown in Figure 1. The rectum wall is made up of many layers while cancer starts in the innermost layer it can grow outward through some of the rectum layers. After surpassing the wall, the cancerous tumor then can grow into blood vessels or the lymph vessels, and thus it can travel to nearby lymph nodes even distant parts of the body over time [2-4].

Hence, early detection is very crucial to cancer treatment. Two or more types of treatment can be used either at the same time or one after the other. These depend on things like the stage of cancer, the chance of the treatment to cure cancer or limit the growth, age of the patients, health problems that the patient might have, the specific genes or protein the patient's cancer might be carrying, and the patient's feeling about the treatment. So, it is imperative we track the findings regarding colorectal cancer and the treatments involving it that are relevant to today's oncological medicine practices. So, we are going to discuss the historical evolution of this review paper.

Recent advancement on colorectal cancer (CRC) research (2000- onward)

Colorectal cancer (CRC) is developed due to defects in various genes and the signal transduction pathways. Around 30 years ago, the multistep genetic model for the development of this cancer has been reported. Nearly 2 years ago, in 2018, a study done with oxaliplatin along with fluoropyrimidine showed as oxaliplatin is associated with cumulative neurotoxicity a shorter therapy has the capability to spare toxic effects [5]. In 2017, a multicenter, randomized, non-blinded, phase 3 non-inferiority trial (Stockholm III) between 1998-2013 with the necessary specification of the patients proved that increasing radiation time and taking time with rectal cancer surgery lowers risks of surgical complications [6]. In 2016, a retrospective analysis of patients with RAS wild type metastatic colorectal cancer from the CRYSTAL and FIRE-3 trials were classified as having left-sided or right-sided metastatic colorectal cancer trial suggesting colorectal tumor location affects prognosis, may inform treatment choice [7].

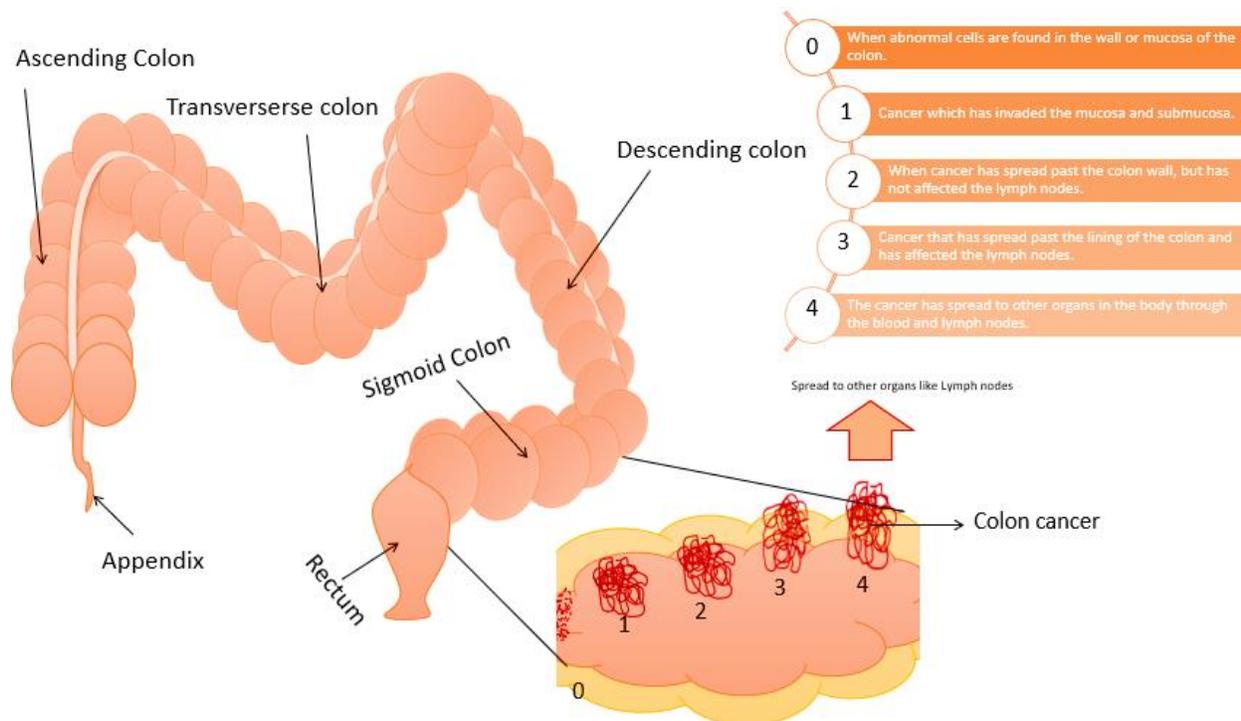


Figure 1: Stages of colorectal cancer.

Four years before this finding, in 2012, after scientists made progress in deciphering the molecular signature of prostate cancer, two new targeted drugs named regorafenib and aflibercept are designed and were approved by the Food and Drug Administration (FDA), thereby providing new options for patients with aggressive colorectal cancers [8].

In 2010, CRCs have been reported to develop along with long time achieving successive accretion of genetic alterations oppressing

- The regulators of cell proliferation
- The cell cycle mechanisms
- Apoptosis, and
- The DNA repair system [9].

This is to be noted that in 2009, the physicians, for the first time, were capable to use the genetic test using gene assay predicts risk of colon cancer recurrence so patients with lower risks can avoid chemotherapy and the other side effects while new cancer patients can just cover with chemotherapy without primary tumor surgery [10].

This is not surprising that lots of significant developments in the CRC research were accomplished before the findings as stated above. In 2008, flat colon growths were noticed to be more likely to be cancerous than more obvious ones but they are difficult to be detected thus molecular markers are required for effectiveness [11]. In 2007, lymph node sampling for staging is refined; and the correlation between dietary nutrients as well as physical exercise with the development of CRC was established [12]. In 2006, a 15-month long study concluding 2053 colonoscopies suggested that taking more time to perform colonoscopy increases screening accuracy after comparing rates of lesions detection with two different withdrawal times [13]; while in 2005, two targeted drugs namely Erbitux and Vectibix are approved for advanced colon cancer although they are only effective in patients with the normal form of a gene known as KRAS while conventional colonoscopy established as optimal screening method from the less invasive ones. Right-sided colon cancers present a challenge for colonoscopy and recommend people to undergo a colonoscopy every 10 years to reduce the risk [14]. In 2004, a German rectal cancer study found that chemotherapy and radiation before surgery reduce side effects for rectal cancer patients while laparoscopic colon cancer surgery is deemed to be more effective better tolerated. FDA approves the first “anti-angiogenic” drug, bevacizumab [15]. In 2003, aspirin and similar anti-inflammatory medications were shown to help to reduce colon cancer risk. New “FOLFOX” chemotherapy is effective for colon cancer. First oral chemotherapy drug Capecitabine which has comparative effectiveness as the widely used IV chemotherapy helps simplify colon cancer treatment [16]. The adjuvant therapy was first employed in 2001 (like short-term preoperative radiotherapy and total mesorectal excision) which showed to improve local control of disease in patients with resectable rectal cancer [17].

Achievements in CRC research before 20th Century

In 1997, hepatic resection surgery was found to cure some patients with advanced colorectal cancer [18]; and interestingly, in 1996, irinotecan was approved for the treatment of advanced-stage colon cancer [19]. In 1994, new genetic tests for hereditary conditions like familial adenomatous polyposis were initiated [20] while in 1990, it was unraveled that treatment after surgery increased the chance of survival against CRC [21]. 1985, the minimal invasive approach using trans-anal endoscopic microsurgery was first performed which in the turn was found to be useful for remediating some rectal cancers [22]. In 1982, a clinical staging system was proposed, comprising four stages; i.e., stage 0: abnormal cells in the mucosa that turn into metastatic tumors.; stage 1: confined to the rectum; stage 2: confined to the rectum or slight extra rectal spread; stage 3: moderate or extensive extra rectal spread; stage 4: involvement of

other organs or unresectability; and it was also noticed that the limited surgery helped the cancer patients avoid colostomies [23]. Prior to all these findings, the previous research in further exploration of an association between colorectal and breast cancers was actually suggested; the screening tests for colorectal cancer were noticed to reduce deaths dramatically [24].

Conclusion

Previous literature reported lots of information regarding the genetic makeup of the colorectal cancer progression, the development cascade in association to the biochemical signaling. The diagnosis and treatment options have also been very well reported; and many of those are in practice now. The present review simply portrayed the historical evolution of the colorectal cancer remedies on a time to time basis which may be easily inferred by the general readers. Although the molecular basis of cancer development, the review of detailed prophylaxis are absent in this review, the time scale basis discovery of the major anti-cancer remedies may aid to the existing vast knowledge about colorectal cancer.

The accelerating number of Covid-19 cases has turned the world upside down. It is neither the first pandemic the world has seen nor will it be the last, but it is the first pandemic in history where technology and social media are being used on a massive scale to keep people safe, informed, productive, and connected. Presently, we all are drowned in an overabundance of information about Covid-19, both online and offline - an infodemic - amidst a pandemic. A huge amount of misinformation and fabricated facts have surfaced across the web. It includes deliberate attempts to disseminate wrong information to undermine the public health response and advance alternative agendas of groups or individuals. This propaganda has led to the development of paranoia and can even compel a layman to experiment with something dangerous in an attempt to protect against or get rid of the virus. Misinformation is disseminated among people for political or financial gain. The campaign against Covid-19 vaccination is a notable example in this regard - the wellness and nutritional supplement companies are advocates of, and directly profit from, antivaccination campaigns.

Infodemic in the form of mis- or disinformation can have far-reaching consequences. It can be harmful to people's physical and mental health or could cost someone's life; threaten precious health gains; increase stigmatization; and lead to poor observance of public health measures, thus reducing their effectiveness and endangering nations' ability to stop the pandemic. Without the appropriate trust and correct information, diagnostic tests go unused, immunization campaigns will not meet their targets, and the virus will continue to thrive. Incoherent

government messaging and reversals in recommendations, based on newly emerging evidence, can be misconstrued as incompetence. This situation is extremely concerning because it undermines trust in health institutions and programs. The outcome is the erosion of public trust and a sense of helplessness, the perfect conditions for the spread of harmful misinformation that begins a vicious circle.

Combatting the infodemic, effectively and promptly, is a critical part of controlling the uncertainty and anxiety associated with the COVID-19 pandemic. A coordinated approach among governments, multilateral organizations, and civil society is vital in this regard. All the nations need to disseminate timely and reliable COVID-19 information, based on science and evidence, to all communities, particularly the high-risk groups and take measures to counter misinformation by leveraging digital technologies accordingly. They also need to empower local communities to develop solutions and resilience against mis- and disinformation.

Immediate, coordinated action is needed from the global political and scientific community to maintain the integrity and credibility of professional expertise and rebuild public trust. Scientific journals should consider actively countering misinformation about themselves and the work that they publish. The research community, all over the world, has also come together to combat the infodemic by making the latest scientific data on Covid-19 readily available and almost all emerging research on COVID-2019 has been made open access.

We can slow down the spread of misinformation and disinformation, at an individual level, by practicing some information hygiene. Measures like assessing the source of information; going beyond the headlines to look at the entire story; identifying the credibility of the author; checking the date of publishing (recent/relevant or up-to-date); examining the supporting evidence; checking one's own biases and making use of fact-checkers focused on debunking misinformation, can help us navigate this tide of infodemic and decide who and what to trust. One needs to remember that panic takes us nowhere; it is always the awareness that helps. Until a brighter day dawns over this infodemic; wash your hands, wear a mask, and maintain social distancing.

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