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Pathophysiology of Colorectal Cancer

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Colorectal Cancer

Colorectal cancer (CRC) is a slow developing preventable cancer that occurs after colon or rectal polyps undergo abnormal cellular changes. Even though CRC is preventable, it remains the third most common cancer in the world (Simonsom, 2018) and the second most diagnosed cancer in developed countries (Cuthbert, Hemmelgarn, Xu, & Cheung, 2018). There were estimates that 140,250 cases of CRC would be diagnosed in 2018 and 50,630 deaths (Montminy, Karlitz, & Landreneau, 2019). Many CRCs can be prevented by early detection of growths or polyps on the colon before they develop into cancer cells, but up to 65% of patients do not complete recommended screenings (Hassan, Kaminski, & Repici, 2018). To prevent occurrences of CRC it is be important to understand the barriers that patients have and reason why they are not compliant with CRC screening recommendations.

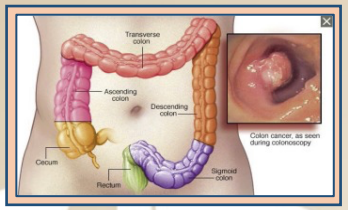

Image 1 (Buccafusca et al., 2019)

Why choose Colorectal Cancer?

The topic CRC was chosen because the author is employed in a gastrointestinal endoscopy unit and is a part of a team that completes routine colorectal cancer screenings. The author would like to gain a deeper understanding of the pathophysiology of this disease.

Case Presentation

A 65 year old Caucasian male presents. to an outpatient colonoscopy center to have his first colonoscopy. He does not have any symptoms and did not want to have the screening. His wife insisted that he completed the screening. He eventually agreed to have a colonoscopy completed. The colonoscopy was performed and there was a 5 cm polyp noted near the cecum. The polyp was removed with a snare and sent to pathology for analysis. The pathology report came back showing adenocarcinoma. The patient was referred to a colorectal surgeon and oncologist for further recommendations.

Underlying Pathophysiology

CRC can be sporadic, hereditary, or from inflammatory bowel disease (Simonsom, 2018). There are multiple mutations that happen to cause CRC, listed below are some of the most common causes. Sporadic causes of CRC occur at 94%, 5% are from inherited mutations, and the remaining 1% are from inflammatory bowel disease (Simonsom, 2018). Image 2 shows normal colon mucosa transforming to adenocarcinoma due to DNA mutations.

Sporadic

- Chromosome instability or suppressor pathway dysfunction
  - A genetic alterations in tumor suppressor genes (APC, KRAS, and p53)
  - When there are mutations in the tumor suppressor genes, tumors are able to proliferate and differentiate into cancer (Simonsom, 2018)
- Microsatellite instability or mutator pathway dysfunction
  - Disruption in the DNA mismatch repair (MMR) genes
  - The MMR system proofreads DNA as it is created. When the MMR system identifies an abnormality in the sequence repairs to the DNA are made.
  - MMR gene dysfunction allow DNA mutations to increase at a rapid pace (Simonsom, 2018)
- CpG island methylator phenotype (CIMP) or serrated pathway dysfunction
  - Tumor suppressor genes switch off
  - When tumor suppressor genes are turned off in the CIMP pathway abnormal cells are able to grow and malignant cells develop (Simonsom, 2018)

Hereditary

- Lynch syndrome (LS) or hereditary nonpolyposis CRC
  - Autosomal dominant
  - Defective MMR gene (Snyder & Hampel, 2019)
  - This mutation has an increased risk for not only CRC but also ovarian, gastric, urothelial, hepatobiliary, pancreatic, small bowel, glioblastomas, and sebaceous skin cancers (Snyder & Hampel, 2019)
- Familial Adenomatous Polyposis (FAP)
  - Autosomal dominant
  - APC gene mutation (Snyder & Hampel, 2019)
  - Patients that have inherited FAP have hundreds of polyps in the colon and 100% of patients with this genetic condition will get CRC by the age of 40 (Simonsom, 2018).
  - These patient must undergo early screening and most need a colectomy due to the number of polyps that develop in their colon and their risk of developing cancer.

Inflammatory Bowel Disease (IBD)

- Crohn's disease or ulcerative colitis
  - Chronic inflammation from cytokines and chemokines alter cell proliferation and survival (Dulia, Sandborn, & Gupta, 2016)
  - The colon experiences molecular changes with inflammation, including cytokine secretion, vascularization, and tumor growth (see Figure 1)
  - Patients with IBD have a 60% higher risk for developing CRC compared to those without IBD (Dulia, Sandborn, & Gupta, 2016)

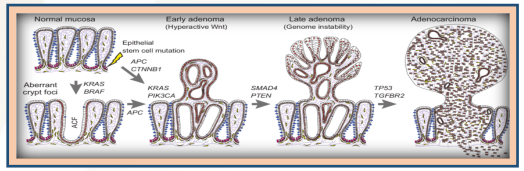

Image 2 (Strubberg & Madison, 2017)

Significance of Pathophysiology

Altered genes and mutations cause cells to proliferate in the colon and polyps develop in the mucosa. The polyps continue to grow and they eventually become malignant growths with the potential to metastasize. Usually CRC is a slow developing cancer. Polyps can take years to turn into cancerous cells (with the exception of FAP/LS which has rapid growth). Polyps that are less than 1 cm in size have a 3% chance of being an advanced adenoma and polyps that are bigger than 2 cm have a 10% chance of being malignant (Harisinghani, Chen, & Weissleder, 2019).

The different types of polyps that can develop are:

- Tubular adenoma
- Villous adenoma
- Tubulovillous adenoma
- Sessile serrated- these polyps may be difficult to discover as they are usually flat (Simonsom, 2018)
- Hyperplastic- these polyps have no malignant potential (Harisinghani, Chen, & Weissleder, 2019)

Treatment of CRC

Treatment of CRC depends on the stage of the tumor when it is discovered. If the tumor has not breeched the submucosa or colon wall it may be sufficient to remove the tumor endoscopically. If the tumor is too large to remove endoscopically surgical resection may be required. When surgical resection is required the patient may need a bowel diversion. Below are the different treatment options for CRC.

- Primary colon cancers without systemic disease are treated mainly by surgery with complete mesocolic excision
- Total mesorectal excision (TME) is indicated for rectal cancer
- Right hemicolectomy transverse colectomy, left hemicolectomy or total colectomy depending on where the tumor is located
- Adjuvant chemotherapy
- Radiation (Buccafusca et al., 2019)

Signs and Symptoms of Colorectal Cancer

- Anemia
- Weight loss
- Weakness
- Abdominal pain
- Changes in bowel habits
- Rectal bleeding and/or melena (Buccafusca et al., 2019)

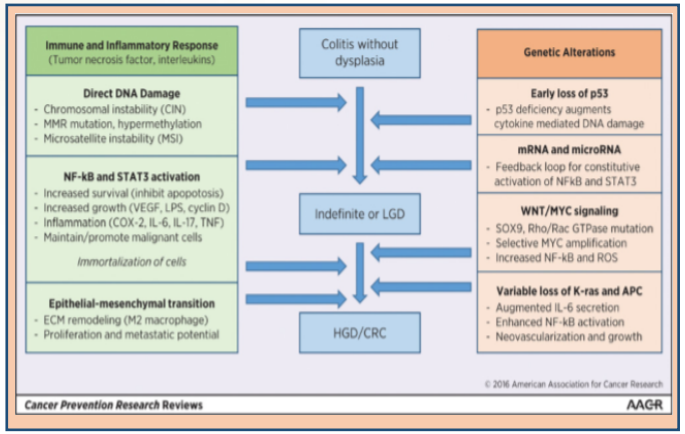

Figure 1 (Dulia, Sandborn, & Gupta, 2016)

Nursing Implications

Nurses are responsible for health promotion. When considering CRC, nurses can promote health by encouraging patients to undergo preventative screenings for CRC. Many CRCs can be prevented by early detection of growths or polyps on the colon before they develop into cancer cells, but up to 65% of patients do not complete recommended screenings (Hassan, Kaminski, & Repici, 2018). It is important for nurses to understand the screening methods and the recommendations that are used to detect CRC. Nurses can help patients overcome barriers they may face when considering CRC screenings. Below is information about the types of screenings and the screening recommendations (see Figure 2) for patients that do not have family history of CRC and are considered to be in a low risk group. These screenings should start at age 50 (Rex et al., 2017). Colonoscopy is recommended for patients that are in the high risk population. Frequency of the screenings depend on each specific case.

CRC screening methods

- Colonoscopy is direct visualization of the entire colon (from the cecum to the rectum) where polyps or growths can be found. If polyps are noted they can be removed or biopsied and sent for analysis at the time of the procedure.
- Fecal Immunochemical Testing (FIT) analyzes stool samples for blood.
- CT colonography is an imaging test that can detect growths in the colon.
- Flexible sigmoidoscopy is a procedure similar to colonoscopy, but the endoscope only visualizes part of the colon, the transverse and ascending colon are not visualized during a sigmoidoscopy.
- FIT-Fecal DNA testing (Cologuard) is a test that is able to detect abnormal DNA that is found in some polyps and adenomas .
- When any of the screening tests come back abnormal or positive a colonoscopy would be recommended. If patients do undergo colonoscopy are found to have polyps the frequency of screenings may increase to every three to five years.

Screening recommendations

Tier 1
- Colonoscopy- to be completed every 10 years
  or
- Fecal Immunochemical Testing (FIT)- to be completed every year

Tier 2- If patient declines colonoscopy or FIT testing
- CT colonography- to be completed every five years
  or
- Flexible sigmoidoscopy- to be completed every five to 10 years
  or
- FIT- Fecal DNA testing- to be completed every three years

Tier 3- If patient declines all other screening methods
- Capsule colonoscopy- to be completed every 3 years (Rex et al., 2017)

Figure 2 (Rex et al., 2017)

Conclusion

CRC is a preventable disease that continues to be one of the leading causes of cancer. Multiple complex genetic mutations take place to turn normal cells into malignant growths. If the abnormal growths are found in the very early stages, they can be removed endoscopically, but once the mass gets too large surgical resection is necessary. Many patients fail to complete screening for CRC. In many cases CRC could be prevented if the screenings were completed. Healthcare providers must ensure their patients understand the importance of screening for CRC and promote the completion of preventative screenings.

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