



Malignant Tumors of Intestine

Lecture 09

430 Pathology Team

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Malignant Tumors of Large Intestine:

Carcinogenesis:

Two pathogenetically distinct pathways for the development of colon cancer, both seem to result from accumulation of multiple mutations:

1- The APC/B-catenin pathway (85 %)

It is a chromosomal instability that results in stepwise accumulation of mutations in a series of oncogenes and tumor suppressor genes.

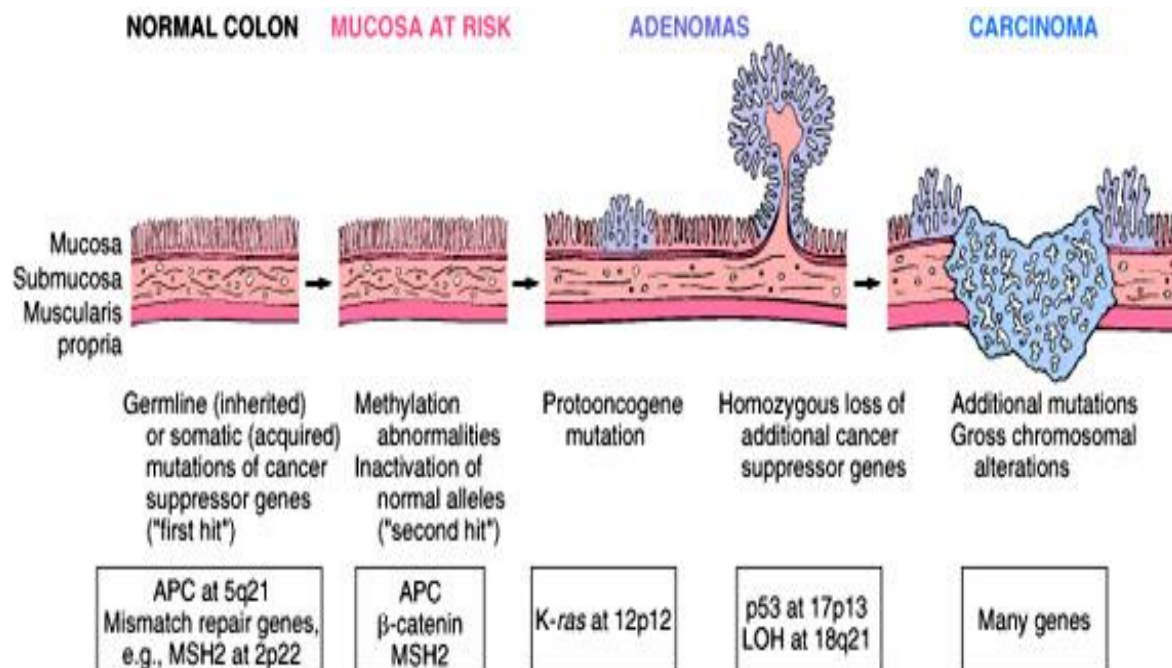
e.g: **Familial Adenomatous Polyposis (FAP):**

Cause: Hereditary mutation of the APC gene.

Prognosis: affected individuals carry an almost 100% risk of developing colon cancer by age 40 years.

2- The DNA mismatch repair genes pathway

- 10% to 15% of sporadic cases.
- There is accumulation of mutations (as in the APC/B-catenin schema)
- Five DNA mismatch repair genes (MSH2, MSH6, MLH1, PMS1, AND PMS2) lead to microsatellite instability
- Give rise to the hereditary non polyposis colon carcinoma (HNPCC)



Adenocarcinoma:

Incidence:

- Adenocarcinoma of the colon is the most common malignancy of the GI tract and is a major cause of morbidity and mortality worldwide.
- Constitutes 98% of all cancers in the large intestine.

Predisposing factors:

1. IBD, adenomas , polyposis syndrome.
2. Diet appears to play an important role in the risk for colon cancer:
 - Low fibre diet.
 - High fat content.
 - Alcohol
 - Reduced intake of vit A, C & E.

Colorectal Carcinoma:

Morphology:

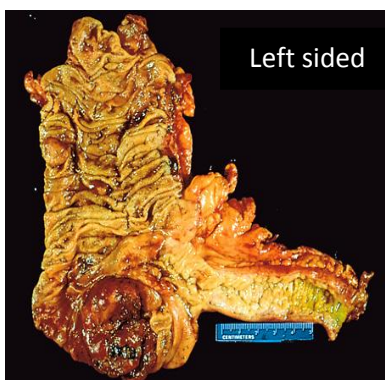
Location: 70% are in the rectum, rectosigmoid and sigmoid colon.

Types:

- **Left-sided carcinomas:** tend to be annular, encircling lesions with early symptoms of obstruction.
- **Right-sided carcinomas:** tend to grow as polypoid, fungating masses, obstruction is uncommon. **Patients usually present with anemia.**

Which one has better prognosis, right sided or left?

The right sided carcinoma has better prognosis than left sided



- Adenocarcinoma
- Mucinous adenocarcinoma secrete abundant mucin that may dissect through cleavage planes in the wall.

Signs and symptoms:

- If located closer to the anus: change in bowel habit, feeling of incomplete defecation, PR bleeding
- A tumor that is large enough to fill the entire lumen of the bowel may cause bowel obstruction
- Right-sided lesions are more likely to bleed while left-sided tumors are usually detected later and could present with bowel obstruction.

Tumor markers:

A **tumor marker** is a substance found in the blood, urine or body tissues that can be elevated in cancer, among other tissue types.

Both carcinoembryonic antigen (CEA) and Carbohydrate antigen (CA-19-9) are useful to assess tumor recurrence.

Serum levels of carcinoembryonic antigen (CEA) are related to tumor size and extent of spread. They are helpful in monitoring for recurrence of tumor after resection. **Before surgery, levels will be high, however, after resection the levels will markedly decrease to normal, but when the disease reoccurs levels will start to increase again).**

These tumor markers are not very specific as they are raised in different conditions, diseases, and even other tumors. Another disadvantage for these markers is that they are only elevated after the tumor has greatly enlarged and metastasized.

Tissue inhibitor of metalloproteinases 1 (TIMP1) is elevated in early and late stages.

Prognosis: by TNM Staging of Colon Cancers, **for more information see table 15-13, page 624 of Robbins basic pathology, 8E**

stage	indication
Tis	The cancer is in the earliest stage (in situ). It involves only the mucosa.
T1	Invasion of lamina propria or submucosa.
T2	Invasion of muscularis propria.
T3	The cancer has grown through the muscularis propria and into the outermost layers of the colon or rectum but not through them. It has not reached any nearby organs or tissues.
T4	Invasion of other organs or structures such as lymph nodes

Malignant Small Intestinal Neoplasms:

In descending order of frequency:

- Carcinoid
- Adenocarcinomas
- Lymphomas
- Leiomyosarcomas.

1- Carcinoid Tumors

Definition: neoplasms arising from endocrine cells found along the length of GIT as well as the respiratory mucosa.

Age group: the peak incidence is in the sixth decade, but they may appear at any age.

Incidence:

- They compose less than 2% of colorectal malignancies (majority is adenocarcinoma)
- almost half of small intestinal malignant tumors.

Location: 60 to 80% appendix and terminal ileum. 10 to 20% rectum.

Behavior:

Aggressive behavior correlates with:

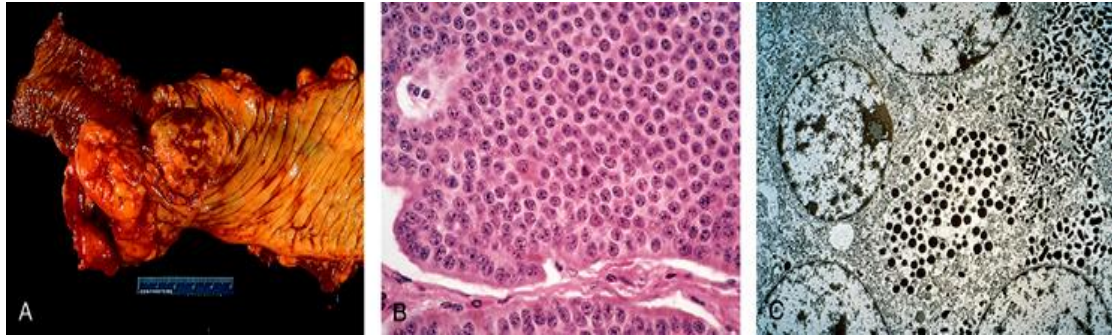
- The site of origin (e.g: in appendiceal or rectal carcinoids are usually benign and rarely metastasis. However, in ileal , gastric, colonic carcinoids they are usually aggressive)
- the depth of local penetration
- and the size of the tumor

Appendiceal and rectal carcinoids infrequently metastasize (local invasion), even though they may show extensive local spread.

90% of ileal, gastric, and colonic carcinoids that have penetrated halfway through the muscle wall have spread to lymph nodes and distant sites at the time of diagnosis, especially those larger than 2 cm in diameter.

Morphology:

- A solid, yellow-tan appearance
- The cells are monotonously similar (having a scant, pink granular cytoplasm and a round-to-oval stippled nucleus).
- Ultrastructural features: neurosecretory (electron dense bodies) in the cytoplasm (produce active peptide)



Clinical features:

- Asymptomatic
- May cause obstruction, intussusception or bleeding.

Intussusception is the enfolding of one segment of the intestine within another. It is characterized and initially presents with recurring attacks of cramping abdominal pain that gradually become more painful.

- May elaborate hormones: Zollinger-Ellison (**gastrin**), Cushing's carcinoid or other syndromes such as carcinoid syndrome.

Carcinoid syndrome:

Incidence: 1% of carcinoid tumor & in 20% of those of widespread metastasis

The syndrome is classically associated with ileal carcinoids with hepatic metastases.

Cause: excessive production of serotonin

N.B: normally serotonin is degraded in the liver to an inactive form. However, in patients with hepatic dysfunction as a result of metastases, serotonin will reach the blood circulation causing most of the symptoms below.

Symptoms:

- paroxymal flushing
- episodes of asthma-like wheezing
- right-sided heart failure
- attacks of watery diarrhea
- abdominal pain

2- Lymphoma:

Types:

- most often low-grade lymphomas arising in mucosal-associated lymphoid tissue (MALT) lymphoma **associated with H.Pylori**
- high-grade non-Hodgkin's lymphomas of B cell type.
- **t-cell lymphoma associated with celiac disease.**

Location:

- May occur in any part of the intestine.
- The ileocecal region as well as the jaws are the favored site for Burkitt's lymphoma.