

RECTAL CARCINOID TUMORS

Slow growing malignancies, derived from neuroendocrine cells, which produce biologically active agents, occurring most frequently in the gastrointestinal tract.

History

- 1867: Langhans first described a carcinoid tumor
- 1890: Ransom provided a full comprehensive description of carcinoid syndrome
- 1907: Oberndorfer first used “karzinoide” to differentiate from adenocarcinomata
- 1914: Gosset and Masson: recognized carcinoids as endocrine-related tumors
- 1963: Williams & Sandler: classification according to embryological origin

Epidemiology:

Modlin et al. 2003 (13,715 patients over 5 decades)

- 0.49% of all malignancies
- age 59.9-61.4 overall. Average age for small intestinal carcinoids 65.4
- female:male 55.1:44.9 % (female predominance for gastric 64.5%, colonic 56.5%, appendiceal 65.7%, bronchopulmonary 63% and gallbladder 75%; male predominance for esophageal 66%, and thymic 76%)
- White:Black ratio overall 6.8
- Although appendiceal has long been recognized as the most frequent occurring carcinoids, their relative frequency decreased from 43.9% to 2.43% (due to decreased surgical commitment to appendectomy?)

Lauffer et al. 1998 74% in GI tract (SB 29%, appendix 19%, rectum 13%)

Classification:

Carcinoids derive from neuroendocrine cell compartments → around 60% arise from the intestine, 25% from bronchopulmonary system

Classification based on site of origin in terms of embryologic divisions of the alimentary tract:

- Foregut (lungs, bronchi, stomach)
 - present with PUD, abdominal pain or bleeding, duodenal or biliary obstruction
 - lung tumors may present with carcinoid syndrome, recurrent pneumonia, cough, hemoptysis
 - Pulmonary carcinoid can secrete other neuroendocrine factors that cause Cushing’s, acromegaly
- Midgut (small intestine, appendix, proximal colon)
 - present with usually abd pain and/ or obstruction
 - carcinoid syndrome less likely due to mesenteric venous flow to liver and clearance of serotonin, but by overwhelming its capacity in the presence of liver metastasis it may appear.

- Hindgut (distal colon, rectum, GU tract)
 - present with changes in bowel habits, obstruction, or bleeding
 - again carcinoid syndrome less likely
 - GU tract tumors may present with renal mass or testicular mass
 - Ovarian tumors are common to present with carcinoid syndrome due to systemic venous outflow

Carcinoid symptoms:

- Skin
 - Flushing, telangiectasias, cyanosis, pellagra
- GI
 - Diarrhea and cramping
- Heart
 - Valvular lesions (right heart > left hear)
- Respiratory
 - Bronchoconstriction
- Symptoms mediated by various humoral factors elaborated by some carcinoid tumors
- Symptoms include: Cutaneous flushing, telangiectasias, secretory diarrhea, bronchospasm, cardiac valvular lesions

Active Agents:

- Serotonin
 - Tryptophan metabolism altered- classically overproduction of serotonin, but for example in some foregut tumors, histamine may be produced (enzyme issue) or in hindgut tumors tryptophan cannot be converted to serotonin and thus no carcinoid syndrome (even if metastasized to liver)
 - May result in tryptophan deficiency
 - Decreased protein synthesis, hypoalbuminemia, niacin deficiency (pellagra)
 - Diarrhea secondary to intestinal stimulation by serotonin
 - Stimulation of fibroblasts and fibrogenesis which may lead to peritoneal and cardiac fibrosis
- Histamine
 - Primary gastric carcinoids
 - Responsible for flushing and pruritis
 - PUD
- Kallekrein
 - Cleaves kinin from plasma kininogens, bradykinin a product is a potent vasodilator and may cause flushing
- Prostaglandins E and F
 - Stimulate gut motility and fluid secretion in the GI tract
- Other polypeptides
 - Insulin, ACTH, Gastrin, VIP

Treatment:

- Symptomatic treatment. Octreotide (analog of somatostatin)

Metastases:

- In 29.4% of autopsies. Lymph nodes 89.8%, liver 44.1% , lung 13.6%, peritoneum 13.6% and pancreas 6.8% (Berge et al. 1976)³

Carcinoid tumors of the rectum

- Mostly small
- 3rd most common of GI carcinoids 13.71% (*Modlin et al. 2003*)
- Black:White 3:1
- Male:Female ratio 1.13 (1.7 *Jetmore et al. 1992*, 2.8 *Matsui et al. 1993*)
- Average age at diagnosis 56.2 (52 *Jetmore et al. 1992*, 48 *Matsui et al. 1993*)

Classification:

- <1 cm (80%, benign), 1-2 cm (10%, aggressive size-independent course with reported risk of metastasis and death in 15-25%), >2 cm (10%, usually malignant)
- Histological:
 - Typical: uniform cell patterns, rare mitotic activity, no evidence of local invasive growth, bloodstream, lymphatic vessels or neuronal structures
 - Atypical: local invasion or cell pleomorphism
 - T1 mucosa or submucosa, T2 muscularis propria, T3 full rectal wall, T4 surrounding tissue

Diagnosis:

- Only 50% cause symptoms (*Stinner et al. 1996*)
 - Transanal bleeding 18%
 - Constipation 17%
 - Rectal pain 7%
 - Pruritus ani 3%
- Known to be hormonally inactive, even with extensive liver metastasis
- Elevated prostatic acid phosphatase (80%) and CEA (25%)
- Most rectal vault tumors lie in the anterior and lateral portion of the lower 1/3, thus the majority is amenable to be palpated on digital rectal examination
- Endoscopic (colonoscopy, sigmoidoscopy, proctoscopy) finding:
 - Usually nodular, polypoid or sessile. Generally as small mobile, submucosal nodule or focal areas of thickened submucosa.
- Lymph nodes and distant metastases: endoluminal rectal sonography, CT, or somatostatin receptor scintigraphy.
- Metastasis on presentation only 14% of cases (overall)
- 60% of biopsied were <1 cm - 2% metastasize, 1-2cm 10-15% mets; >2cm 60-80% mets. (*Mani et al 1994*)

Treatment: *Shindl et al. 1998* (n=31)

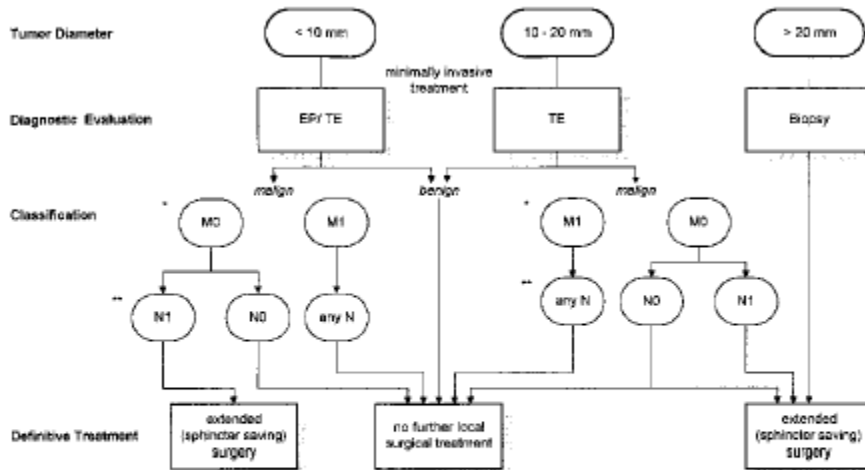


Fig. 2. Algorithm for stage-dependent treatment of rectal carcinoid tumors. EP: endoscopic polypectomy; TE: transanal excision. Preoperative evaluation by *abdominal CT scan and somatostatin receptor scintigraphy; **endosonography and somatostatin receptor scintigraphy.

- 16/17 patient with “benign” lesions underwent minimally invasive surgery with no recurrence or progression
- The above algorithm was designed from the outcomes of 14 patients with “malignant” lesions
Mani et al. 1994:
- Tumors > 2cm or with invasion of muscularis → treatment as adenocarcinoma

Chemotherapy:

- Role limited. Streptosotozin, 5-fluorouracil, doxorubicin, beta interferon and cyclophosphamide have not shown any benefit.

Outcomes/Prognosis

- Rectal carcinoids have low propensity to metastasize, overall 5-year survival rate 88.3
- Not sufficient data to support that extensive surgical treatment can improve prognosis of disseminated disease. Only palliative for local symptoms such as bleeding or obstruction (*Stinner et al. 1996*)

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