

CARCINOID TUMORS OF THE APPENDIX

1% of all appendectomy specimens contain a neoplasm. Most common tumor is the carcinoid (0.3%). Rare tumors also include benign and malignant mucoceles, adenocarcinoma, and adenocarcinoids or *goblet cell carcinoid*.

Carcinoids represent 2/3 of all appendiceal neoplasms. Of all those within the GI tract, ½ arise from the appendix. They appear yellow and have a surrounding desmoplastic reaction although usually found incidentally. Most carcinoids present in ages 15-29. Goblet cell carcinoids typically present at mean age 52 years.

Mucocele of the appendix can be either cystadenomas or cystadenocarcinomas. They usually obstruct the appendiceal lumen with mucin. On CT, one sees a mucin filled lumen with a surrounding calcified wall. If a benign tumor causes appendiceal rupture and mucinous ascites, appendectomy is cure. If malignant with mucinous ascites → *pseudomyxoma peritonei*. The difference is that in malignant condition there is tumor implantation in peritoneum with mucin producing cells.

Appendiceal adenocarcinoma is rare and found unexpectedly at time of appendectomy. 50% of these patients have metastases at time of diagnosis. Dukes A (mucosa and submucosa) lesions can be treated by appendectomy. B and C lesions need right hemicolectomy.

Presentation/Symptoms/Signs

Usual presentation is that of appendicitis and tumor is found incidentally. Most of the time tumor (62%) is found at tip and is not the cause of the appendicitis. Can also be diagnosed at time of routine cholecystectomy or benign pelvic surgery.

Goblet cells often found in *diffusely inflamed* appendix.

Carcinoid syndrome: carcinoids produce serotonin, histamine, kallikrein, bradykinin and prostaglandins. Confirmed by 24-hour urinary excretion of 5-HIAA.

Vasomotor- flushing during stress, alcohol, sex, or large meal. Lasts 5-10 minutes begins on face and then goes to trunk.

GI-diarrhea

Cardiac-endocardial fibrosis of tricuspid and pulmonary valves.

If have carcinoid syndrome from GI tumor then have metastatic disease to the liver. Liver has MAO which deactivates serotonin. Treatment for carcinoid syndrome includes surgery, and/or radiation, hepatic artery embolization, and octreotide. **RARELY SEEN IN APPENDICEAL CARCINOIDS, NOT SEEN IN GOBLET CELL CARCINOIDS.**

Pathology

Carcinoid tumors originate from neuroendocrine tissue found along the primitive GI tract. They do not arise from neural crest origin, rather from same progeny as other GI cells. Appendix is most common site in GI tract for carcinoids, ileum is second.

Goblet cell carcinoid is variant of appendiceal carcinoid, aka *adenocarcinoid*. Originate from pluripotent GI cells that differentiate into mucinous and neuroendocrine cells.

Primary route of spread of all carcinoids is via lymphatics.

Grading: Benign, borderline malignant, low-grade malignant, and high-grade malignant.
But majority of metastases occur in tumors that were graded low-grade malignant!!

Tumor characteristics predicting aggressive behavior include: size, histological type, and mesoappendiceal involvement.

Size: metastatic spread unlikely if tumor less than 2cm. In Moertel et al.'s series of 150 patients, 127 had lesions less than 2cm., none had metastasized.

Mesoappendiceal extension: correlates with nodal metastases and tumor size. Serosal involvement is unrelated to outcome in several studies, except in Goblet cell tumors.

Histological subtype: Goblet cell carcinoids are unique. 65% of these patients show invasion of mesoappendix, or extension to adjacent organs. *Serosal involvement is more predictive of outcome in these cases.* Can also present as Krukenberg tumors to ovaries.

Mitotic activity: Assessing the mitotic activity in low-grade malignant tumors can be useful. This includes Ki67 expression (a proliferation marker). Ki67 index is higher in tumors greater than 2cm. Over expression of p21 and E-cadherin correlates with malignant behavior.

Prognosis and Staging

Prognosis/10-year survival rate: most important factor is extent of disease at TIME of diagnosis.

Carcinoids <1cm and benign: ~100%

Malignant Carcinoid: 80%

Goblet Cell: 60%, in McCusker et al.'s study, 65% showed serosal involvement, 51% with mesoappendiceal involvement.

Adenocarcinoma: 50%

Treatment

Appendectomy: for lesions <2cm

Right hemicolectomy: positive margins on appendectomy, greater than 2cm, mesoappendiceal involvement, mitotic index of more than 2cells per mm², high Ki67 index, angioinvasion.

References

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November 22, 2004