APPENDICEAL CARCINOID

- 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
  - **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.

- **Mucoceles** 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 appendicial 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:

- Size:
    - metastatic spread unlikely if tumor less than 2cm.
    - In Moertel series of 150 patients, 127 had lesions less than 2cm., none had metastases
- 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.
    - Overexpression of p21 and E-cadherin correlates with malignant behavior.

Prognosis and Staging

- most important factor is extent of disease at TIME of diagnosis.
    - *Carcinoids <1cm are 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 indicated when:
  - positive margins on appendectomy
  - size greater than 2cm
  - mesoappendiceal involvement
  - mitotic index of more than 2 cells per mm^2
  - high Ki67 index
  - angioinvasion.

Sources

- Aizawa et al. Adenocarcinoid of the Appendix: Report of Two Cases. Surgery Today. 2003.
- Goede et al. Carcinoid Tumour of the Appendix. British Journal of Surgery. 2003.
- McCusker et al. Primary Malignant Neoplasms of the Appendix. Cancer 2002.
- Moertel et al. Carcinoid Tumor of the Appendix: Treatment and Prognosis. NEJM. 1987.

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