Epithelial Neoplasms of the Appendix

Laura H. Tang, MD, PhD

Objective.—To review clinical and diagnostic issues for 3 pathologic types of epithelial neoplasms of the appendix:

- Mucinous adenocarcinoma, with specific focus on mucinous neoplasm; (2) goblet cell carcinoid tumor and associated adenocarcinoma; and (3) typical carcinoid tumor.

Data Sources.—Case-derived material and literature review.

Conclusion.—The most important issue in pathologic assessment of epithelial tumors of the appendix is to understand the clinical implications inherent in the diagnosis.

(Arch Pathol Lab Med. 2010;134:1612–1620)

Epithelial tumors of the appendix essentially resemble, with more or less fidelity, their counterpart epithelial-cell types of the normal mucosa. Appendiceal adenocarcinomas have a phenotype similar to that of conventional colonic adenocarcinomas, although mucinous neoplasms are more common in the appendix than in the colon. Because of its association with the clinical condition of pseudomyxoma peritonei (PMP), appendiceal mucinous neoplasm is associated with complex clinical and pathologic issues concerning its nomenclature, tumor staging, and clinical decisions about the management of local and disseminated disease. Typical carcinoid tumors of the appendix exhibit an exclusive neuroendocrine phenotype with the capacity for amine and peptide hormone production. In contrast, goblet cell carcinoid tumors of the appendix are rare, and they have a mixed phenotype with partial neuroendocrine differentiation and intestinal-type goblet cell morphology. As such, they have been classified together with other neoplasms that show both neuroendocrine and glandular differentiation. It remains controversial whether goblet cell carcinoid tumors should be considered as variants of appendiceal adenocarcinoma or as part of the carcinoid tumor spectrum.

MUCINOUS NEOPLASMS OF THE APPENDIX

A mucinous adenocarcinoma of the appendix may be 1 of 2 major types: 1 type resembles conventional colonic adenocarcinoma and possesses the potential for destructive growth and nodal or solid organ metastasis; the other is associated with predominantly low-grade mucinous neoplasms and possesses the potential for peritoneal dissemination. Among epithelial neoplasms of the appendix, mucinous neoplasm is the most common tumor and is the focus of this review. Pseudomyxoma peritonei is a clinical condition of gelatinous ascites, which is usually secondary to an appendiceal mucinous neoplasm, although in rare situations it may be associated with a mucinous tumor of other primary sites. Primary appendiceal mucinous neoplasms exhibit a spectrum of histopathologic features and have been variably designated as ranging from mucinous cystadenoma, low-grade mucinous neoplasm, and disseminated peritoneal adenomucinosis to cystadenocarcinoma, mucinous carcinoma, and peritoneal mucinous carcinomatosis. The dilemma of tumor classification and nomenclature will most likely continue to be the subject of debate; as a consequence, there continues to be considerable confusion in our daily pathology practice and in the clinical management of the disease.

1. Precursor Lesions

Mucinous adenocarcinoma is believed to arise in association with dysplastic mucinous epithelium. In contrast to conventional tubular adenoma of the colon, appendiceal mucinous cystadenoma commonly presents as circumferential luminal involvement by villous or serrated adenoma (Figure 1, A). Identification of these preexisting dysplastic epithelia in appendiceal mucosa supports an appendiceal primary tumor for pseudomyxoma peritonei, as opposed to a primary tumor from other anatomic sites.

Mucocele is not a histopathologic diagnosis, and the epithelial lining in a mucocele may or may not be dysplastic in nature. Mucocele usually denotes gross
dilatation of the appendiceal lumen, with mucin accumulation in the presence or absence of luminal obstruction secondary to neoplasia, or denotes a nonneoplastic process such as fecalith, postinflammatory scarring, endometriosis, or a carcinoid tumor. A nonneoplastic mucocele is the least common cause of appendiceal luminal mucin retention. Thus, the use of the term *mucocele* should be eliminated in pathology reports to avoid the confusion about the etiology of this group of lesions.

Simple hyperplastic polyps are rare in the appendix when compared to the colon, and they are not precursors of mucinous adenocarcinoma. However, since most adenomatous polyps of the appendix contain abundant intracellular mucin, which can render the nuclear pseudostatification of an adenoma less apparent, the distinction between a mucinous adenoma and a hyperplastic polyp can be challenging.

### Table 1. Summary of Staging Issues for Appendiceal Mucinous Neoplasm

<table>
<thead>
<tr>
<th>Noninvasive</th>
<th>Uncertain Malignant Potential</th>
<th>Invasive</th>
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<tbody>
<tr>
<td>Cystadenoma</td>
<td>Adenoma with focal stromal acellular mucin dissection</td>
<td>Confined to Appendix (pT1-T4)</td>
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<tr>
<td>Adenoma with diverticulum</td>
<td>Adenoma with extramural acellular mucin</td>
<td>Local Peritoneum Malignant epithelium outside appendix</td>
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<tr>
<td>Adenoma with mucin extrusion secondary to rupture</td>
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<td>Extensive Peritoneum Pseudomyxoma peritonei</td>
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A diverticulum or mucosal herniation into the appendiceal wall can commonly simulate the appearance of an invasive carcinoma (Figure 1, B); this is particularly challenging because most mucinous adenocarcinomas of the appendix are well differentiated and display minimal cytologic atypia, and they are often indistinguishable from the epithelium of the noninvasive counterpart. The presence of a rim of lamina propria around the epithelium is a feature associated with a diverticulum (Figure 1, B). In contrast, the presence of desmoplasia surrounding the epithelium in question would support the interpretation of invasive carcinoma; unfortunately, desmoplasia is not often present in invasive carcinomas, even in cases of metastatic carcinoma (Figure 2). Additional deeper tissue sections may help to demonstrate connection of the epithelium of a diverticulum to the luminal surface.
The presence of stromal mucin noticeably raises the concern for an invasive carcinoma, and in some situations, it is impossible to prove otherwise. In fact, identification of acellular mucin dissecting into extra-appendiceal stroma raises concerns about the presence of an invasive mucinous carcinoma that has been incompletely sampled. Detection of a gross or microscopic rupture site would help to determine the noninvasive nature of mucin extrusion. In addition, other histologic features of these mucin pools, if observed in the appropriate context, may be of help in determining their etiology. Mucin pools with an associated inflammatory response and histiocytic reaction suggest mucin spillage secondary to rupture (Figure 1, C). In contrast, “clean” stromal mucin that lacks

Figure 2. Well-differentiated mucinous adenocarcinoma with extensive mucin pools partially lined with mucin containing neoplastic epithelium (A and B). Even in an ovarian metastasis, desmoplasia is not apparent (C); an immunostain with CK20 confirms the presence of metastatic intestinal epithelium amalgamated with ovarian epithelium (D). Adenocarcinoma presents as extramural carcinoma without mural involvement (upper right) (E) (hematoxylin-eosin, original magnifications ×200 [A through D] and ×100 [E]).
an inflammatory/histioytic reaction and dissect between numerous small bands of stroma is more commonly seen in an invasive carcinoma (Figure 2).

The diagnosis of mucinous cystadenoma should be reserved for adenomatous lesions unequivocally confined to the appendiceal lumen without intramural or extramural mucin or neoplastic epithelium. This necessitates diligent handling of appendectomy specimens by both the surgeon and the pathologist. Particular care must be taken when aspirating or extruding mucin from the cyst to prevent extramural contamination by cyst contents, which may complicate the microscopic evaluation and the assessment of margin status. The final diagnosis of a cystadenoma should be established after microscopic examination of the entirely submitted appendectomy specimen to ensure the absence of extraluminal and extramural disease. When mucin is found outside the appendix, alternative terminology is suggested, depending upon whether there are neoplastic cells detected within the mucin (see below).

3. Invasive Mucinous Adenocarcinoma

When neoplastic epithelium and mucin are found within the wall, or especially outside the wall of the appendix, and the possibility of a diverticulum cannot be proven, there is a risk for progression of the disease to pseudomyxoma peritonei. Although numerous other terms have been proposed to describe this clinical situation (Table 2), we believe that the clinical course of the disease justifies its designation as mucinous adenocarcinoma, which should be staged and graded like other gastrointestinal adenocarcinomas for the appropriate guidance of clinical management and prognosis (Table 1). Thus, the condition of PMP is the clinical manifestation of a mucinous adenocarcinoma, since the locally spilled acellular mucin from rupture of a noninvasive cystadenoma should not cause excessive mucin production and accumulation in the peritoneal cavity. When there is obvious PMP outside the immediate periappendiceal region, there is less of an issue in establishing a diagnosis of malignancy even though the neoplastic epithelium is difficult to sample. When the invasive adenocarcinoma is confined to the appendiceal wall without evidence of disseminated PMP, one should stage the tumor by assessment of the depth of invasion, as for colonic adenocarcinoma (Table 1). The chief issue is that it may be difficult to identify neoplastic epithelium within extraluminal mucin. It is well recognized that the malignant epithelium is often very scanty in well-differentiated mucinous adenocarcinomas, in which the ratio of malignant epithelium to extracellular mucin is extremely low. In these cases, the scant floating strips of malignant epithelium in mucin lakes are not always evident on a 2-dimensional tissue section, and deeper sections of areas of suspicion may uncover malignant glands (Figure 2, A and B). When invasive carcinoma is detected, additional pathologic information, such as tumor grade, may provide guidance for further clinical management and outcome.21 Well-differentiated mucinous adenocarcinomas have relatively scant epithelium arranged predominantly in strips, either floating in the mucin or attached to the stroma at the edge of the mucin pools; the nuclei are only moderately atypical, and cellular polarization is preserved. Moderately differentiated mucinous adenocarcinomas are more cellular and have complex architecture, including gland formation and cribriform pattern, and there is more obvious nuclear atypia and loss of polarity. Focal invasion of the fibrotic stroma in the absence of extracellular mucin can be found. Poorly differentiated adenocarcinomas are much more cellular and have individual cells (sometimes with a signet-ring-cell configuration) or solid nests and sheets of cells. There is necrosis and areas lacking mucin accumulation are common. Invasive growth is also more pronounced. Unlike conventional intestinal-type adenocarcinoma, desmoplasia is not a typical feature in well-differentiated mucinous adenocarcinoma, either at the primary site or in metastases (Figure 2, B through D). The adenocarcinoma may also present as extramural carcinoma without mural involvement (Figure 2, E). In contrast, desmoplasia is better appreciated in moderately and poorly differentiated carcinomas (Figure 3). When the malignant epithelium is identified outside the appendiceal wall, a diagnosis of mucinous adenocarcinoma should be established even in the absence of high-grade luminal epithelial dysplasia, and all sites of mucin accumulation outside the appendix are then regarded as reflecting the presence of carcinoma, even when that mucin lacks malignant epithelium.

4. Uncertain Malignant Potential or Uncertain in Your Assessment?

The most difficult cases to categorize are those with apparent acellular mucin outside the appendiceal wall when no clear connection to a diverticulum or site of

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<tr>
<th>Source, y</th>
<th>Well Differentiated</th>
<th>Conventional Classification</th>
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<tr>
<td>Ronnett et al, 1995</td>
<td>Disseminated peritoneal adenomucinosis</td>
<td>Peritoneal mucinous carcinomatosis intermediate or discordant</td>
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<tr>
<td>Misraji et al, 2003</td>
<td>Low-grade mucinous neoplasm</td>
<td>Discordant</td>
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<tr>
<td>Pai &amp; Longacre, 2005</td>
<td>Mucinous neoplasm of low-grade/ uncertain malignant potential</td>
<td>Mucinous adenocarcinoma</td>
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<tr>
<td>Pai et al, 2009</td>
<td>Low-grade noninvasive mucinous neoplasm</td>
<td>Mucinous adenocarcinoma</td>
</tr>
<tr>
<td>Bradley et al, 2006</td>
<td>Low-grade mucinous carcinoma peritonei</td>
<td>High-grade mucinous carcinoma peritonei</td>
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rupture is detectable. Available follow-up data suggest that when the acellular mucin is limited to the periappendiceal region, the risk of progression to PMP after appendectomy is extremely low. However, given the extreme hypocellularity of some well-differentiated mucinous adenocarcinomas, there may remain a small concern about the possibility that the malignant epithelia may have been missed, especially if the specimen was not submitted in its entirety for histologic examination. Thus, the term mucinous neoplasm of uncertain malignant potential has been used for this scenario (Table 1), to reflect the fact that although the strong suspicion is for a favorable outcome, it is difficult to completely exclude the possibility of occult invasive carcinoma. The uncertainty associated with this term more accurately reflects our concerns when no clear evidence exists to diagnose a benign behavior neoplasm. In many instances, these uncertainties are associated with lack of clinical information about the possibility of mucin elsewhere in the peritoneum, mishandling and inadequate sampling of appendectomy specimens, poor orientation of the histologic sections, or unclear gross pathology descriptions. We usually classify a tumor as mucinous neoplasm of uncertain malignant potential in the following circumstances: (1) an adenoma with acellular mucin focally present outside the appendiceal wall, with no apparent evidence of rupture or (2) an

Figure 3. Appendiceal mucinous adenocarcinomas are classified as follows: well-differentiated with low-grade cytologic features (A); moderately differentiated with loss of intracellular mucin, increased cytologic atypia, and architectural complexity (B); and poorly differentiated with irregular glands/signet-ring-cell clusters and significant cytologic atypia (C) (hematoxylin-eosin, original magnifications ×200).

Figure 4. Typical goblet cell carcinoid (GCC) (A). Adenocarcinoma ex GCC, signet-ring-cell type (B). Poorly differentiated adenocarcinoma ex GCC (C) with focal typical GCC (lower right) suggests a morphologic transformation from GCC to adenocarcinoma (hematoxylin-eosin, original magnifications ×200).
adenoma with focal mucin dissection into the appendiceal wall, without the presence of associated intramural or extramural malignant epithelium. Obviously, in the absence of malignant epithelium beyond the appendiceal lumen, one cannot definitively render a diagnosis of invasive or disseminated carcinoma. However, certain morphologic features of these acellular mucin pools may suggest the presence of an invasive carcinoma in which the malignant epithelium is not represented in sections examined. It has been suggested that organizing acellular serosal mucin with neovascularization and mesothelial hyperplasia probably represents extramural tumor extension rather than benign mucinosus extrusion secondary to rupture or manipulation of the specimen.\(^{21}\) However, serosal neovascularization and mesothelial hyperplasia may be observed when there is coexisting acute appendicitis in a noninvasive mucinous cystadenoma. Stromal mucin dissection lacking associated inflammatory/histiocytic response at the periphery of mucin pools is also more often associated with invasive carcinoma.

One should make every necessary effort to carefully handle and thoroughly inspect the gross specimen, submit the entire appendix with optimal orientation, and examine multiple deeper tissue sections until the pathologic assessment is satisfactory. When a diagnosis of adenocarcinoma is determined, regardless of the stage and grade, it is considered to have the potential for producing disseminated disease of pseudomyxoma peritonei. In the absence of reliable evidence of carcinoma, these lesions should be considered in the “uncertain malignant potential” category until their clinical course reveals the nature of the disease.\(^{8}\)

5. Stratification of Prognostic Groups of Appendiceal Mucinous Adenocarcinoma

The prognosis of mucinous adenocarcinoma of the appendix is dictated by multiple clinical and pathologic attributes. Any appendiceal mucinous neoplasm that is capable of progressing to the clinical condition of pseudomyxoma peritonei should be designated as an adenocarcinoma, and the associated peritoneal disease should be graded as well-, moderately, or poorly differentiated, as the differentiation has prognostic implications. Like other carcinomas at most sites in the gastrointestinal tract, tumor stage is a reliable predictor of its clinical course. This is particularly pertinent in the absence of clinical evidence of PMP, which inevitably predicts an aggressive clinical course. In the group of low-grade mucinous neoplasm with so-called uncertain malignant potential, the clinical outcome is largely dependent on meticulous pathologic assessment of the initial appendectomy specimen, since the identification of either acellular mucin or cellular mucin confined to the right lower quadrant implies incidence of disease recurrence or dissemination to PMP. Recent investigations\(^{21,22}\) show that the incidence of disease recurrence is 4% to 8% and 33% to 75% in cases with identifiable, localized acellular or cellular mucin, respectively. It is important to emphasize that even if the recurrence risk is very low in cases with limited extra-appendiceal acellular mucin, the rate of disease-free survival is not 100%. In addition, the amount of neoplastic epithelium sampled can be extremely limited, such that this epithelium is often not represented in the sections examined, even when the appendix is submitted in its entirety. The clinical management of appendiceal mucinous neoplasm with uncertain malignant potential is controversial. There have been no compelling data to indicate recurrence-free advantage by performing right-sided hemicolectomy or intraperitoneal chemotherapy after appendectomy in patients with either localized acellular mucin or scant cellular mucin. Many clinicians at our institution choose close observation of patients with localized disease, particularly with the support of pathologists, to demonstrate no adverse features for recurrence in thoroughly examined appendectomy specimens.

Tumor grade has also been associated with survival and recurrence in disseminated cases of PMP.\(^{4,6,15}\) Other parameters, such as patient’s age, resection margin status, and the volume andcellularity of ascites should be assessed in conjunction with clinical information.\(^{23}\) The clinical management of appendiceal mucinous adenocarcinomas is not identical to that of conventional colorectal adenocarcinoma.\(^{24}\) The treatment decisions for right-sided hemicolectomy after appendectomy, cytoreductive surgery, perioperative or adjuvant chemotherapy are dependent not only on tumor stage, but also on tumor grade and classification.\(^{4,6,15,21}\) Furthermore, pathologic classification has primarily been the basis for stratification of prognostic groups of appendiceal mucinous adenocarcinomas. While the classification system and the nomenclature for these tumors will continue to be the subject of debate, most investigators have recognized that disseminated peritoneal mucinous adenocarcinoma comprises fundamentally 2 groups of adenocarcinoma. These groups are determined primarily by tumor grade at the low end and at the high end of the spectrum of lesions (Table 2).\(^{17,22}\) Tumors with intermediate and hybrid features are also recognized. To be consistent with the terminology used for most adenocarcinomas of the gastrointestinal tract, we choose to designate appendiceal mucinous tumors as well-differentiated, moderately differentiated, and poorly differentiated adenocarcinomas (Figure 3, A through C, respectively). We fully acknowledge other nomenclatures applied to these tumors, based on similar morphologic criteria (Table 2). Until a uniform classification system becomes available, it is reasonable to use a nomenclature for appendiceal mucinous adenocarcinomas that is understood by the local disease management community.

GOBLET CELL CARCINOID TUMORS AND ASSOCIATED ADENOCARCINOMAS

In contrast to typical carcinoid tumors of the appendix, tumors exhibiting both neuroendocrine differentiation and glandular differentiation are uncommon. Nevertheless, these entities can cause difficulty in pathologic classification, prediction of prognosis, and clinical management. Goblet cell carcinoids (GCCs) of the appendix have a mixed phenotype, with partial neuroendocrine differentiation and intestinal-type goblet cell morphology. As such, they have been classified, along with other neoplasms that show both neuroendocrine and glandular differentiation, as adenocarcinoid tumors, a term that includes biologically diverse neoplasms such as tubular carcinoid tumor and mixed carcinoid-adenocarcinoma. Goblet cell carcinoids are rare tumors of the appendix, with differing reports concerning their prognosis and clinical management.\(^{25}\) Whether goblet cell carcinoid tumors should be considered as variants of appendiceal adenocarcinoma or as part of carcinoid tumor spectrum...
has been controversial. Despite a number of plausible hypotheses, the histogenesis of GCCs is not clear. Morphologically, GCCs arise in the base of epithelial crypts of the appendiceal mucosa, without coexisting epithelial dysplasia. Both the clinical and pathologic features of GCCs are sufficiently distinctive, and it has been suggested that they represent a separate entity, distinct from both classic carcinoids and conventional appendiceal adenocarcinomas.

In addition to their morphologic diversity and complexity, tumors of GCC origin also display a wide spectrum of clinical behavior. At the time of initial diagnosis, more than 50% of patients present with metastatic disease, and an appendiceal primary tumor is not considered in most cases with disseminated disease. This is particularly relevant in female patients, since more than 80% of these patients have ovarian metastasis of GCC neoplasm and an initial impression of an ovarian primary malignancy is usually entertained. Despite the presentation of metastatic disease, the clinical outcome of GCC tumors is more favorable than that of stage-matched conventional colonic-type adenocarcinoma of the appendix or colon, and despite morphologic similarities with these adenocarcinomas, an adenocarcinoma ex GCC does not exhibit an adenoma-carcinoma sequence and may originate from a neuroendocrine cell.

In addition to displaying evidence of glandular/mucinous differentiation, GCCs can also progress to frank adenocarcinoma, which is morphologically indistinguishable from a poorly differentiated adenocarcinoma, usually the signet-ring-cell type. Our recent study, based on a retrospective investigation of the pathologic features and clinical outcomes of such cases, has led us to propose a subclassification of GCC of the appendix into typical goblet cell carcinoid and adenocarcinoma ex GCC (Table 3 and Figure 4, A through C). On the basis of the proposed classification criteria, these tumors can be stratified into prognostically significant groups even at the advanced stage. However, we fully recognize that, similar to criteria for morphologic classification of any tumors, there will always be challenging cases which are difficult to classify by the criteria provided (Table 3). In these situations, the final analysis and clinical decision should be rendered based upon not only the judgment of an experienced pathologist but also the combined clinical and pathologic information.

Tumors in the group adenocarcinoma ex GCC often exhibit predominant features of an adenocarcinoma with only minimal evidence of a residual GCC component; they behave as an adenocarcinoma, with peritoneal dissemination as a dominant pattern of disease spread. The adenocarcinomas arising in GCC commonly have signet-ring-cell morphology, but sometimes a more conventional tubular pattern or a poorly differentiated adenocarcinoma pattern can occur. Thus, GCCs and their derivative adenocarcinomas display a spectrum of well-differentiated to poorly differentiated histologic features and possess the potential to transform into an adenocarcinoma phenotype. In contrast to conventional adenocarcinomas of the appendix or colon, and despite morphologic similarities with these adenocarcinomas, an adenocarcinoma ex GCC does not exhibit an adenoma-carcinoma sequence and may originate from a neuroendocrine cell.

| Table 3. Pathologic Classification of the Family of Goblet Cell Carcinoid (GCC) Tumors* |
|---------------------------------------------|-----------------------------------------------|
| **Tumor**                                   | **Morphologic Criteria**                       |
| Typical low-grade GCC (group A)             | Well-defined goblet cells arranged in clusters or linear pattern |
|                                             | Minimal cytologic atypia                       |
|                                             | Minimal to no desmoplasia                      |
|                                             | Minimal architectural distortion of the appendiceal wall |
|                                             | Degenerative change with extracellular mucin is acceptable |
| Adenocarcinoma ex GCC, signet-ring-cell type (group B) | Goblet cells or signet ring cells arranged in irregular large clusters and sheets |
|                                             | Single cell–infiltrating pattern               |
|                                             | Significant cytologic atypia                   |
|                                             | Reduced intracellular mucin                    |
|                                             | Marked desmoplasia                            |
|                                             | Destruction of appendiceal wall                |
| Adenocarcinoma ex GCC, poorly differentiated (group C) | Requires at least focal evidence of goblet cell morphology |
|                                             | A component (≥1 low-power field or 1 mm²) is not otherwise distinguishable from a poorly differentiated/undifferentiated adenocarcinoma |

* The grading is based upon morphologic features at the primary site (appendix) only.

| Table 4. Recommended Management of Goblet Cell Carcinoid Tumors of the Appendix |
|---------------------------------------------|-----------------------------------------------|
| **Tumor Presentation**                     | **Management**                                |
| Localized tumor (pT1 or pT2), and Low histologic grade, and Negative appendectomy resection margin No evidence of perforation | Inadequate data to recommend (appendectomy and observe?) |
| Tumor spread beyond appendiceal wall (pT3/pT4), or Histology of an adenocarcinoma ex GCC, or Localized perforation (secondary to inflammation), or Positive appendectomy resection margin Intraperitoneal spread (stage IV), or Presence of poorly differentiated adenocarcinoma component | Right-sided hemicolectomy Consider oophorectomy Chemotherapy in stage III/IV Debunking surgery Consider oophorectomy Systemic and intraperitoneal chemotherapy |

Modified with permission from Tang et al.12
These lesions are usually no more than a few millimeters in size and are confined to the appendiceal tip, sometimes next to an obliterated lumen, than a few millimeters in size and are confined to the

typical carcinoid tumor of the appendix (Figure 5, A). In this tumor, the cell of origin is, in most cases, the L-cell, which produces enteroglucagons and peptide YY; thus, these lesions usually stain for glucagon-family peptides. The presence of the tubules obviously leads to differential diagnosis of a metastatic carcinoma. The tubules in L-cell carcinoid are usually small, with a sharp luminal contour, and are uniform in size; the tumor cells are cuboidal with centrally located nuclei and are cytologically bland. Immunohistochemistry can distinguish an adenocarcinoma from a tubular carcinoid tumor, and the latter is diffusely positive for chromogranin and or synaptophysin.

Metastases are extremely unusual in typical appendiceal carcinoids, particularly in those with low to no mitotic activity (<1 mitosis per 50 high-power fields). It has been estimated that tumors 2 cm or larger are at risk for lymph node or distant metastases, whereas tumors 1 cm or smaller rarely metastasize. For this reason, many surgeons elect to proceed with right-sided hemicolectomy after initial appendectomy with tumors that are larger than 2 cm, with subserosa or mesoappendix invasion, with lymphovascular invasion by tumor, or with identification of increased mitotic activity (>2 mitoses per 50 high-power fields) in rare cases.

References

Figure 5. Typical carcinoid tumor of the appendix (A). Tubular carcinoid tumor of the appendix (B) (hematoxylin-eosin, original magnifications ×200).


