Pseudoneoplasms of the Gastrointestinal Tract

Giovanni De Petris, MD; Stanley T. Leung, MD

Pseudoneoplasms of the gastrointestinal tract are unusually alarming lesions that result from morphologically worrisome outcomes of the gut’s response mechanisms to injury or from the heterotopic nature of the tissue. They may manifest as abnormal intestinal soft tissue reactive changes (eg, inflammatory fibroid polyp [IFP]), exuberant prolapse-induced changes (eg, colitis cystica profunda), unusual-appearing cellular changes (eg, malakoplakia, bizarre stromal cells [BSC], or benign signet ring cells), and morphologic findings made unusual by their location (heterotopias). The goal of this necessarily short review is to explain why pseudoneoplasms can appear in association with, or be caused by, a malignancy. The pathologist plays the leading role in distinguishing pseudoneoplasms from truly neoplastic lesions by analyzing morphologic features of pseudoneoplasms by abnormal patterns and distinguishing them from malignancies. The histopathologic features of pseudoneoplasms by abnormal patterns of response and heterotopias are discussed, with particular emphasis on inflammatory fibroid polyp, malakoplakia, atypical cellular infiltrates, and prolapse-related pathology. Because the gut reacts to insults with a limited repertoire of tissue changes, it is not surprising that many pseudoneoplasms can appear in association with, or because of, a malignancy.

Pseudoneoplasms of the gastrointestinal tract can be classified by their most likely location (Table 1) or by useful histopathologic or etiologic features (Table 2). Whereas numerous conditions in the gut may be considered pseudoneoplastic because of endoscopic or radiologic manifestations, this review focuses mainly on entities selected for their histologic mimicry (and the resulting possibility of diagnostic pitfalls) and for their clinical relevance.

Objective.—This review was conducted to heighten awareness of pseudoneoplasms, to help differentiate among the various types of pseudoneoplasms, and to help distinguish pseudoneoplasms from malignancies.

Context.—The pathologist plays the leading role in distinguishing pseudoneoplasms from truly neoplastic lesions in the gastrointestinal tract.

Conclusions.—A classification of pseudoneoplasms, according to the mechanism of injury to the gastrointestinal tract, morphologic patterns, and heterotopia, may be useful in providing a diagnostic framework in which ancillary techniques often have a diagnostic role. Several pseudoneoplasms may be closely associated with true neoplasms (eg, malakoplakia, prolapse-type lesions) because of the nonspecific nature of the response of the intestine to injury.

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Inflammatory Fibroid Polyp

Inflammatory fibroid polyp is a rare mesenchymal pseudoneoplasm of the digestive system with unclear histogenesis. First found in the stomach by Jiri Vanek in 1949, it was initially called submucosal granuloma with eosinophilic infiltration. It has subsequently been identified in the duodenum, small intestine, esophagus, colon, rectum, and gallbladder. The most common site is the stomach, especially the antrum, where it often appears as a polyp (≥4.5% of all gastric polyps are IFPs); the next-most-common site is the small intestine. Inflammatory fibroid polyps of the esophagus (where they are more likely to occur in the distal third) and of the colon (where they are more likely in the cecum) are uncommon, whereas IFPs are exceptionally rare in the gallbladder. The familial occurrence of IFP, unique to date, has been described in a Devon family (Devon polyposis syndrome). Inflammatory fibroid polyps occur in adults, with a peak incidence occurring between ages 60 and 70 years. The size may reach 5 cm.

Clinical presentation depends on the size and location of the lesion. Gastric IFPs cause epigastric pain and bleeding, whereas colicky pain, occult bleeding, and intussusception are associated with intestinal IFPs. Duodenal IFPs can cause obstruction of the common bile duct, and melena and dysphagia have been reported in esophageal IFPs.

Microscopically, an IFP appears as a submucosal proliferation of mononucleate and monomorphic, bland, spindle, and stellate cells in fibromyxoid stroma with an inflammatory infiltrate often dominated by eosinophils (Figure 1). Nuclear pleomorphism is considered quite unusual. In a substantial minority of cases, multinucleated giant cells are also observed (Figure 2, A). Lymphoid fol-
There is some evidence that the histologic pattern of gastric and small bowel IFPs may be determined by the age of the lesion. Smaller lesions have a better-developed, concentric distribution of spindle-shaped cells (Figure 2, C and D), and as the lesion grows, the dominant histologic type progresses through the different phases to become sclerotic in larger IFP.8 Different histologic patterns may coexist in the same lesion, and the edematous pattern has been suggested as an artifact of intestinal obstruction.8

The CD34 immunostain is the most useful immunostain to confirm the diagnosis of IFP. The stromal cells of IFP stain positive for CD34, especially around vessels (Figure 2, C). Occasionally, CD34 stain is negative, especially in cases with no onion skinning in the small bowel, which may represent older evolutionary stages of the lesion.4 The expression of fascin, CD35, cyclin D1, vimentin, and calponin is also found. A few IFP express smooth muscle actin; CD117 is negative (although mast cells in the lesion will be positive), and no abnormalities of exons 9 and 11 of the c-kit gene have been found.4 The S100 protein is not present. Pantanowitz et al9 demonstrated uniform staining for CD35 and overexpression of cyclin D1. They concluded that the proliferating stromal cells are of dendritic cell origin with myofibroblastic differentiation and a possible defect in cell cycle regulation. Electron microscopy reveals no specific findings.10

The reactive rather than the neoplastic nature of this lesion is suggested by its low mitotic activity, low recurrence rate, absence of necrosis, and metastases. Inflammatory fibroid polyp may be a form of reparative tissue response to injury. The detection of IFP in association with Crohn disease,11 diaphragm disease,12 previous surgery,13 and areas adjacent to carcinoma14 supports this hypothesis. Genotype profiling of 12 predominantly gastric IFPs showed no loss of heterozygosity at any of 14 commonly analyzed tumor suppressor gene loci,15 strengthening the view that these lesions are not neoplastic. Symptom treatment and resolution of diagnostic uncertainty may require surgical resection of the IFP. Endoscopic polypectomy is the ideal technique for polypoidal and accessible lesions in the stomach and colon. However, because IFPs arise from the submucosa and may be sessile, there is risk of perforation or incomplete resection after endoscopic treat-

Data from Fitzgibbons.35

### Table 1. Pseudoneoplasms in Various Portions of the Gastrointestinal Tract

<table>
<thead>
<tr>
<th>Site</th>
<th>Pseudoneoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire alimentary tract</td>
<td>Inflammatory fibroid polyp</td>
</tr>
<tr>
<td>Xanthoma</td>
<td></td>
</tr>
<tr>
<td>Lipoma-like lesions</td>
<td></td>
</tr>
<tr>
<td>Ectopias and heterotopias</td>
<td></td>
</tr>
<tr>
<td>Pseudotumors due to infections</td>
<td>Benign signet ring cells infiltrate</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Fibrovascular polyp</td>
</tr>
<tr>
<td>Melanos of the esophagus</td>
<td></td>
</tr>
<tr>
<td>Pseudodiverticulosis</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>Gastritis cystica profunda</td>
</tr>
<tr>
<td>Inverted hyperplastic polyp</td>
<td>Russell bodies gastritis</td>
</tr>
<tr>
<td>Intestines</td>
<td>Mucosal prolapse-related lesions</td>
</tr>
<tr>
<td>Malakoplakia</td>
<td></td>
</tr>
<tr>
<td>Tumefactive endometriosis</td>
<td>Prolapsing mucosal folds of diverticular disease</td>
</tr>
<tr>
<td>Hypertrrophic and papilla</td>
<td>Elastofibromatous lesions</td>
</tr>
</tbody>
</table>

### Table 2. Useful Histopathologic or Etiologic Features of Intestinal Pseudoneoplasms

<table>
<thead>
<tr>
<th>Pseudoneoplasm</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudosarcomas</td>
<td>Granulation tissue-like</td>
</tr>
<tr>
<td></td>
<td>Bizarre stromal cells</td>
</tr>
<tr>
<td></td>
<td>Vascular proliferations</td>
</tr>
<tr>
<td></td>
<td>Elastofibromatous abnormalities</td>
</tr>
<tr>
<td></td>
<td>Lipomatous changes</td>
</tr>
<tr>
<td>Cellular infiltrate of benign cells</td>
<td>Eosinophilic cells</td>
</tr>
<tr>
<td></td>
<td>Foamy cells</td>
</tr>
<tr>
<td></td>
<td>Signet ring cells</td>
</tr>
<tr>
<td></td>
<td>Lymphoid nodules and hyperplasia</td>
</tr>
<tr>
<td></td>
<td>Melanocytes</td>
</tr>
<tr>
<td></td>
<td>Bizarre stromal cells</td>
</tr>
<tr>
<td>Prolapse and entrapment</td>
<td>Mucosal prolapse syndromes</td>
</tr>
<tr>
<td></td>
<td>Entrapment of glands</td>
</tr>
<tr>
<td></td>
<td>Gastritis cystica profunda</td>
</tr>
<tr>
<td></td>
<td>Enteroitis cystica profunda</td>
</tr>
<tr>
<td></td>
<td>Collitis cystica profunda</td>
</tr>
<tr>
<td></td>
<td>Entrapment of air</td>
</tr>
<tr>
<td></td>
<td>Pneumatosis intestinalis</td>
</tr>
<tr>
<td></td>
<td>Pseudolipomatosis</td>
</tr>
<tr>
<td>Heterotopias</td>
<td>Normal tissue in unusual sites</td>
</tr>
<tr>
<td></td>
<td>Diseases of the “normal” tissue appearing in unusual sites</td>
</tr>
</tbody>
</table>
ment. It is unclear whether the occasional reported recurrence of IFP after attempted removal is due to incomplete excision.16

The differential diagnosis includes the various mesenchymal tumors of the gastrointestinal tract (Table 3) and inflammatory conditions (eg, granulation tissue or eosinophilic inflammatory processes). The abundant inflammatory component of the IFP is distinctive and easily differentiates it from leiomyoma and desmoid. Eosinophilic gastroenteritis does not form masses and consists of eosinophilic infiltrates in the various layers of the gut, mainly in young patients with a history of asthma and peripheral eosinophilia. Inflammatory myofibroblastic tumor (IMT) is a myofibroblastic neoplasm that, like IFP, shows an admixture of inflammatory infiltrate with spindle-shaped cells set in myxoid or collagenized stroma (Figure 3) with occasional large cells resembling histiocytes or ganglions. The distinction between IFP and IMT is relevant because IMT is a neoplasm of intermediate biologic potential with occasionally aggressive behavior and as much as a 25% rate of recurrence.17-20 Inflammatory myofibroblastic tumor occurs mainly in the soft tissue of the abdomen, retroperitoneum, and lung; it rarely arises in the gastrointestinal tract.17,18 Coffin et al17 identified 3 main histologic patterns in IMT: (1) myxoid, resembling granulation tissue, and often rich in inflammatory cells; (2) compact spindle cells, resembling fibromatosis or fibrous histiocytoma; and (3) a dense collagen in a platelike pattern.17 These patterns can be found within the same tumor. Eosinophils can be prominent in IMT, especially in the myxoid subtype resembling fasciitis, but plasma cells are the most common inflammatory cells overall. Makhlouf and Sobin18 have shown that IMT and IFP have different clinical, histopathologic, and immunohistochemical features. Inflammatory myofibroblastic tumor is less common and typically forms larger tumors than IFP. Persons affected by IMT are younger than those with IFP. Inflammatory myofibroblastic tumor is associated with systemic symptoms (eg, fever, abdominal pain, and weight loss) more commonly than IFP, which more often presents with bowel obstruction. Plasma cells predominate most commonly in IMT, whereas eosinophils are numerous in IFP. Perivascular onion skinning in IMT is much less pronounced in the stomach. Immunophenotypically, IMT reacts more commonly than IFP for smooth muscle markers (86% versus 13%)18 but fails to express CD34. Immunohistochemical expression of anaplastic lymphoma kinase occurs in IMT19,20 and is detected in 50% to 60% of...

Figure 2. Inflammatory fibroid polyp. Features include A, multinucleated giant cells; B, dumbbell shape; and C and D, circumferential arrangement of constitutive cells around vessels (hematoxylin-eosin, original magnification ×200 [A and D], with reactivity for CD34 immunostain, original magnification ×200 [C]). Figure B courtesy of Thomas C. Smyrk, MD, Mayo Clinic, Rochester, Minnesota.
cases. No study of anaplastic lymphoma kinase expression in IFP has been published to date, to our knowledge.

Fibroblastic polyp is a recently described bland proliferation of mitotically inactive, vimentin-positive fibroblastic cells in the lamina propria of the left colon21 (Figure 4, A). The colonic crypts are widely separated by the proliferation and may be serrated. Fibroblastic polyp presents as a small polyp with no specific disease or associated symptoms. In the original report by Eslamí-V arzaneh et al21 of 14 cases, the cells showed rare, focal CD34 and actin immunoreactivity but were negative for S100, epithelial membrane antigen, c-kit, CD31, and desmin. The spindle cells may spare the upper aspect of the lamina propria and may show a focal pericytial and perivascular concentric arrangement similar to that of IFP or perineurioma; however, they do not seem to extend into the submucosa.22

Perineuriomas in the intestine, most often in the left colon, have recently been described.23 They are composed of bland spindle cells with ovoid to tapered nuclei (Figure 4, B) and weakly eosinophilic cytoplasm that may involve the mucosa and the submucosa. They characteristically surround hyperplastic colonic glands and express epithelial membrane antigen and claudin-1 but are negative for S100, neurofilament, and CD34. Relying on histologic findings alone makes it difficult to distinguish between a perineurioma and a fibroblastic polyp. Groisman and Polak-Charcon24 recently suggested that fibroblastic polyp and perineurioma of the colon represent the same entity because of additional ultrastructural evidence (the presence of external lamina and long, slender cytoplasmic processes with pinocytotic vesicles) and immunohistochemical evidence (epithelial membrane antigen immunopositivity when high antibody concentration and modified antigen retrieval are applied, and GLUT-1 and collagen IV immunopositivity are found in fibroblastic polyp).

Table 3. Mesenchymal Lesions of the Gastrointestinal Tract

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Location</th>
<th>Site</th>
<th>IHC</th>
<th>Diagnostic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFP</td>
<td>Submucosal</td>
<td>Antrum, SB, col-</td>
<td>CD34⁺, CD35⁺, CD117⁻, S100⁻, SMA⁺ in &lt;50% of cases</td>
<td>Dumbbell shape; eosinophilic infiltrate; perivascular skinning; loose stroma; regular vascular pattern; heterogeneous cell population</td>
</tr>
<tr>
<td>GIST</td>
<td>Mural (Muscula-</td>
<td>Stomach, SB, col-</td>
<td>CD117⁺, CD34⁺, CK⁻</td>
<td>Nonprotruding; cellular, spindle, and epithelioid cells; perinuclear vacuolization; nuclear palisading; homogeneous cell population</td>
</tr>
<tr>
<td>IMT</td>
<td>Mesenteric, rarely</td>
<td>Colon, SB, stom-</td>
<td>CD34⁻, ALK⁻ (50% of cases), SMA⁺</td>
<td>Young patients; large tumor; diffuse inflammation with plasma cells often dominant; multiple patterns; scattered ganglion-like cells</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>Mesenteric, rarely</td>
<td>Stomach, colorectum, E, SB</td>
<td>S100⁺ (strong and diffuse), SMA⁺, CD117⁺, CD34⁺, GFAP⁺</td>
<td>Separates crypts that may be serrated; may spare upper mucosa; it may, in fact, be peri-neurinoma</td>
</tr>
<tr>
<td>Fibroblastic polyp</td>
<td>Mucosal</td>
<td>Left colon</td>
<td>S100⁺, CD117⁻ (faint or rare), CD34⁺</td>
<td>Peripherly lymphoid cuffing</td>
</tr>
<tr>
<td>Mesenteric fibro-</td>
<td>Mesenteric, retroper-</td>
<td>SB, colon, stom-</td>
<td>β-catenin⁺, CD34⁺, SMA⁺/−, desmin⁺/−, CD117 (usually −)</td>
<td>Infiltrative borders; low cellularity; collagen deposition; no cystic degeneration or necrosis; small muscular arteries and dilated thin veins with sparse perivascular lymphocytes</td>
</tr>
<tr>
<td>Perineurioma</td>
<td>Mucosal, sub-mucosal</td>
<td>Left colon, jejunum</td>
<td>EMA⁺, claudin-1⁺ (50% of cases), GLUT1⁺, S100⁻, CD117⁻</td>
<td>Entraps hyperplastic glands; bland spindle cells with pale eosinophilic cytoplasm; no lymphoid cuffing</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>Mucosal, sub-</td>
<td>Esophagus, stomach</td>
<td>CD117⁺, AE1/AE3⁺, CD34⁺, S100⁺, CK⁻</td>
<td>Rare tumor; high cellularity; tapestry pattern with ropey collagen; SYT-SSX gene fusion transcript present</td>
</tr>
<tr>
<td>F and I dendritic cell sarcoma</td>
<td>Mesenteric or, rarely, mural</td>
<td>Stomach, duodenum, SB, col-</td>
<td>F: CD21⁺, CD35⁻, I: S100⁺</td>
<td>Rare; evenly distributed inflammatory infiltrate admixed with spindle cells</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>Mural</td>
<td>Rare; found from esophagus to rectum</td>
<td>SMA⁺, desmin⁺ (70%–100%), CD117⁻, CD34⁺, β-catenin⁺, S100⁻</td>
<td>Cellular atypia; mitotic activity high (&gt;50/50 HPF) in most cases</td>
</tr>
</tbody>
</table>

Abbreviations: “−”, negative; “+”, positive; “++.−”, positive >50% of the time; “++,−”, negative >50% of the time; ALK, anaplastic lymphoma kinase; E, esophagus; F, follicular; GFAP, glial fibrillary acidic protein; GIST, gastrointestinal stromal tumor; HPF, high-power field; I, interdigitating; IHC, immunohistochemistry; IFP, inflammatory fibroid polyp; IMT, inflammatory myofibroblastic tumor; SB, small bowel; SMA, smooth muscle actin.

Figure 3. Inflammatory myofibroblastic tumor. Typical features are plump, ovoid myofibroblastic cells with pale eosinophilic cytoplasm in a collagenous background with numerous lymphocytes and plasma cells and few eosinophils (hematoxylin-eosin, original magnification ×200).
Bizarre Stromal Cells

The presence of BSC has been noted in many different organ systems (eg, upper respiratory tract, urinary bladder, endometrium and lower gynecologic tract, prostate, and gut) in association with granulation tissue and in benign inflammatory polypoid lesions and ulcerated mucosa. Large cells that may be spindled, stellate, or epithelioid make up BSC; they have an alarming vesicular nucleomegaly, nuclear pleomorphism, and occasional multinucleation (Figure 5). The amount of cytoplasm, which is usually eosinophilic, varies. Bizarre stromal cells can be widely scattered or clustered along the base of an ulcer. They may resemble cells infected with cytomegalovirus or ganglion cells and, thus, may be so strikingly atypical that the differential diagnosis includes malignant cells of high-grade carcinoma, sarcoma, and melanoma. In the gut, BSC has been found in ischemic colitis, in esophageal polyps, in the distal esophagus in patients with reflux esophagitis, in gastric ulcers, in pseudopolyps of inflammatory bowel disease, in granulation tissue near surgical anastomoses, and in anal fibroepithelial polyps. Mitoses are rarely found in BSCs but are not atypical. Immunohistochemical tests reveal reactivity for vimentin and occasionally for smooth muscle actin, consistent with a fibroblastic or myofibroblastic cell origin.

Pseudoneoplastic Vascular Proliferations of the Gastrointestinal Tract

The proliferation of benign capillaries in the gut can give origin to visible lesions and can be sufficiently florid to mimic neoplasms. Benign vascular proliferations have been found in association with gastrointestinal tumors (benign and malignant) and intussusception with ulceration. They are often accompanied by microscopic changes caused by prolapse. Intermittent ischemic damage to the mucosal and submucosal layers that occurs during intussusception or prolapse may give rise to exuberant vascular proliferation in the granulation tissue that can be misinterpreted as neoplastic, especially on biopsy specimens. Paraneoplastic florid angiogenesis of the mucosa surrounding an ileal carcinoid may cause multiple small polyps. These changes have been ascribed to angiogenic factors secreted by the tumor. Angiosarcoma is based on the clinical history (angiosarcoma is a rare primary neoplasm of the intestine), on the lobular arrangement of the capillary proliferation found in benign conditions (reminiscent of pyogenic granuloma), and on cytologic features. The endothelial cells lack significant hyperchromasia and nuclear pleomorphism, whereas mitotic figures are encountered infrequently and are not atypical in benign vascular proliferations. Muscular fibroplasia of the mucosa (an indication of prolapse), in association with vascular proliferation, should alert the pathologist to the possibility that the vascular lesion may be a benign reactive condition.

Elastosis and Elastofibromatous Abnormalities of the Gastrointestinal Tract

Elastosis (diffuse or focal increase in elastic fibers in the submucosal and muscularis mucosae layers of the gut) and elastofibromatous change (if there is an accompanying increase in fibrous tissue) are harmless abnormalities that can occasionally develop in the alimentary tract and may form polypoid lesions. Hobb et al found that most cases (10 of 13; 77%) of elastosis or elastofibroma occurred in the colon. In 8 of 13 patients (62%), they manifested as yellow or lipoma-like polyps, sometimes with large submucosal vessels (3 of 13; 23%). These changes do not simulate a neoplasm but are indistinguishable from amyloidosis on routine hematoxylin-eosin staining. They appear as granular or fibrillar, amphophilic, pale eosinophilic to gray material occasionally centered on blood vessels. A negative Congo red stain and a strongly positive elastin stain are diagnostic. The etiology is unclear, but elastosis or elastofibroma may be related to previous injury.

CELLULAR INFILTRATE OF BENIGN CELLS

Benign Eosinophilic Cell or Pink Cell Infiltrates

Malakoplakia—Malakoplakia is the best example of a pseudoneoplasm characterized by an eosinophilic cell infiltrate. Diseases consisting of an infiltrate of eosinophilic cells in the alimentary tract are listed in Table 5. Malakoplakia is a rare condition (fewer than 500 cases in the United States as of 2007), but this well-characterized inflammatory disease has been well described since it was first mentioned in 1902 by Michaelis and Gut-
Malakoplakia affects people along the entire age spectrum (6 weeks to 88 years), but pediatric cases are rare. It occurs most frequently in the genitourinary tract (about 60% of cases) but is also found in many other organs (eg, gastrointestinal tract, lungs, liver, pancreas, lymph nodes, adrenal gland, skin, salivary glands, and brain), with the gastrointestinal tract being the second-most-common site. In the intestine, it occurs most frequently in the descending colon, sigmoid, and rectum; it is found less commonly in the terminal ileum, stomach, appendix, and cecum.

Malakoplakia is composed of sheets of oval histiocytes with abundant granular eosinophilic cytoplasm (von Hansemann histiocytes) that contain basophilic, periodic acid-Schiff (PAS)–positive, diastase-resistant inclusions, and calcified Michaelis-Gutmann bodies (Figure 6). These often have a targetoid appearance with a darker central core and can also be extracellular. Michaelis-Gutmann bodies stain blue with hematoxylin-eosin and are positive for calcium and iron with the von Kossa stain and the Perls stain, respectively. The histiocytes stain positively for the CD68 antibody and for α1-antichymotrypsin. Gram stain may identify gram-negative bacteria. Electron microscopy has shown curved membrane-bound phagolysosomes containing whorled and parallel lamellar phospholipids in the histiocytes.

The pathogenesis of malakoplakia is not completely understood, but evidence supports the hypothesis that immunosuppression associated with defective phagolysosomal digestion of bacteria is necessary. The defective bacterial digestion seems related to decreased intracellular cyclic guanosine monophosphate (cGMP). Decreased cGMPs alter microtubule function and lower the release of β-glucuronidase, with resulting impairment in phagolysosomal digestion. Michaelis-Gutmann bodies appear in phagolysosomes by sequential, concentric calcifications around bacterial debris, caused by deposition of calcium and iron on the bacterial glycolipids. An altered or deficient immunoresponse is a contributing factor in the development of malakoplakia. Gram-negative bacteria, such as Escherichia coli and Klebsiella pneumoniae, are the most common bacteria involved in the genesis of malakoplakia. Interestingly, different bacteria are implicated in different clinical conditions (eg, Rhodococcus equi and Pasteurella multocida are associated with malakoplakia in acquired immunodeficiency syndrome). Fibrosis and immune responses also play a role in the development of malakoplakia. The gross appearance varies from unifocal, multiple, and even widespread nodular lesions to a large, soft, yellow (at least initially) mass, usually covered by intact mucosa that may be centrally depressed. Symptoms at presentation may be absent or may include abdominal pain, hemorrhage, diarrhea, obstruction, and, in extensive disease, fistulae. Malakoplakia can be found in association with several diseases in the alimentary tract (Table 6). In particular, as many as 30% of cases of malakoplakia are reported to be associated with colonic adenocarcinoma.

Malakoplakia can be the origin of clinical conditions that mimic an aggressive neoplasm (eg, involvement of an organ and its regional lymph nodes, extension into an adjacent organ, appearance after treatment of adenocarcinoma, and involvement of multiple organs mimicking metastases). Erroneous clinical upstaging of carcinoma because of coexisting malakoplakia involving lymph nodes or other organs is a possible clinical pitfall. As with other pseudoneoplasms of the gastrointestinal tract, it is important to be aware that the diagnosis of malakoplakia may indicate an associated malignancy.

**Other Eosinophilic Pink Cell Infiltrates.**—Crystal-storing histiocytosis and Russell bodies gastritis are among the most unusual conditions composed of eosinophilic cells in the gastrointestinal tract. Crystal-storing histiocytosis is characterized by an infiltrate of eosinophilic histiocytes containing crystalline material. It mainly involves bone marrow and lymph nodes but has been described in lung, thyroid, kidney, and soft tissue. In the gastrointestinal tract, crystal-storing histiocytosis has been diagnosed in the stomach and colon, where it can form polyoid lesions. Crystal-storing histiocytosis of the gastrointestinal tract is usually associated with an underlying...
lymphoplasmacytic neoplasm producing monoclonal light chains or, less commonly, with rheumatoid arthritis, *Helicobacter pylori* infection, use of clofazimine (a leprosy drug), and, exceptionally, with eosinophilic colitis. In the case of eosinophilic colitis, the crystalline material was found to be Charcot-Leyden crystals.46

In 1998, Tazawa and Tsutsumi47 described a peculiar, localized accumulation of plasma cells with cytoplasmic Russell bodies (Mott cells) in the lamina propria of the gastric mucosa, which can cause raised polypoid lesions; they named it Russell bodies gastritis.47,48 Plasma cells of Russell bodies gastritis are monomorphous but polyclonal. The high density and localized nature of the infiltrate also distinguish Russell bodies gastritis from chronic gastritis. Absence of clonality, lymphoepithelial lesions, mitoses, and atypia help distinguish Russell bodies gastritis from both cyto-keratin and human placental lactogen.

Eosinophilic cellular infiltrate in the gut must also be distinguished from granular cell tumor (GCT), which can arise anywhere in the gastrointestinal tract, with the esophagus and colon being the most common sites.51 Endoscopic examination of GCT shows whitish nodules or sessile lesions that can be confused with hemorrhoids when they occur in the anal canal. These lesions usually have indistinct margins and small dimensions, although in rare cases they can reach 5 cm. Granular cell tumors are composed of nests and sheets of large polygonal to elongated cells with granular eosinophilic cytoplasm and distinct cell borders; the nuclei are small and round. Granular cell tumor cells originate in Schwann cells, react with antibodies to S100 protein, and stain positive with PAS. Pseudop epitheliomatous hyperplasia of the esophagus in the area affected by GCT, with GCT cells

### Table 4. Pseudoneoplastic Vascular Proliferation of the Gut

<table>
<thead>
<tr>
<th>Entity</th>
<th>Site</th>
<th>Association</th>
<th>Endoscopic and Gross Findings</th>
<th>Diagnostic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign vascular proliferation of the colon in intussusception and mucosal prolapse</td>
<td>Colon (cecum favored)</td>
<td>Mucosal prolapse, intussusception, A-V malformation, lipoma leading to intussusception</td>
<td>Colonic mass</td>
<td>Lobular proliferation of small vascular channels from submucosa through thickness of entire intestinal wall; features of mucosal prolapse</td>
</tr>
<tr>
<td>Angiogenic polypoid proliferation of the small bowel</td>
<td>Small bowel, adjacent to neoplasm</td>
<td>Small-intestine neoplasm (carcinoid, primary and metastatic adenocarcinoma, GIST, lymphoma) and prolapse</td>
<td>Sessile polyps adjacent to tumor</td>
<td>Club-shaped villi with prominent intramucosal capillaries; features of mucosal prolapse</td>
</tr>
</tbody>
</table>

### Table 5. Pathologic Processes Characterized by Infiltrates of Eosinophilic Cells or Foamy Cells in the Alimentary Tract

<table>
<thead>
<tr>
<th>Infiltrate</th>
<th>Pathologic Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophilic cells</td>
<td>Malakoplakia, Crystal-storing histiocytosis, Plasma cell dyscrasias, Lymphoproliferative disorders, Clofazimine-induced histiocytosis, Eosinophilic colitis, Russell bodies gastritis, Granular cell tumor, Decidual reaction, Histiocytic infiltrate of infections</td>
</tr>
<tr>
<td>Foam cells</td>
<td>Xanthoma, Muciphages, Whipple disease, Infections, Histoplasmosis, <em>Rhodococcus equi</em>, <em>Mycobacterium avium-intracellulare</em> complex, Melanosis coli, Hereditary metabolic storage disorders</td>
</tr>
</tbody>
</table>

### Table 6. Gastrointestinal Conditions Associated With the Pseudoneoplasms Malakoplakia or Benign Epithelial Signet Ring Cells

<table>
<thead>
<tr>
<th>Pseudoneoplasm</th>
<th>Gastrointestinal Condition</th>
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<tbody>
<tr>
<td>Epithelial signet ring cells</td>
<td>Pseudomembranous colitis, Ulcerated tubular adenoma, Peutz-Jeghers polypl, Ischemia, Acute erosive gastropathy, Mucosa-associated lymphoid tissue, Cystic fibrosis, Ulcerative colitis</td>
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close to the epithelium, is a notorious pseudoneoplastic lesion that can mimic squamous cell carcinoma (Figure 8; see also ‘‘Selected Pseudoneoplastic Lesions of the Skin’’ by Wick and Patterson in this special section). Careful examination of the mucosa and submucosa for GCT is important in patients for whom the diagnosis of squamous cell carcinoma is being considered on the basis of a biopsy of the esophagus.

Benign Signet Ring Cells Infiltrate

Signet ring cells are characterized by a cytoplasmic vacuole or inclusion that pushes a crescent-shaped nucleus to the cytoplasmic periphery. They are the hallmark of signet ring cell adenocarcinoma. Epithelial signet ring cells, however, may appear in reactive processes or in association with nonepithelial neoplasms, such as mucosa-associated lymphoid tissue lymphoma; as a result, they can present a diagnostic challenge. Table 6 includes a list of diseases of the gastrointestinal tract associated with nonepithelial signet ring cells.

Nonneoplastic epithelial signet ring cells appear to be associated with ulcerations or ischemia (caused, eg, by torsion in a Peutz-Jeghers polyp) and are limited to the mucosa. An awareness of the association among nonneoplastic epithelial signet ring cells and degenerated or necrotic mucosa, and the lack of infiltrative growth should prevent an automatic diagnosis of malignancy when there are bland-appearing signet ring cells (ie, cells lacking nuclear atypia, hyperchromasia, prominent nucleoli, and mitosis) in the gastrointestinal tract.

Nonetheless, the benign nature of nonneoplastic epithelial signet ring cells remains difficult to ascertain, especially in biopsy specimens, because signet ring cells carcinoma can be cytologically bland. Nonneoplastic epithelial signet ring cells will express cytokeratins consistent with their gastrointestinal segments of origin. In a report on pseudomembranous colitis associated with signet ring cells, Wang and colleagues recommended the use of immunostains for p53, Ki-67, and E-cadherin in difficult cases. Nonneoplastic epithelial signet ring cells showed strong reactivity for E-cadherin but failed to react with antibodies for p53 and Ki-67. Nonneoplastic epithelial signet ring cells are not always epithelial in nature: Macrophages (ie, macrophages with mucin in their cytoplasm that can appear packaged in vacuoles). Schwannoma

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**Figure 7.** Decidual cells. A, Decidual cells with abundant eosinophilic cytoplasm, central nucleus, and no atypia. B, Florid decidual reaction involving small intestine resected during cesarean section (hematoxylin-eosin, original magnification ×400 [A] and ×200 [B]; Courtesy of Fausto J. Rodriguez, MD, Mayo Clinic, Rochester, Minnesota. Used with permission.)

**Figure 8.** Pseudoepitheliomatous hyperplasia. A, Squamous cell proliferation with keratin pearls deep in lamina propria. B, Granular cell tumor adjacent to surface epithelium with abundant eosinophilic cytoplasm and small, centralized nuclei (hematoxylin-eosin, original magnification ×200 [A] and ×400 [B]).
cells, and adipocytes (eg, S100-positive signet ring cells in the subserosa)\textsuperscript{66} may present as nonneoplastic signet ring cells. Neoplastic signet ring cells have also been reported in numerous extraintestinal neoplasms (eg, in melanoma, lymphoma, or ovarian tumors). Awareness of the presence of mimickers of malignant signet ring cells and attention to cytomorphologic details are necessary for proper interpretation.

**Foam Cell Infiltrates**

Foam cell infiltrates are often found in the gastrointestinal tract, especially in the mucosa of the stomach and the rectum. Conditions characterized by foam cell infiltrates are listed in Table 5. Xanthomas and muciphages are the most common cell constituents of foam cell infiltrates.

Xanthomas are innocuous lesions composed of foamy macrophages characterized by abundant vacuolated cytoplasm because of the accumulation of lipids and cholesterol and centrally placed nuclei (Figure 9). Xanthoma cells reside mainly in the mucosa but occasionally extend into the submucosa. They are found most frequently in the stomach as small (usually <3 mm), yellowish or white flat lesions, frequently in clusters scattered along the lesser curvature and in the pyloric region. Xanthomas in the colon and rectum may appear polyoid.\textsuperscript{57} Xanthomas have been associated with chronic inflammatory states but also with malignancies.\textsuperscript{56,59}

Xanthoma cells may be difficult to distinguish from signet ring cells of adenocarcinoma without the aid of special stains (xanthoma cells are immunoreactive for CD68 and are negative for cytokeratin and S100 protein; they stain negatively for mucicarmine and PAS).\textsuperscript{60} Xanthoma cells also have to be distinguished from the other entities listed in Table 5 and from granular cell tumors.

Muciphages are mucin-rich macrophages originating from the ingestion of mucin released by mucosal damage; they are digested PAS-positive and Alcian blue-positive, whereas xanthoma cells are negative for these mucin stains.\textsuperscript{58} Bejarano et al\textsuperscript{57} found muciphages in 38% of rectal biopsy specimens, mainly from the upper mucosa. Muciphages may occasionally appear as nodules or polyps.\textsuperscript{62} They may resemble signet ring cells of adenocarcinoma, and they may be found in lymph nodes.\textsuperscript{59} As expected, however, they show no labeling for cytokeratin immunostains, whereas histiocytic markers are positive.

The foam cells in Whipple disease are replenished with mucosal damage; they are digested PAS-positive and Alcian blue-positive, whereas xanthoma cells are negative for these mucin stains.\textsuperscript{63} The epithelium may show ulceration, regenerative and ischemic changes, and pseudomembranes. The crypts often take on a diamond-shaped or angulated appearance rather than maintaining their normal rounded contours. The repeated injury of prolapse results in villiform-appearing mucosa with hemosiderin deposition and in distorted or serrated glandular architecture. Glands may become trapped in the submucosa or deeper layers of the wall and appear cystic (ie, colitis cystica profunda; see also “Entrapped Glands’’).

The villiform appearance and the deep glands with reactive atypical epithelium may suggest villous adenoma and invasive adenocarcinoma: The distinction from dysplastic epithelium relies on clinical and histologic clues. Recurrent lesions at the anal verge in a patient with straining are typical of mucosal prolapse. Maturation of the epithelium from the deep to the superficial aspect of the mucosa, superficial fibrin and granulation tissue, and the presence of intramucosal smooth muscle and diamond-shaped crypts are indicators of prolapse rather than dysplastic epithelium.

Bleeding may require removal of polyps, but the polyps of prolapse are benign. Patient outcome depends on the underlying disorder.

**Entrapped Glands: Colitis Cystica Profunda, Enteritis Cystica Profunda, and Gastritis Cystica Profunda**

Glandular epithelium displaced into the submucosa or the deeper layers of the intestinal wall defines colitis cystica profunda, enteritis cystica profunda, and gastritis cystica profunda. These lesions in the various portions of the gastrointestinal tract are fundamentally similar and can be considered together. The most common type is colitis
Cystic Changes of the Gastrointestinal Tract

Cystic changes of the gastrointestinal tract are not true neoplasms. These abnormalities are the result of injury or infection leading to stagnation and cystic dilatation of glands or cyst formation in the wall of the intestine. Entrapped glands can reach all the way into the subserosa. Patients may be asymptomatic or may present with signs and symptoms of the underlying condition. Intestinal lesions can enlarge and cause obstruction or intussusception.

Figure 9. Xanthoma. Foamy lipid-laden histiocytes with bland-appearing nuclei in a gastric biopsy specimen (hematoxylin-eosin, original magnification ×400).

Figure 10. Prolapse-induced changes in colon mucosa. Changes are indicated by perpendicular smooth muscle fibers streaming from the muscularis mucosae into the lamina propria with no evidence of arborization. Some crypts appear pointy rather than rounded (hematoxylin-eosin, original magnification ×100).

Figure 11. Hamartomatous polyp of the small bowel. This hamartomatous polyp led to intussusception in a patient with Peutz-Jeghers syndrome. Asterisk (*) indicates entrapped cystic gland in the wall of the intestine (enteritis cystica profunda; hematoxylin-eosin, scanning magnification).

Figure 12. Colitis cystica profunda. Rounded mucin pools with peripheral epithelium are displaced in the submucosa in a case of mucosal prolapse of the colon (hematoxylin-eosin, original magnification ×100).

cystica profunda, followed by enteritis cystica profunda and then gastritis cystica profunda. Because chronic persistent injury leads, through ulceration and repair, to entrapment of glands deep in the intestinal wall, these changes can be found in conditions such as prolapse, severe infection, ischemia, inflammatory bowel disease, and Peutz-Jeghers syndrome (Figure 11), in irradiated tissue and along surgical anastomotic lines. The mechanisms of misplacement may include herniation, implantation after ulceration, mucosal microdiverticula, and reepithelialization of fistulae (eg, in Crohn disease). Entrapped glands in the intestine can reach all the way into the subserosa.

Patients may be asymptomatic or may present with signs and symptoms of the underlying condition. Intestinal lesions can enlarge and can cause obstruction or intussusception.

Colitis cystica profunda is generally localized and only rarely diffuse. The localized form is more likely in the rectum because of its association with rectal prolapse. The findings at gross examination include thickened intestinal wall and cysts in submucosal spaces. Glands entrapped in the walls of the intestine commonly undergo dilatation and cystic change and often have a loss of epithelium because of pressure atrophy. Acellular mucin pools are then left behind and may show calcium deposition or even ossification.

The differential diagnosis is invasive adenocarcinoma. Diagnosis may be complicated by the occasional association of carcinoma with colitis cystica profunda.

The cytologic features of the entrapped benign glands in colitis cystica profunda (Figure 12) are usually bland and, in most cases, easily distinguished from those of carcinoma. If sections show a connection to the surface epithelium or the presence of luminal material in the glan-
Endometriosis may mimic epithelial carcinoma, or when it consists only of endometriotic stroma. In the usual change (see also “Benign Eosinophilic Cell Infiltrate”) diagnostic challenges when it is affected by decidua, tumor, such as Kaposi sarcoma (which is, however, CD10 negative), whereas in the second case, it may mimic a soft tissue tumor, such as Kaposi sarcoma. In 1901, Lubarsch was the first to use the term esophageal pseudodiverticulosis to indicate what today is referred to as esophageal intramural pseudodiverticulosis (Figure 13). Prolapse is not at play in this rare disease, but unusual-appearing intramural changes are found in it. Esophageal intramural pseudodiverticulosis is characterized by multiple flask-shaped outpouchings in the esophageal wall that are only a few millimeters in size and that communicate with the esophageal lumen by a short neck. These pseudodiverticula represent dilated excretory ducts of deep submucosal glands of the esophagus. Endoscopic and radiologic images typically show, respectively, the tiny ostia of the pseudodiverticula (in about 20% of cases) and, with contrast medium, the outpouchings into the wall. Esophageal intramural pseudodiverticulosis causes dysphagia. It is thought to follow esophageal motility disorders or esophagitis (including candidiasis or esophagitis due to herpesvirus), causing squamous metaplasia of the ducts of the esophageal glands with plugging.

Esophageal intramural pseudodiverticulosis is unlikely to be confused with a neoplasm, except perhaps with the recently described carcinoma cuniculatum of the esophagus (Figure 14), a variant of well-differentiated esophageal squamous cell carcinoma. Carcinoma cuniculatum lacks the typical endoscopic and radiologic appearance of esophageal intramural pseudodiverticulosis.

Empty Spaces: Pneumatosis Intestinalis

Pneumatosis intestinalis is defined by the collection of gas in the intestinal wall and the formation of clear cystic spaces lined by histiocytes and giant cells in the submucosa (Figure 15), along with pseudolipomatosis (small, air-filled, clear, cystic spaces of the lamina propria, often in the proximity of lymphoid nodules), disarray of crypts, and eosinophilia. Pneumatosis intestinalis is rare, and its...
etiology is unknown. Pneumatosis intestinalis is found more often in the small bowel than in the colon (especially the left). In 80% of patients, pneumatosis intestinalis is associated with gastrointestinal conditions that cause compromised mucosal integrity or increased luminal pressure (eg, traumatic, infectious, inflammatory, or drug-induced conditions) or it is associated with extraintestinal diseases, especially obstructive pulmonary disease. Pneumatosis intestinalis can be asymptomatic, or it can cause obstruction, intussusception, volvulus, and blood in the stool. Polyps or mucosal folds are soft, bluish, and often sessile and are the most common gross manifestations of pneumatosis intestinalis; such features may resemble colonic polyposis. A “bubble wrap” crackling noise produced by handling the specimen is typical. Pneumatosis intestinalis can be difficult to diagnose by biopsy, especially if the cystic spaces are collapsed. Pneumatosis intestinalis is seldom confused with a neoplasm at microscopic examination, with perhaps the exception of acellular mucin of colloid carcinoma. In that case, negative stains for mucin would facilitate diagnosis.

HETEROTOPIAS

Heterotopia indicates findings of the presence of normal tissue at a site where it usually does not reside and where it lacks anatomic and vascular connections with the parent organ. The mechanism of formation of heterotopia is obscure; hypotheses include errors in embryologic development (eg, incomplete regression of vestigial structures, abnormal differentiation of local tissues, or dislocation of a portion of a definitive organ rudiment during development). The most commonly reported heterotopias in the gut are gastric and pancreatic heterotopias (Table 7).81,82 Sebaceous heterotopia of the esophagus is less common; rarer still are salivary gland heterotopia of the rectum, prostate gland heterotopia of the anal canal, and thyroid and parathyroid glands heterotopia of the upper esophagus.61,62

### Gastric Heterotopia

Gastric heterotopia has been found throughout the bowel, but it is mainly encountered in the upper esophagus (the so-called inlet patch, found in 1%–10% of patients at endoscopy but more frequently at autopsy),79 the duodenum (especially the bulb), Meckel diverticulum, and the rectum. Gastric heterotopia may manifest as polyps, nodules, or thickening of the mucosa and ulcerations. In exceptional cases, gastric heterotopia appears disseminated and can be associated with celiac disease.63,64

### Inlet Patch

Schmidt85 first described the inlet patch in 1805. Endoscopically, it appears to be salmon-colored mucosa with a sharp edge positioned just at or below the upper esophageal sphincter, and it is usually no more than 3 cm. The gastric mucosa can be oxyntic or less commonly antral. Its neoplastic potential is low, but there are several reports of adenocarcinoma arising in inlet patch.66,87 There are no data reported in the medical literature, to our knowledge, that would justify regular biopsies or follow-up.

### Pancreatic Heterotopia

The frequency of pancreatic heterotopia in autopsy series shows large variability (0.55%–25%), which indicates that the lesion often goes undetected and is largely harmless. Symptomatic pancreatic heterotopia has a peak incidence in the fourth to sixth decades of life with a male to female ratio of 3:1. Pancreatic heterotopia can cause pain, bleeding, obstruction, and intussusception, and it can be complicated by the development of virtually any disease of the orthotopic pancreas, including neoplasms and pancreatic intraepithelial neoplasias. Pancreatic heterotopia is most common in the duodenum, the upper jejunum, and the stomach (typically the prepyloric region, the greater curvature, and the posterior wall). It can be found

<table>
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<th>Table 7. Heterotopias of the Gastrointestinal Tract</th>
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<td><strong>Type</strong></td>
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<tr>
<td>Gastric</td>
</tr>
<tr>
<td>Pancreatic</td>
</tr>
<tr>
<td>Sebaceous glands</td>
</tr>
<tr>
<td>Salivary glands</td>
</tr>
<tr>
<td>Prostate gland</td>
</tr>
<tr>
<td>Thyroid and parathyroid glands</td>
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*In decreasing order of frequency.*
throughout the alimentary tract, including the tongue, and in the spleen, liver, gallbladder, biliary tract, mesentery, lungs, mediastinum, fallopian tube, umbilicus, submandibular salivary glands, and lymph nodes. In the gut, pancreatic heterotopia appears as round or lobulated intramural nodules usually measuring less than 3 cm. It is usually found in the submucosa but has also been found in the muscularis propria or subserosa. The overlying mucosa can show umbilication at the site of the draining duct and yet remain normal. In many cases, the deep location prevents diagnosis by endoscopic biopsy.

Pancreatic heterotopia may contain any type of pancreatic tissue in various proportions (total heterotopia), it may be composed only of ducts (Figure 16), or it may comprise only acinar cells (exocrine heterotopia) or islet cells (endocrine heterotopia). When pancreatic ducts predominate, there is often a proliferation of thick smooth muscle bundles of the muscularis around the ducts. Thus, additional descriptive terms (eg, myoglandular hamartoma, adenomyomatous hamartoma, or adenomyoma) may be used to indicate this type of pancreatic heterotopia, which is usually found in the periampullary region of the duodenum or in the gastric antrum.

Pancreatic heterotopia can pose various diagnostic problems. Table 8 lists the most common diagnostic dilemmas and provides clues to their correct diagnosis. These include, for example, the correct interpretation of the benign heterotopic glands during laparoscopic examination in a patient with a mass in the pancreas, the distinction from well-differentiated adenocarcinoma, the distinction from a neuroendocrine tumor of an endocrine heterotopia in the stomach, the distinction of the cystic change in pancreatic heterotopia from a duplication, the presence of pancreatic adenocarcinoma in an ectopic site, the possibility of false-positive cytologic findings at laparoscopy, and the distinction from Paneth cells and from pancreatic acinar metaplasia.

Neuroendocrine markers (eg, synaptophysin or chromogranin), hormone markers (eg, insulin, glucagon, or somatostatin in physiologic isletlike distribution), and exocrine markers (eg, trypsin, lipase, or chymotrypsin) can aid diagnosis. Cytokeratin 7 (ie, the cytofilament of pancreatic centroacinar and ductal cells) may help highlight excretory ducts in stains of biopsy specimens from the stomach.

Sebaceous glands are found occasionally in the epithelium and lamina propria of the esophagus where they form flat, yellowish bumps (Figure 17); they are likely to be more frequent in this location than suggested by reports in the medical literature. In individual cases, they may be quite numerous. The heterotropic and, therefore, congenital nature of sebaceous glands in the esophagus has been questioned by various observations suggesting that they are metaplastic. In a large necropsy study that examined the esophagi of 1000 pediatric subjects, no cases of sebaceous glands heterotopia were found. In another, more recent, study, bulbous nests of proliferating basal cells with sebaceous differentiation were found to express CK14 (a cytokeratin found in the progeny of dormant basal stem cells), which is suggestive of metaplastic change.

<table>
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CONCLUSION

In summary, awareness of the various pseudoneoplasms that may present in the gastrointestinal tract and awareness of their possible pathogenetic mechanisms allow for recognition of these entities. Immunohistochemistry and molecular techniques are sometimes helpful. The main goal of the pathologist is to distinguish pseudoneoplasms from maligantomas. This is particularly important when pseudoneoplasms (e.g., malakoplakia or prolapse lesions) are associated with a true neoplasm.

We thank F. Bilbao, Department of Pathology, University of the Basque Country (Bilbao, Spain) and F. J. Rodríguez, MD, of the Department of Pathology, Mayo Clinic (Rochester, Minnesota), for their insightful comments on esophageal intramural pseudodiverticulosis and deciduosis of the gastrointestinal tract.

References


