Hector H. Li-Chang
Richard Kirsch · James Conner
Aysegul Sari · Aaron Pollett
Hala El-Zimaity · Dhanpat Jain
Romulo Celli · Stephanie L. Reid
Robert H. Riddell

Atlas of Intestinal Pathology

Volume 1: Neoplastic Diseases of the Intestines

Springer

Atlas of Anatomic Pathology

Series Editor

Liang Cheng
Indianapolis, Indiana, USA

This Atlas series is intended as a "first knowledge base" in the quest for diagnosis of usual and unusual diseases. Each atlas will offer the reader a quick reference guide for diagnosis and classification of a wide spectrum of benign, congenital, inflammatory, nonneoplastic, and neoplastic lesions in various organ systems. Normal and variations of "normal" histology will also be illustrated. Each atlas will focus on visual diagnostic criteria and differential diagnosis. It will be organized to provide quick access to images of lesions in specific organs or sites. Each atlas will adapt the well-known and widely accepted terminology, nomenclature, classification schemes, and staging algorithms. Each volume in this series will be authored by nationally and internationally recognized pathologists. Each volume will follow the same organizational structure. The first Section will include normal histology and normal variations. The second Section will cover congenital defects and malformations. The third Section will cover benign and inflammatory lesions. The fourth Section will cover benign tumors and benign mimickers of cancer. The last Section will cover malignant neoplasms. Special emphasis will be placed on normal histology, gross anatomy, and gross lesion appearances since these are generally lacking or inadequately illustrated in current textbooks. The detailed figure legends will concisely summarize the critical information and visual diagnostic criteria that the pathologist must recognize, understand, and accurately interpret to arrive at a correct diagnosis. This book series is intended chiefly for use by pathologists in training and practicing surgical pathologists in their daily practice. The atlas series will also be a useful resource for medical students, cytotechnologists, pathologist assistants, and other medical professionals with special interest in anatomic pathology. Trainees, students, and readers at all levels of expertise will learn, understand, and gain insights into the complexities of disease processes through this comprehensive resource. Macroscopic and histological images are aesthetically pleasing in many ways. This new series will serve as a virtual pathology museum for the edification of our readers.

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Hector H. Li-Chang
Pathology and Laboratory Medicine
University of British Columbia
Royal Victoria Regional Health Centre
Barrie, ON
Canada

James Conner
Department of Pathology and Laboratory
Medicine, Mount Sinai Hospital
University of Toronto
Toronto, ON
Canada

Aaron Pollett
Department of Laboratory Medicine
and Pathobiology, Mount Sinai Hospital
University of Toronto
Toronto, ON
Canada

Dhanpat Jain
Department of Pathology
Yale New Haven Hospital
New Haven, CT
USA

Stephanie L. Reid
Discipline of Laboratory Medicine
Health Sciences Centre, Memorial University
of Newfoundland
St. John's, NL
Canada

Richard Kirsch
Department of Pathology and Laboratory
Medicine, Mount Sinai Hospital
University of Toronto
Toronto, ON
Canada

Aysegul Sari
Department of Pathology and Laboratory
Medicine, Mount Sinai Hospital
University of Toronto
Toronto, ON
Canada

İzmir Katip Celebi University Ataturk Training
and Research Hospital
İzmir, Turkey

Hala El-Zimaity
Dynacare Laboratories
Brampton, ON
Canada

Romulo Celli
Department of Pathology
Yale New Haven Hospital
New Haven, CT
USA

Robert H. Riddell
Department of Laboratory
Medicine and Pathobiology
University of Toronto
Toronto, ON
Canada

Pathology and Laboratory Medicine
Mount Sinai Hospital
Toronto, ON
Canada

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Series Preface

One Picture Is Worth Ten Thousand Words

— Frederick Barnard, 1927

Remarkable progress has been made in anatomic and surgical pathology during the last 10 years. The ability of surgical pathologists to reach a definite diagnosis is now enhanced by immunohistochemical and molecular techniques. Many new clinically important histopathologic entities and variants have been described using these techniques. Established diagnostic entities are more fully defined for virtually every organ system. The emergence of personalized medicine has also created a paradigm shift in surgical pathology. Both promptness and precision are required of modern pathologists. Newer diagnostic tests in anatomic pathology, however, cannot benefit the patient unless the pathologist recognizes the lesion and requests the necessary special studies. An up-to-date atlas encompassing the full spectrum of benign and malignant lesions, their variants, and evidence-based diagnostic criteria for each organ system is needed. This atlas is not intended as a comprehensive source of detailed clinical information concerning the entities shown. Clinical and therapeutic guidelines are served admirably by a large number of excellent textbooks. This atlas, however, is intended as a "first knowledge base" in the quest for definitive and efficient diagnosis of both usual and unusual diseases.

The *Atlas of Anatomic Pathology* is presented to the reader as a quick reference guide for diagnosis and classification of benign, congenital, inflammatory, nonneoplastic, and neoplastic lesions organized by organ systems. Normal and variations of "normal" histology are illustrated for each organ. The atlas focuses on visual diagnostic criteria and differential diagnosis. The organization is intended to provide quick access to images and confirmatory tests for each specific organ or site. The atlas adopts the well-known and widely accepted terminology, nomenclature, classification schemes, and staging algorithms.

This book series is intended chiefly for use by pathologists in training and practicing surgical pathologists in their daily practice. It is also a useful resource for medical students, cytotechnologists, pathologist assistants, and other medical professionals with special interest in anatomic pathology. We hope that our trainees, students, and readers at all levels of expertise will learn, understand, and gain insight into the pathophysiology of disease processes through this comprehensive resource. Macroscopic and histological images are aesthetically pleasing in many ways. We hope that the new series will serve as a virtual pathology museum for the edification of our readers.

Indianapolis, IN, USA — Liang Cheng

Preface

Intestinal neoplasia comprises a large part of a surgical pathologist's workload. Pathologists play a key role not only in the classification of malignancies but also in assisting screening programs, identifying incidental neoplasms, and guiding treatment by providing essential prognostic features for individual entities. A large variety of neoplasms affect the intestines, and there is ongoing discovery of new entities and prognostic features for known diseases. Pathologists and trainees should have a solid understanding of key morphologic features, pitfalls, and differential diagnoses. Importantly, pathologists should recognize and communicate features that will help their clinical colleagues in making treatment decisions, with the ultimate goal of benefiting the patient first and foremost.

This atlas provides a comprehensive yet concise, primarily visual review of intestinal neoplasms. It should also serve as a useful resource primarily for pathologists and trainees in pathology by providing a concise yet comprehensive summary of the morphology of intestinal neoplasia. Clinical practitioners and trainees will also benefit from an understanding of the pathologic correlates to the diseases they manage.

Barrie, ON, Canada — Hector H. Li-Chang
Toronto, ON, Canada — Richard Kirsch
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Toronto, ON, Canada — Aaron Pollett
Brampton, ON, Canada — Hala El-Zimaity
New Haven, CT, USA — Dhanpat Jain
New Haven, CT, USA — Romulo Celli
St. John's, NL, Canada — Stephanie L. Reid
Toronto, ON, Canada — Robert H. Riddell

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Contents

1 Epithelial Polyps 1
1.1 Inflammatory Polyps 1
1.2 Hamartomatous Polyps 3
1.3 Hyperplastic Polyps 5
1.4 Sessile Serrated Adenomas 6
1.5 Traditional Serrated Adenomas 7
1.6 Duodenal/Periampullary Adenomas 7
1.7 Tubular Adenomas 8
1.8 Villous and Tubulovillous Adenomas 10
1.9 Adenoma Variants 11
1.9.1 Clear Cell Changes 11
1.9.2 Paneth Cells 11
1.9.3 Composite Adenoma-Microcarcinoid 11
1.9.4 Eroded Adenomas 11
1.9.5 Epithelial Misplacement 12
References 13

2 Colorectal Carcinoma 15
Reference 25

3 Mesenchymal Neoplasms 27
3.1 Gastrointestinal Stromal Tumors 27
3.2 Tumors of Neural Origin 35
3.3 Tumors of Smooth Muscle Origin 43
3.4 Tumors of Fibroblastic or Myofibroblastic Origin 47
3.5 Tumors of Vascular Origin 53
3.6 Tumors of Adipocytic Origin 55
3.7 Other Mesenchymal Tumors of the Small and Large Bowel 57
3.8 Other Neoplasms and Reactive Conditions Mimicking Mesenchymal Tumors 59
References 63

4 Appendiceal Tumors 65
4.1 Introduction 65
4.2 Normal Appendix and Serrated Hyperplasia, Dysplasia, and Carcinoma 67
4.3 Mucinous Neoplasms 72
4.4 Goblet Cell Carcinoids and Carcinomas ex Goblet Cell Carcinoid 83
4.5 Other Primary Appendiceal Polyps 88
4.6 Other Diseases Involving the Appendix 88
References 91

5 Neuroendocrine Tumors of the Gastrointestinal Tract 93
5.1 Well-Differentiated Endocrine Tumors 94
5.2 Duodenum 94
5.2.1 Gastrin-Producing NETs 95
5.2.2 Somatostatin-Producing NETs. 95
5.2.3 Gangliocytic Paraganglioma 95
5.3 Jejunal and Terminal Ileum NETs 98
5.4 Appendix 100
5.5 Large Intestine 101
5.6 Neuroendocrine Carcinoma (NEC) 103
References. 108

6 Lymphoproliferative Disorders of the Small and Large Intestine 111
References. 128

7 Anal Neoplasms. 131
7.1 HPV-Associated Squamous Intraepithelial Lesions. 131
7.2 Squamous Cell Carcinomas 132
7.3 Adenocarcinomas. 134
7.4 Anal Fistula Carcinoma 135
7.5 Paget Disease 135
7.6 Hidradenoma Papilliferum. 136
7.7 Melanoma 136
References. 137

Index. 139

Contributors

Romulo Celli, MD Department of Pathology, Yale New Haven Hospital, New Haven, CT, USA

James Conner, MD, PhD Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

Hala El-Zimaity, MD Dynacare Laboratories, Brampton, ON, Canada

Dhanpat Jain, MD Department of Pathology, Yale New Haven Hospital, New Haven, CT, USA

Richard Kirsch, MBChB, PhD Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

Hector H. Li-Chang, MD Pathology and Laboratory Medicine, University of British Columbia, Royal Victoria Regional Health Centre, Barrie, ON, Canada

Aaron Pollett, MD, FRCPC Department of Laboratory Medicine and Pathobiology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

Stephanie L. Reid, MD, FRCPC Discipline of Laboratory Medicine, Health Sciences Centre, Memorial University of Newfoundland, St John's, NL, Canada

Robert H. Riddell, MD Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada

Aysegul Sari, MD Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

İzmir Katip Celebi University Ataturk Training and Research Hospital, İzmir, Turkey

1 Epithelial Polyps

Hector H. Li-Chang

The vast majority of polyps arising in the small and large intestines are derived from epithelial cells. These are routinely sampled by endoscopists during screening and diagnostic procedures, and hence they comprise a large proportion of the work done by pathologists. The proper diagnosis of intestinal polyps is required to gauge the risk of subsequent intestinal malignancy, either through the enumeration and classification of premalignant polyps, or less commonly through the identification of polyps that may alert clinicians to an underlying neoplastic syndrome. Although polyps from the small bowel are relatively rare specimens, most of the principles from the colorectum can be extended to this site.

Our understanding of the significance of epithelial polyps continues to evolve. For example, the malignant potential of sessile serrated adenomas/polyps (SSA/Ps) often went unrecognized in the relatively recent past, as they were often diagnosed as hyperplastic polyps. Recent studies suggest a relationship between at least some hyperplastic polyps, SSA/Ps, and traditional serrated adenomas.

Despite their frequency in daily practice, certain diagnostic challenges persist even in the diagnosis of the most commonly encountered types of polyps. There continues to be some uncertainty on occasion in distinguishing hyperplastic polyps from SSA/Ps. There is also disagreement on the architectural classification of adenomas and dysplasia grading. The high amount of interobserver variability that exists in this space has led some pathologists to suggest that these qualifiers not be reported. More than occasionally, benign submucosal epithelial misplacement of adenomatous epithelium is difficult to distinguish from invasive adenocarcinoma. Finally, abnormal findings are sometimes not initially appreciated in initial sections because of specimen orientation, requiring deeper levels to arrive at adequate diagnoses.

This chapter attempts to describe and illustrate diagnostic features of epithelial polyps, with special attention paid to highlighting helpful features in challenging situations.

1.1 Inflammatory Polyps

Inflammatory polyps in the small intestine arise as a result of a variety of conditions, most commonly NSAID injury, gastric *Helicobacter* infection, and inflammatory bowel disease [1]. The example in Fig. 1.1 is characterized by abundant gastric foveolar-type metaplasia, lamina propria expansion by a chronic inflammatory infiltrate, and architectural distortion (villous blunting and crypt elongation/branching). A neutrophilic infiltrate may be present, and the foveolar metaplasia may harbor an ectopic *Helicobacter* infection.

Foveolar metaplasia is not always readily identified by beginners. Note that the native duodenal epithelium on the left side of Fig. 1.2 is composed of absorptive cells with abundant eosinophilic cytoplasm, and goblet cells whose cytoplasm is composed of a large mucin droplet. In contrast, the metaplastic foveolar cells on the right contain a cap of mucin with pink cytoplasm in between this droplet and the nucleus.

Colonic inflammatory polyps may arise from a wide range of conditions, and they are occasionally solitary idiopathic findings. They are characterized by irregularly shaped crypts, a variably mixed chronic and neutrophilic inflammatory infiltrate, and expansion of the lamina propria by edema and inflammatory cells [2]. Figure 1.3 shows marked expansion of the lamina propria by a mixed infiltrate rich in plasma cells. The crypts are elongated and irregular in their shape and distribution, and the surface has begun to acquire an undulating, villous-like appearance. In severe conditions, inflammatory polyps may reach large sizes and have such villous-like architectures.

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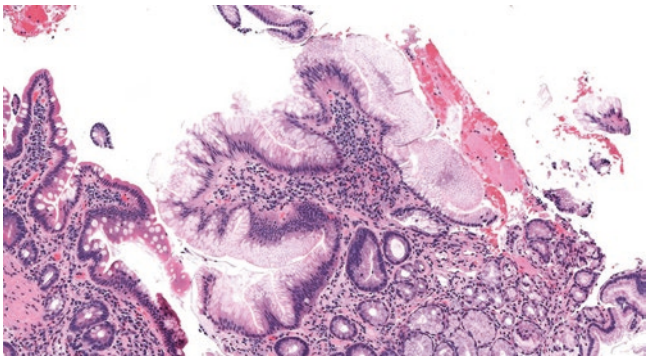

Fig. 1.1 Duodenal inflammatory polyp

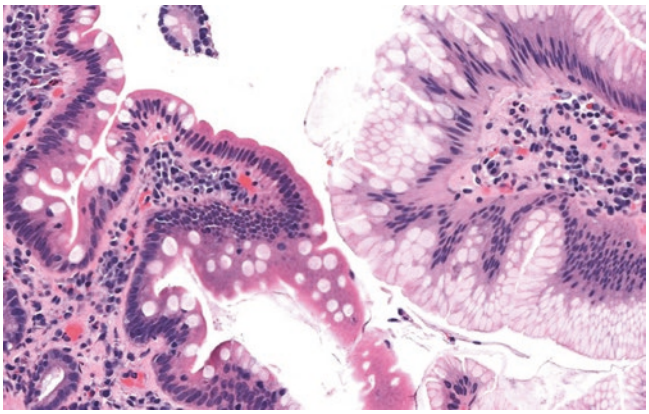

Fig. 1.2 Duodenal inflammatory polyp

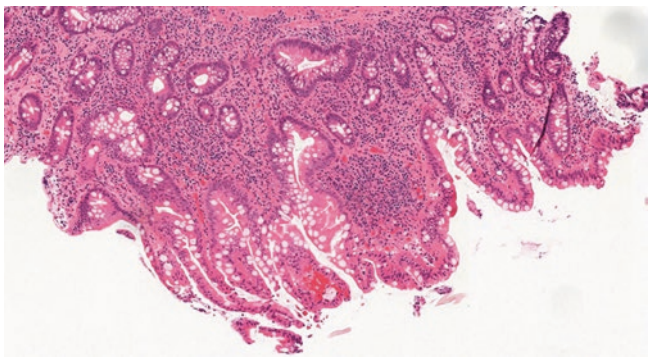

Fig. 1.3 Colonic inflammatory polyp

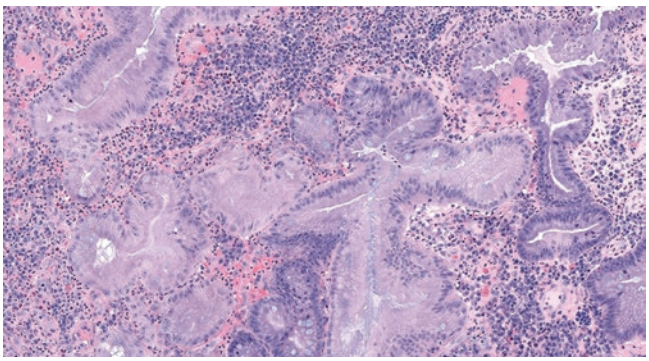

Fig. 1.4 Colonic inflammatory polyp

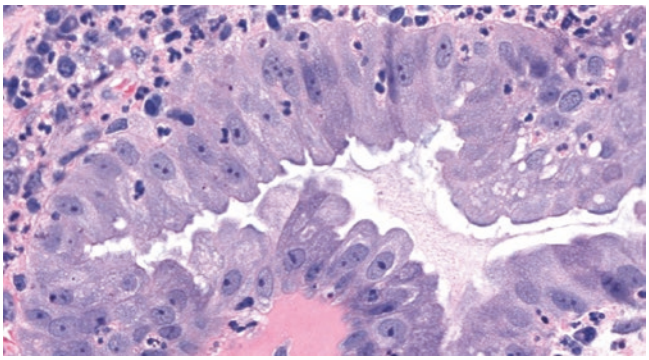

Fig. 1.5 Colonic inflammatory polyp

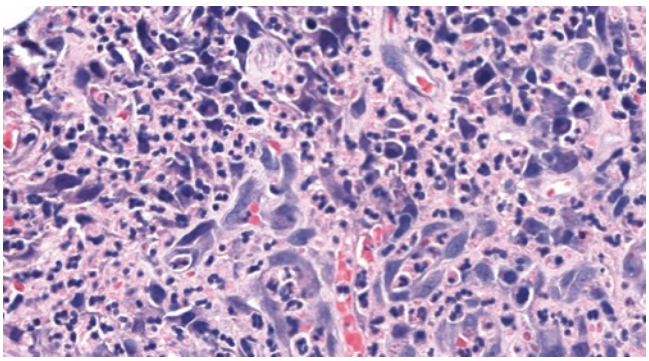

Fig. 1.6 Colonic inflammatory polyp

Inflammatory polyps may occasionally show ongoing active inflammation, often in the setting of an overlying or adjacent erosion. Figure 1.4 shows prominent neutrophilic inflammation in an example associated with inflammatory bowel disease; the architectural changes can also be striking.

The epithelial changes associated with active inflammation can be significant, as in Fig. 1.5, which shows enlarged nuclei and markedly prominent nucleoli. Within intestinal epithelium, a vesicular chromatin pattern with prominent nucleoli is usually, but not always, a reactive phenomenon rather than a neoplastic one. The association with neutrophils, gradual changing to merge with the surrounding epithelium, and association with other inflammatory changes in the polyp and background mucosa help in distinguishing such changes from those of dysplasia.

Erosions and ulcers in the gastrointestinal tract, including those occurring within inflammatory polyps, can result in marked reactive changes within the fibroblasts and endothelial cells (Fig. 1.6). Such cells (humorously referred to by some as "ulcerocytes") are characterized by nucleomegaly, multinucleation, anisocytosis, smudgy chromatin, mitotic

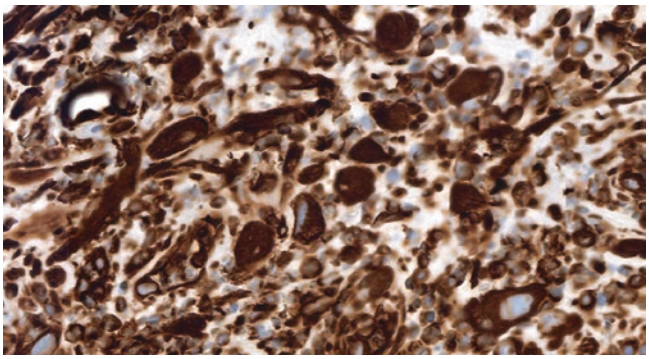

Fig. 1.7 Colonic inflammatory polyp (vimentin stain)

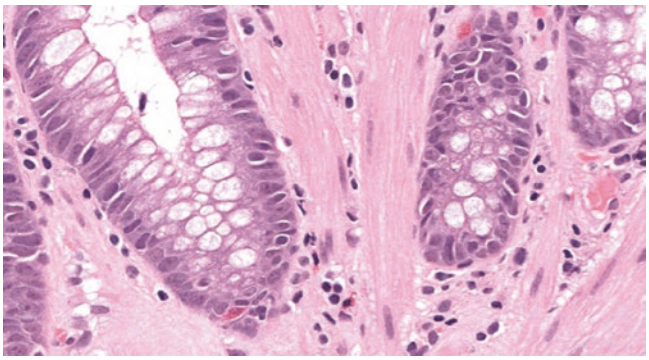

Fig. 1.9 Mucosal prolapse polyp

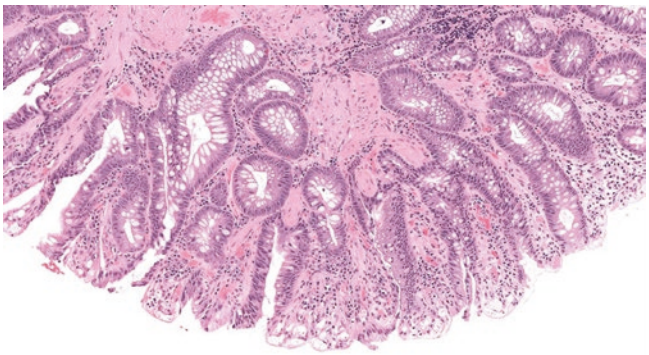

Fig. 1.8 Mucosal prolapse polyp

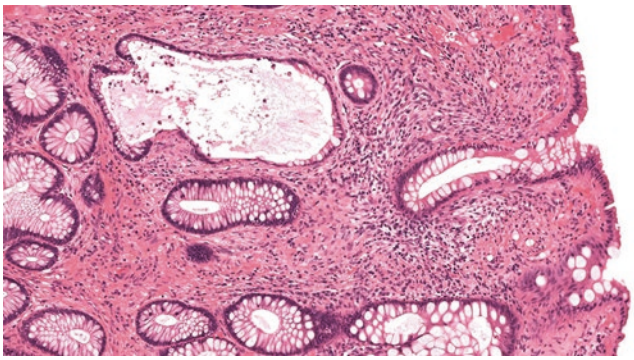

Fig. 1.10 Inflammatory myoglandular polyp

figures, and prominent nucleoli. Such marked reactive changes should not be confused with those of malignancy, and a high threshold for diagnosing malignancy should be employed in the setting of ulcers.

A vimentin stain highlights the reactive, atypical fibroblasts in Fig. 1.7. In contrast, a broad-spectrum cytokeratin stain and melanoma stains are completely negative. This helps to confirm the fibroblastic and reactive nature of these atypical cells in cases where there is concern for malignancy.

Mucosal prolapse polyps can be considered a subtype of inflammatory polyps, seen almost exclusively in the distal colon and rectum (Fig. 1.8). They are thought to result from trauma to the mucosa being dragged into the colonic lumen. They are characterized by a hamartoma-like admixture of thickened, disorganized smooth muscle and crypts, particularly at the crypt bases, with a variable degree of ischemia-like surface epithelial attenuation, erosion, and granulation tissue. Other terms applied to variants of this polyp include "inflammatory cap polyp" (depending on the prominence of surface erosion) and "inflammatory cloacogenic polyp" (depending on the prominence of hamartoma-like features).

The smooth muscle fibers in prolapse polyp splay perpendicularly and superficially to form a cup under the crypt bases (Fig. 1.9). The epithelium in these polyps usually shows regenerative atypia, with hyperchromasia and increased mitotic activity mimicking those of an adenoma. In contrast to adenomas, the nuclear features are most marked at the bases and dissipate superficially, whereas adenomas are characterized by top-down atypia, as described below [3].

Inflammatory myoglandular polyps are rare polyps seen in the ileum and distal colon; they are usually solitary and pedunculated. They are characterized by variable amounts of granulation tissue, irregular and branching dilated glands, and a smooth muscle proliferation in the lamina propria (Fig. 1.10). They may be confused with Peutz-Jeghers polyps, but in contrast to Peutz-Jeghers polyps, inflammatory myoglandular polyps lack villous architecture and arborizing smooth muscle [4].

1.2 Hamartomatous Polyps

Juvenile polyps are the most common type of hamartomatous polyp arising in the colorectum (Fig. 1.11). These are characterized by expansion of the lamina propria by edema and a mixed inflammatory infiltrate, along with dilatation and branching of the crypts. In many cases, a definitive distinction between juvenile polyps and inflammatory polyps is

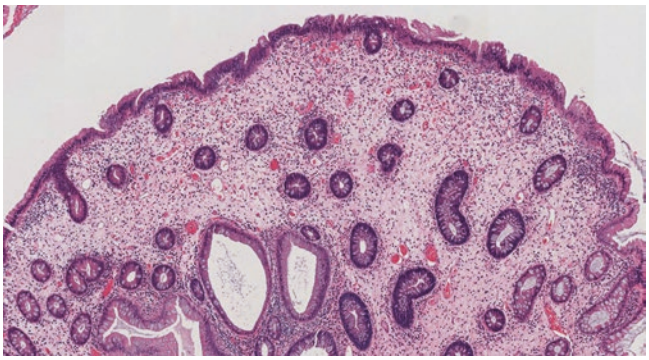

Fig. 1.11 Hamartoma (juvenile polyp and *PTEN* hamartoma tumor syndrome)

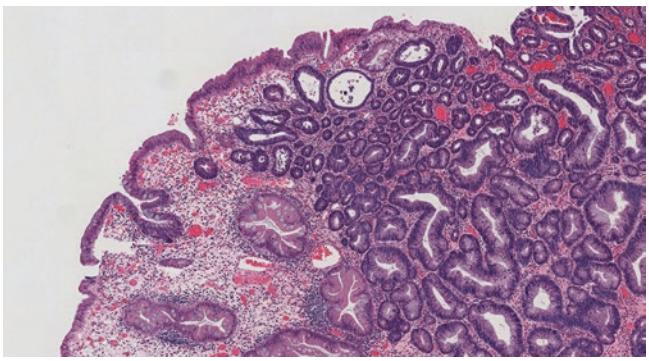

Fig. 1.12 Hamartoma (juvenile polyp and *PTEN* hamartoma tumor syndrome)

not possible. Juvenile polyps such as this one are essentially indistinguishable from those identified in *PTEN* hamartoma tumor syndrome (Cowden syndrome and related syndromes). Subtle histologic differences have been described that may allow pathologists to diagnose *PTEN* hamartoma syndrome, juvenile polyposis, or nonsyndromic polyps [5] but these are difficult to implement in practice.

When multiple hamartomatous polyps are identified, or when a mix of hamartomas and adenomas are present simultaneously, pathologists may play a role in raising the possibility of an underlying tumor predisposition syndrome. Occasionally hamartomatous polyps develop dysplasia in such settings, as in this case of suspected Cowden syndrome in Fig. 1.12, though frank malignancies directly arising from hamartomas are rare.

Cronkhite-Canada syndrome is a rare sporadic condition that can result in multiple polyps very similar to those seen in juvenile polyposis and *PTEN* hamartoma tumor syndrome [6]. Figure 1.13 demonstrates that the nonpolypoid mucosa in such cases can also show identical changes of edema and lamina propria chronic inflammation, so that correlation with clinical endoscopic findings is required to correctly classify such changes.

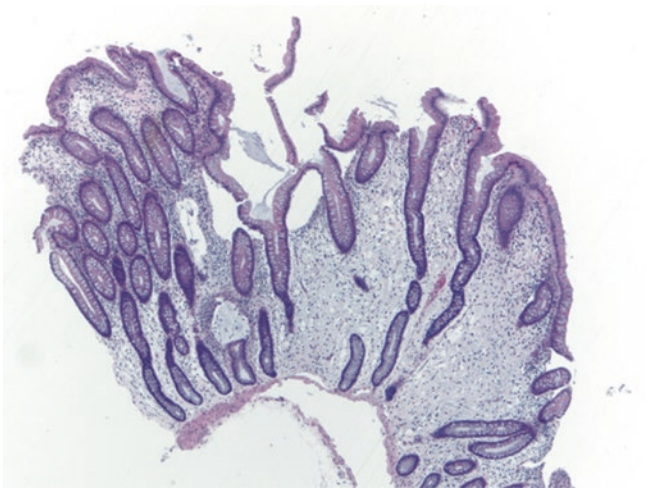

Fig. 1.13 Cronkhite-Canada syndrome (*Image courtesy of* Dr. Rish Pai)

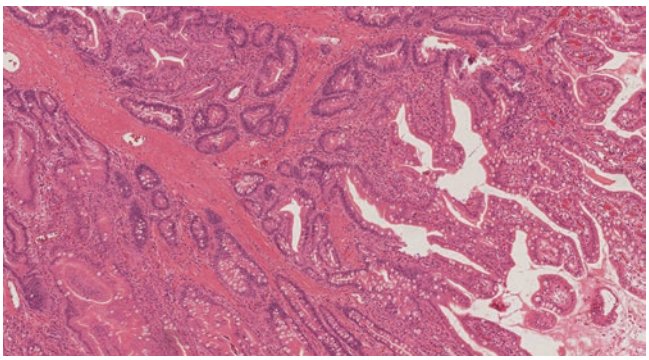

Fig. 1.14 Peutz-Jeghers polyp from the jejunum

The other major subtype of hamartomatous polyps is Peutz-Jeghers (PJ) polyps, which are most commonly found in the jejunum. A genetic predisposition to mucosal prolapse may underlie their development [7]. Some data suggest that *bona fide* PJ polyps may occur only in the small bowel, with gastric and colorectal instances perhaps representing examples of sporadic mucosal prolapse. The polyps are characterized by a tree-like hierarchical branching ("arborizing") pattern of smooth muscle lined by otherwise normal native mucosa. Figure 1.14, an example from the jejunum, demonstrates the presence of normal villi and crypts along the mucosa.

The suspected example of a colonic PJ polyp in Fig. 1.15 is lined by architecturally distorted and inflamed colonic mucosa. A diagnosis of mucosal prolapse polyp (inflammatory cloacogenic polyp) is also a consideration. Such polyps in the colorectum have not been shown to be associated with an increased systemic risk of malignancy, in contrast to *bona fide* PJ polyps arising in the small bowel. As such, a diagnosis of Peutz-Jeghers syndrome should be made with caution, if ever, in patients with colorectal PJ polyps.