Histopathology: Colorectal polyps and carcinoma

These presentations are to help you identify, and to test yourself on identifying, basic histopathological features. They do not contain the additional factual information that you need to learn about these topics, or necessarily all the images from resource sessions.

This presentation contains images of basic histopathological features of colorectal polyps and carcinoma.

Before viewing this presentation you are advised to review relevant histology, relevant sections on neoplasia and gastrointestinal pathology in a pathology textbook, relevant lecture notes, relevant sections of a histopathology atlas and the histopathology power point presentation on neoplasia.

Copyright University of Adelaide 2011
Colonic polyps

- Polyps are lesions that protrude into a lumen, whether on a stalk (pedunculated) or from a broad base (sessile). Polyp, pedunculated and sessile are descriptive terms. They convey no information about the nature or diagnosis of the polyp. There are many different types of polyp (determined microscopically). In the colon, these are:
  - Non-neoplastic
    - Hyperplastic (metaplastic) - most common
    - Juvenile
    - Hamartomatous
    - Inflammatory
  - Neoplastic (premalignant and malignant)
    - Adenomatous/dysplastic
    - Serrated adenomas (often flat elevations of elongated glands rather than polyps)
    - Malignant
  - Sometimes occur as familial syndromes
While squamous dysplasia does not form a mass, glandular dysplasia developing in a lining epithelium often forms a polyp - a protuberance of tissue elevated from the surrounding mucosa. Such dysplastic polyps are often referred to as adenomatous polyps or in the colon, just adenomas. Colorectal adenomas may have a tubular, tubulovillous or villous architecture and the dysplasia histologically is graded as mild, moderate or severe. N.B. Adenomas in the GIT are dysplastic and thus premalignant, but adenomas in other sites are not necessarily dysplastic or premalignant e.g. breast, thyroid. Understanding the specific terminology is thus important, as the natural history and potential outcomes of the lesions are different.
Low power view of a tubular adenomatous polyp in the colon.

Black star: stalk including submucosa.
Note how the glands of the adenomatous polyp (blue arrows) are elongated and have a disorganised architecture compared to the normal colonic glands in the adjacent mucosa (yellow arrows).
Note intact muscularis mucosae: black arrows
Edge of a tubular adenomatous polyp in the colon (low power). Normal glands are present on the right side of the image and dysplastic glands on the left (separated by the black line). The dysplastic glands are more elongated, branched and disorganised. There are also fewer goblet cells indicating less differentiation. The yellow lines outline parts of several glands and indicate (very approximately) the location of their epithelial basement membranes. MM: muscularis mucosae.
Compare the epithelial cells from the normal colonic gland on the left to those of the benign neoplastic (dysplastic) gland on the right. Note that the normal epithelial cells have small nuclei that are similar in size to each other (yellow arrows) and only take up about one third or less of the cell. The well differentiated but neoplastic nuclei (red arrows) are larger and more crowded and take up a larger proportion of the cell. There is only mild nuclear pleomorphism. The basement membranes are outlined in black. Note the capillaries (blue arrows) and plasma cells (black arrows) in the lamina propria.
Very low power view of an adenomatous polyp in which an invasive adenocarcinoma (black stars) has arisen. The carcinoma has destroyed some of the polyp and has invaded through muscularis mucosae (black arrows) into submucosa (yellow star). It is because of this potential complication that adenomatous polyps in bowel are removed when found. Larger villous type adenomatous polyps and those demonstrating severe dysplasia microscopically are more likely to become malignant.

Red stars: edge of adenomatous polyp (showing dysplasia but not invasive adenocarcinoma).
Blue stars: adjacent normal bowel wall.
Most neoplastic lesions form a mass that is composed not only of neoplastic cells but also supportive stroma, blood vessels and often chronic inflammatory cells. The image on the left is a macroscopic view of an adenocarcinoma of the colon (red star). The tumour surface is ulcerated. The image on the right is a very low power histopathological view of the edge of such a lesion. The tumour is on the left side of the black line and normal colon is on the right side. Note how the tumour cells (seen as dark blue/purple areas due to their high N:C ratio) invade deeply into the adventitia (A). The eosinophilic staining between the groups of tumour cells represents the tumour stroma. (M: mucosa, MP: muscularis propria). Note that muscularis propria can be seen macroscopically (black arrows, left image) as a pale line, approx. 1mm thick. Even from the macroscopic specimen it can be seen that this lesion is at least an ACP or Duke’s Stage B.
Compare the epithelial cells from the normal colonic glands in the image on the left to those in the colonic adenocarcinoma on the right. Note that the normal epithelial cells have small nuclei that are similar in size to each other (black arrows) and only take up about one third of the cell. The malignant nuclei are larger (red arrows) and take up a larger proportion of the cell (higher nuclear:cytoplasmic (N:C) ratio), and there is much greater variability in size between nuclei (pleomorphism). The malignant cells, however, still show their glandular nature by the formation of glandular lumina (red stars). This is a moderately differentiated malignancy. Benign lesions and well differentiated malignancies will show nuclear features in between those of the 2 micrographs demonstrated here.
In addition to showing cytological (cellular) atypia, neoplastic lesions (especially malignant) also show architectural atypia i.e. there is disorganisation of the components of the lesion. The image above is from a biopsy of a colonic mass. A few normal glands are present (outlined in black) at the edge of the lesion. They are somewhat crosscut but you can see the simple glandular structures and many goblet cells. The remainder of the tissue is invasive adenocarcinoma. Note how the malignant glands (red star) are more closely packed and disorganised, the glands are probably branching. Note also how, although this is fairly low power, goblet cells are seen in the normal epithelium, but not in the malignant epithelium. This indicates that the malignant epithelium is not as well differentiated. The tumour stroma (black stars) is very dense and cellular.
Invasive adenocarcinoma of the colon
As malignant cells grow they need a blood supply and supportive connective tissue stroma. The stroma that develops looks different to the normal connective tissue of the region that the tumour invades. The stromal response around the cells of an invasive malignancy is known as desmoplasia. When florid, this stromal response makes the tumour very firm and pale (e.g. schirrous ductal carcinoma of the breast). A desmoplastic stromal response is seen here in the invasive colonic adenocarcinoma (image on left) where there are more fibroblasts and denser connective tissue (red stars) than in the lamina propria and submucosa (black arrows) of normal colon (image on right). Chronic inflammatory cells also infiltrate malignant and often benign lesions.
There are different types of adenocarcinoma that have different prognostic significance. While most demonstrate their glandular nature by the formation of glandular lumina (black arrows, lower picture), in others the malignant cells contain a large droplet of mucin that pushes the nucleus to the side (yellow arrows, picture top right). These are known as signet ring cells and thus signet ring carcinomas. In others the cells secrete abundant mucin (red stars) and the malignant cells float about within it (red arrows, picture top left). These are known as mucinous or colloid carcinomas. By far the majority of colorectal carcinomas are of ‘no special type’ (lower picture).
Metastases. Malignant cells are able to metastasise to a wide variety of sites. They mainly do this by invading lymphatics and/or capillaries or small veins. Malignant cells (red stars) from a colorectal carcinoma are seen in the image above in small vessels either side of the muscularis mucosae (MM) in the colon. It is not possible to determine if these are lymphatic vessels or dilated capillaries. Compare the size of the tumour cell nuclei to those of the normal colonic epithelium (black stars). The tumour is an adenocarcinoma - as seen here by the large mucin droplets in a number of the cells (e.g. black arrows). It is important for pathologists reporting cancer specimens to look for vascular invasion as it has prognostic significance - it suggests that the tumour may already have metastasised even if no metastases can be identified radiologically. Also note the lymphocytes and plasma cells (normal) of the lamina propria, but some now infiltrate into submucosa around the tumour (bottom of image).
Metastatic tumour (black star) colorectal adenocarcinoma in the liver.
Yellow star: adjacent liver tissue.
To make a histopathological diagnosis, the pathologist needs to examine many features of the lesion. In the case of neoplastic or potentially neoplastic lesions, they examine the arrangement/architecture and cytological features of the cells and assess whether they are invasive or not to determine if it is benign or malignant. In difficult cases they may also need to look for necrosis, the features of the stroma, or to count mitotic figures. They also need to determine the type of lesion, or its line of differentiation (glandular, melanocytic, lymphocytic etc) and to grade malignant lesions (depending on the type) as these features also influence the management of the patient and prognosis. Other prognostic features may also need to be assessed.
Many features affect the prognosis and management of malignancies. The pathologist provides much of this information in the pathology report of the surgically excised specimen with lymph nodes. This often detailed information is usually presented in a consistent fashion in a synoptic report. These differ somewhat depending on the malignancy. You don’t need to memorize the details of the following synoptic report, which at this stage, is for information only. Note, however, the extent of information that is provided by the pathologist following examination of the specimen and sections to the referring clinician. Medical students should get into the habit of reading the pathology reports in patient notes, as doctors you will be expected to understand them. You should, however, have a general understanding of the features that are important in assessing the prognosis and management of malignancies (tumour type and subtype, grade, stage, presence of lymphovascular invasion, other depending on malignancy), including some specific information about the major malignancies.
Colorectal carcinoma synoptic report

**Nature of specimen:** Right hemicolecotomy

**Tumour site:** Ascending colon

**Size:** 20mm x 25mm

**Proximal dilation (obstruction):** Absent

**Perforation:** Absent

**Tumour type:** Adenocarcinoma NOS

**Grade:** Moderately differentiated

**Margin of tumour:** Infiltrative

**Inflammatory infiltrate:** Peritumoral lymphoid aggregates present
LOCAL SPREAD:
Depth of invasion: Beyond muscularis propria
Excision margins: Proximal and distal margins are free of tumour. Distance of tumour to nearest margin (distal) 40mm
Neural invasion: Absent

DISTANT SPREAD:
Lymph nodes: Total number of nodes found: 14
Total number of nodes involved by tumour: 2
Apical node: Involved
Vascular invasion: Present
Mesenteric deposits: Absent
Adjacent bowel: 2x adenomatous polyps 8 and 10mm in dimension, showing moderate dysplasia
Very low power view of a lymph node from the mesocolon that has been almost entirely replaced with metastatic adenocarcinoma from the colon.
ANCILLARY INVESTIGATIONS:
Immunohistochemistry studies were performed on paraffin sections of tumour with antibodies to MLH1 and MSH2. There was no expression of MLH1 gene product by the tumour cells.

Comments: Lack of expression of MLH1 as demonstrated by immunohistochemistry suggests the possibility of underlying mismatch repair gene abnormality and further gene mutation studies may be indicated.
Only in certain cases are such ancillary investigations (previous slide) performed i.e. if there is a suspicion of hereditary non-polyposis colorectal carcinoma (HNPCC). The following slide shows the immunohistochemical staining for MLH1 and MSH2, and a normal H&E of the tumour. The tumour is not expressing the MLH1 protein, yet the normal epithelial cells are, indicating that the tumour cells have a mutation in the encoding gene and that the patient could have HNPCC.
Black stars: tumour
Yellow stars: normal mucosa
MLH1 and MSH2 are 2 of the family of mismatch repair (MMR) genes that encode proteins involved in DNA repair. Both alleles of one or more members of this family of genes need to be mutated for the protein not to be produced. Loss of the protein means that spontaneous errors occurring in DNA replication, especially in microsatellite repeats, some of which are located in the coding or promoter regions of genes controlling cell growth, are not all repaired, thus ultimately allowing uncontrolled cell growth. Mutations in MMR genes may arise spontaneously or be inherited. In HNPCC, a defect in one allele of one of the genes is inherited and if a defect develops in the other allele in a colonic epithelial cell after birth, the specific MMR protein is not produced -> high risk of developing carcinoma.