International Academy of Pathology
Malaysian Division

FINAL REPORT

QUALITY ASSURANCE PROGRAM
GENERAL DIAGNOSTIC HISTOPATHOLGY
CYCLE 02/2017

NOTES FROM THE COORDINATOR

1. For this cycle 02/2017, a total of 24 sets of DVDs had been circulated. Twenty institutions responded by the closing date of 15 November 2017.

2. Excerpts of previously circulated information about this quality assurance program are reproduced here:
    - IAP-MD QAP provides a platform via the evaluation reports to compare and identify diagnostic insufficiency based on the outcomes of submitted diagnoses and targeted diagnoses.
    - In the evaluation reports of each cycle, the targeted diagnosis for each case is provided, followed by a tabulated list of diagnoses submitted by participating laboratories and followed by discussion and possible differential diagnoses on the case.
    - Evaluation of performance of each laboratory is conducted by participating laboratory by comparing own submitted diagnoses with the diagnoses provided in the evaluation reports. Evaluation of performance shall be the responsibility of each participating laboratory.

3. Any queries regarding this final report for cycle 02/2017 could be directed to Dr. Ch'ng Ewe Seng, e-mail: iapmdqap@gmail.com.

4. The coordinator would like to acknowledge the contributions from Prof. Dr. Nor Hayati Othman, Dato Dr. Norain Karim, Dr. Hakimah Mahsin, Datin Dr. Nik Raihan Nik Mustapha, Dr. Norizal Mohd Noor, Dr. Suhaila Abdullah, Dr. Fazilah Hassan, Dr. Herni Talib, and Dr. Nurul Akmar Misron.

Prepared by,

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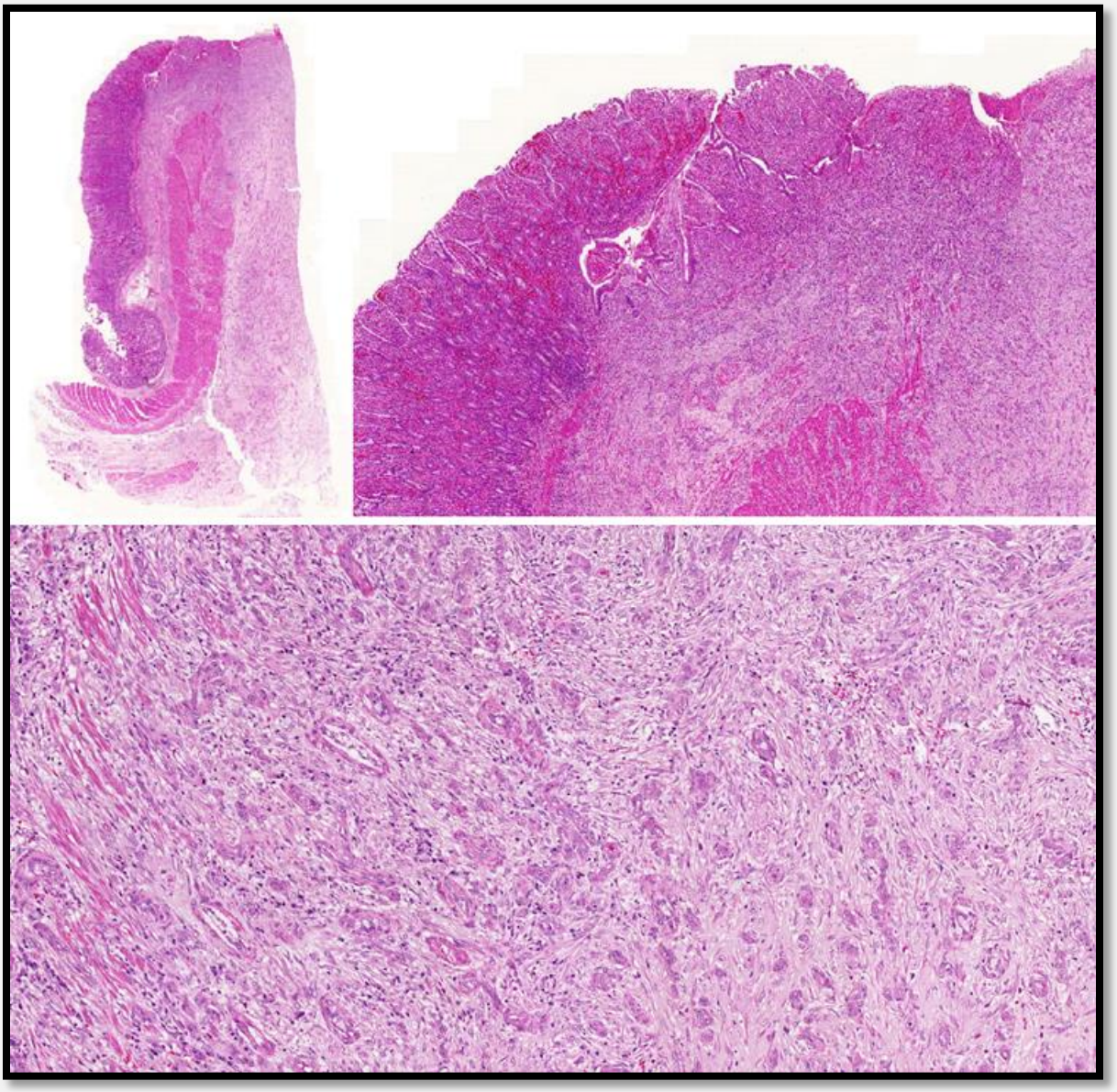
Coordinator for IAP-MD QAP

Case 11

49-year-old female, polypoidal mass (2cm) at small bowel with intussusception. One representative section.

Targeted Diagnosis: **Inflammatory fibroid polyp**



Case 11

Submitted Diagnoses by Participating Institutions	Number
Inflammatory fibroid polyp	17
Inflammatory pseudopolyp	1
Ectopic gastric mucosa	1
Exuberant granulation tissue with mucosal ulceration ?pyogenic granuloma	1

Educational notes:

1. This inflammatory fibroid polyp is composed of spindle cells extending from the submucosal layer deep beyond the muscularis propria while ulcerating the overlying mucosa. The spindle cells have plump vesicular nuclei, streaming around the prominent capillary network. Scattered inflammatory infiltrates with a significant number of eosinophils are observed.
2. Inflammatory fibroid polyps are benign. They occur throughout the gastrointestinal tract; the antrum of the stomach is the most common site. In the small intestine, inflammatory fibroid polyps occur most commonly at the terminal ileum, causing obstruction by intussusception.
3. PDGFRA activating mutations are observed in more than 50% of the cases.
4. Differential diagnoses include inflammatory myofibroblastic tumor (IMT) and gastrointestinal stromal tumor (GIST). Both IMT and GIST lack the prominent capillary network. In IMT, the inflammatory infiltrates are predominantly lymphoplasmacytic infiltrates with lesser eosinophils. GIST in general lacks the inflammatory background.

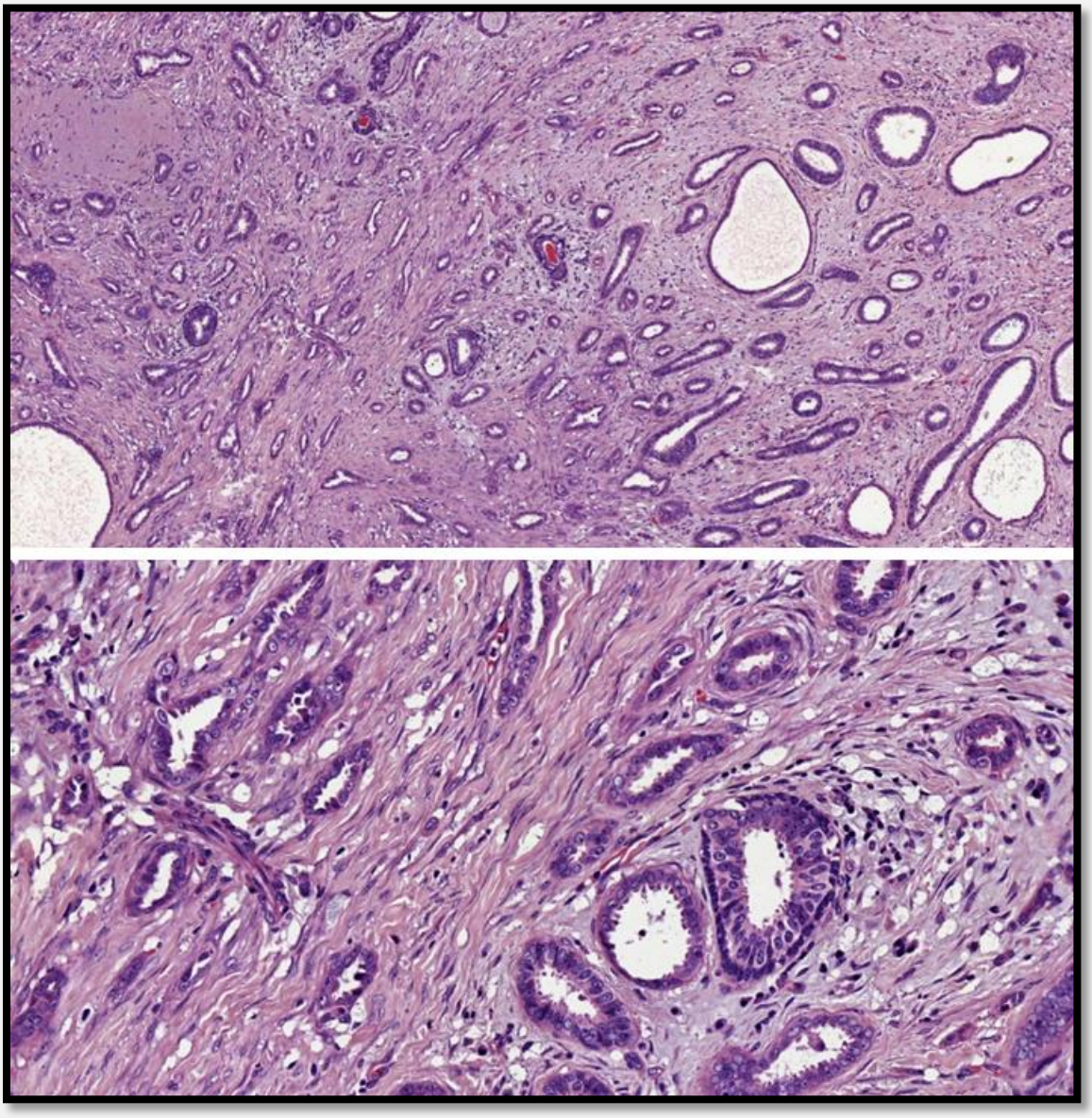
Reference:

1. World Health Organization. (2010). WHO classification of tumours of the digestive system. Fred. T. Bosman (Ed.). Internat. Agency for Research on Cancer.

Case 12

48-year-old female, breast lump (1.8cm). One representative section.

Targeted Diagnosis: **Tubular carcinoma, Grade 1**



Case 12

Submitted Diagnoses by Participating Institutions	Number
Tubular carcinoma/ Tubular carcinoma, Grade 1	12
Tubular carcinoma with fibrocystic change	3
Tubular carcinoma with FEA	1
Sclerosing adenosis, columnar cells change and FEA with areas suspicious of tubular carcinoma. Further IHC staining (p63) needed to help with the assessment/ Radial scar. To rule out invasive tubular carcinoma by immunohistochemistry (SMMHC / p63 / SMA)	2
Sclerosing adenosis with microcalcification/ Complex sclerosing lesion	2

Educational notes:

1. The breast tissue harbors a tubular carcinoma displaying haphazard, infiltrative tubular glands in oval, round or angulated shapes separated by desmoplastic stroma. These tubular glands are single-layered, composed of mildly pleomorphic cells with rare mitoses. In contrast, dilated mammary ducts lined by similar cells with presence of outer layer of myoepithelial cells are also observed, consistent with flat epithelial atypia (FEA).
2. Tubular carcinoma is a special type of breast cancer with excellent prognosis (10-year overall survival rate after resection: 99%-100%). This carcinoma, by definition, is grade 1. According to NCCN practice guidelines in oncology, tubular carcinoma is one of the favorable histologies, which does not require adjuvant chemotherapy, regardless of tumor size provided that there is no lymph node metastasis.
3. Tubular carcinoma commonly occurs in association with FEA, low grade DCIS, and also lobular neoplasia. "Rosen triad" specifically refers to the association with columnar cell lesions (FEA) and lobular neoplasia.
4. Sclerosing adenosis and complex sclerosing lesions/radial scars are differentiated from the tubular carcinoma by the virtue of myoepithelial cells present surrounding the tubules, which could be confirmed by immunostaining. Although microglandular adenosis lacks the myoepithelial cells, the tubules are round and regular, which often contain colloid-like secretory materials.

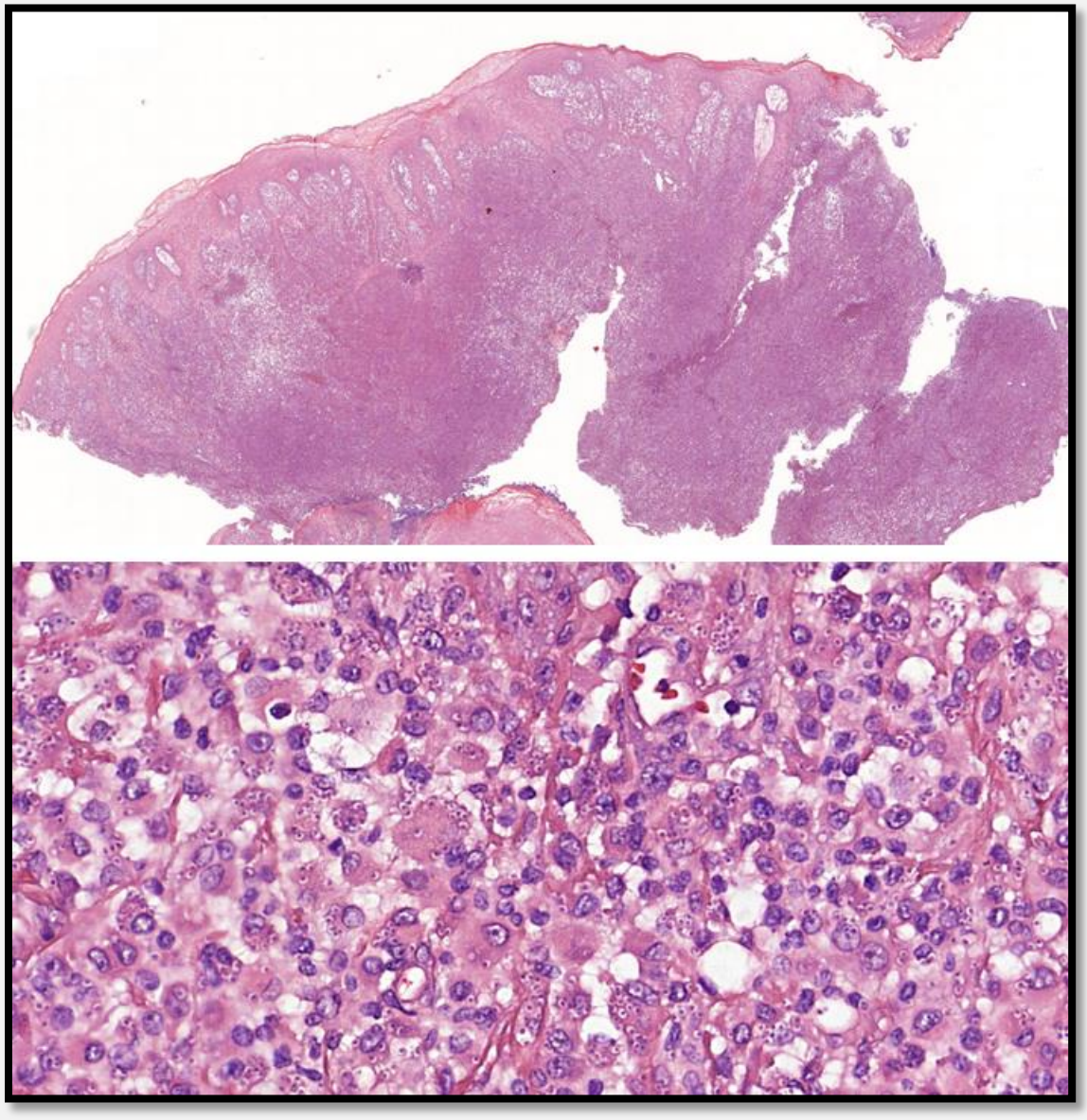
Reference:

1. World Health Organization. (2012). WHO classification of tumours of the breast. Sunil. R. Lakhani (Ed.). Internat. Agency for Research on Cancer.
2. NCCN guidelines - Breast Cancer Version 3. 2017

Case 13

73-year-old female, multiple growths at tongue.

Targeted Diagnosis: **Histoplasmosis**



Case 13

Submitted Diagnoses by Participating Institutions	Number
Histoplasmosis/ Fungal infection, histoplasmosis	10
Fungal infection, morphology suggestive of Histoplasmosis. Requires correlation with microbiology/ Fungal infection suggestive of Histoplasmosis. Please correlate with culture/ Intracellular fungal infection, yeast form, histomorphology resembling Histoplasmosis capsulatum.	3
Fungal infections, histoplasmosis or penicillium/ Fungal infection with differential of Histoplasmosis or Peniciliosis. Correlation with special stain and microbiological culture studies needed.	5
Fungal infections either Histoplasmosis or Cryptococcosis. Comment: need PAS staining to differentiate.	1
Mucocutaneous Leishmaniasis	1

Educational notes:

1. There are sheets of histiocytes in the subepithelial stroma. Fungal bodies in yeast form are observed within these histiocytes. These fungal bodies are smaller than the size of the nucleus of a small lymphocyte.
2. *Histoplasma capsulatum* var. *capsulatum* in tissue is oval **2- to 4-µm** yeasts that may show narrow-based buds. The yeast cytoplasm is separated from the surrounding tissue by a clear zone - the cell wall, which is highlighted with GMS and PAS stains. Clustering of the yeasts within the cytoplasm of histiocytes is an important diagnostic feature.
3. *Penicillium marneffei* is differentiated from *H. capsulatum* as the former shows formation of a transverse septum due to fission rather than budding.
4. Histopathologic identification of fungi in tissue sections is however prone to error that all reports should include a suggestion to correlate with culture results.

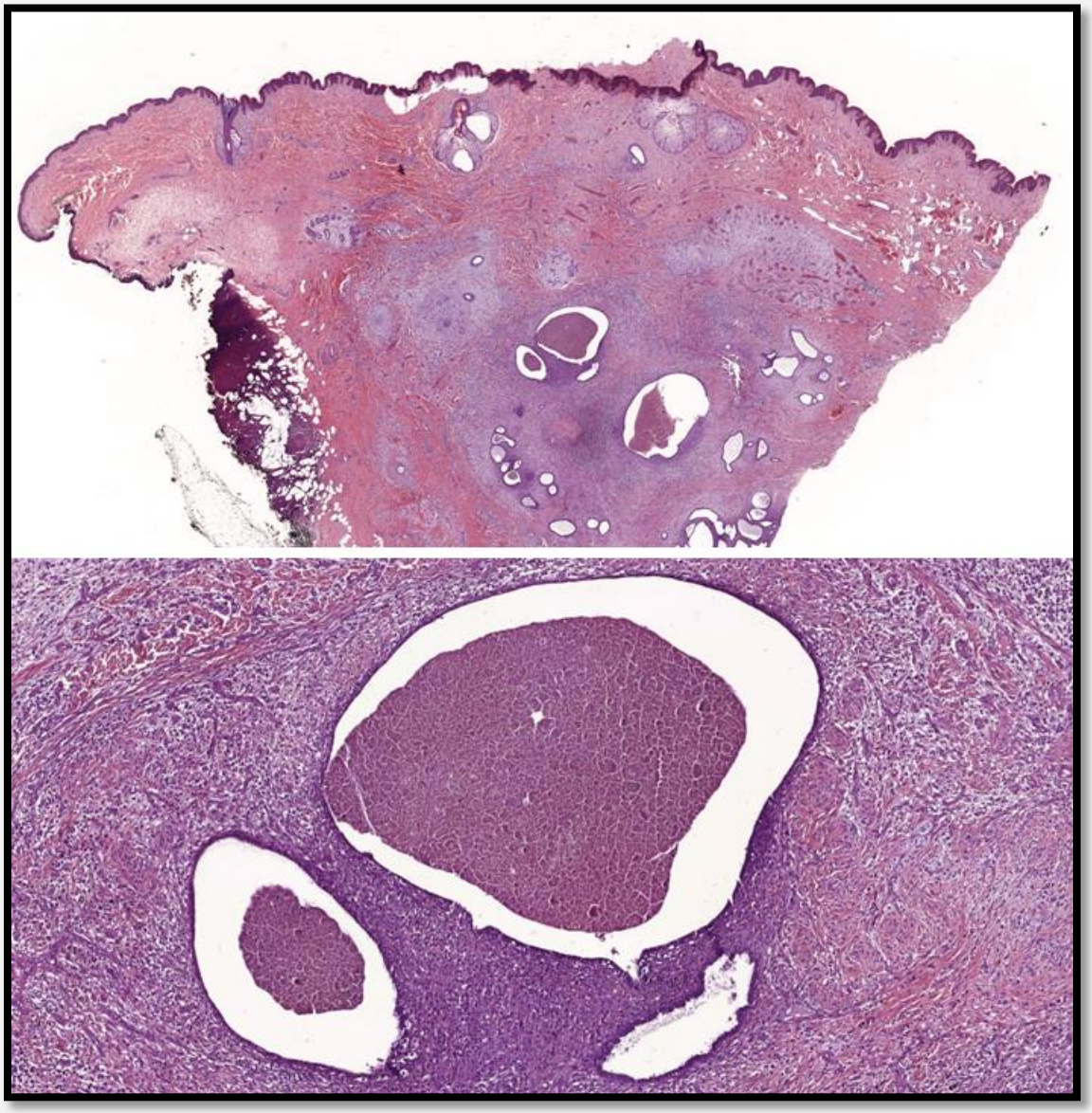
Reference:

1. Guarner, J., & Brandt, M. E. (2011). Histopathologic diagnosis of fungal infections in the 21st century. Clinical microbiology reviews, 24(2), 247-280.

Case 14

24-year-old female, skin nodule at abdomen.

Targeted Diagnosis: **Cutaneous endometriosis**



Case 14

Submitted Diagnoses by Participating Institutions	Number
Endometriosis/ Endometriotic nodule/ Endometriotic cyst	20

Educational notes:

1. Section shows cutaneous endometriosis composed of variable dilated proliferative endometrial glands associated with endometrial stroma in the dermis.
2. Cutaneous endometriosis commonly associated with gynecologically induced abdominal or pelvic scars. Histologically, cutaneous endometriosis responds similarly to hormonal fluctuations and displays proliferative, secretory or menstrual changes. Rarely marked decidualization of the stroma might pose diagnostic difficulties.

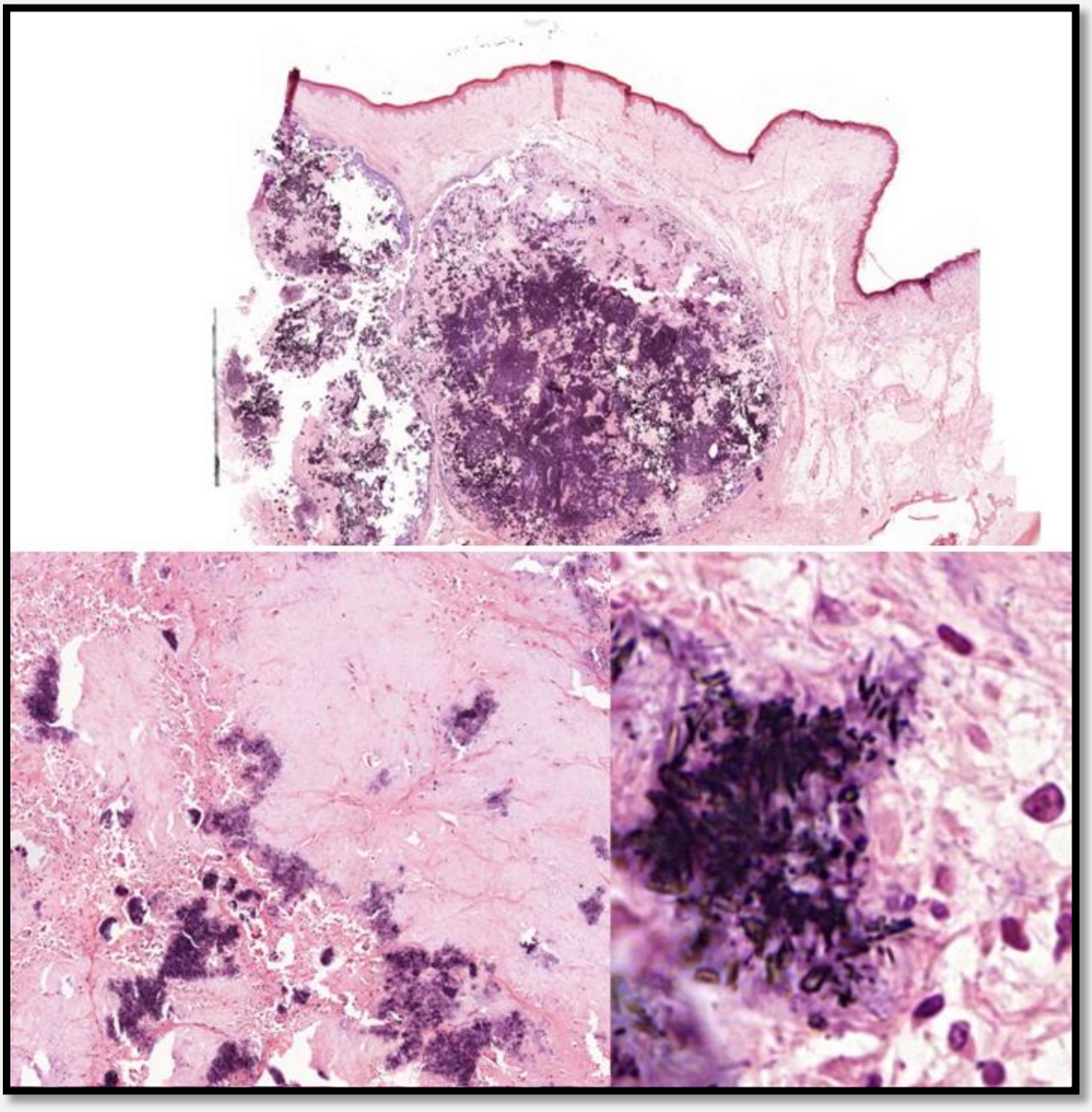
Reference:

1. Barnhill, R., Crowson, A. N., Magro, C., & Piepkorn, M. (2010). Dermatopathology. McGraw Hill Professional.

Case 15

71-year-old. female, left thumb mass.

Targeted Diagnosis: **Calcium pyrophosphate deposition disease**



Case 15

Submitted Diagnoses by Participating Institutions	Number
Calcium phyrophosphate deposition disease / Chondrocalcinosis/ pseudogout/ Tumoral calcium crystalline calcium pyrophosphate dehydrate crystal deposition disease	11
Benign calcified lesion suggestive of gouty tophi/ Gouty tophi/ Calcified gouty tophi/ Gout with calcification	5
Calcinosis cutis/ Tumoral calcinosis	3
Oxalosis of bone	1

Educational notes:

1. Section shows lobulated basophilic aggregates of crystals in the dermis associated with chondroid metaplasia and foreign body giant cell reaction.
2. Differential diagnoses include calcium pyrophosphate deposition disease (CPPD), gout and oxalosis.
3. CPPD is also known as chondrocalcinosis (terminology by radiologists) and pseudogout (terminology by rheumatologists). Crystals in CPPD are basophilic, rhomboid in shape and weakly positive birefringent.
4. In contrast, the gout crystals (sodium urate monohydrate deposits) usually dissolve in tissue fixed with formalin, leaving behind amorphous pale pink areas corresponding to the sites of crystal deposition. Within these amorphous deposits, there is often a feathery appearance. The brown, needle-shaped gout crystals are preserved in alcohol fixation.
5. In oxalosis, the calcium oxalate crystals are light yellow-brown in various shapes: rosettes, ellipses, nprisms, and radial patterns. They are birefringent.

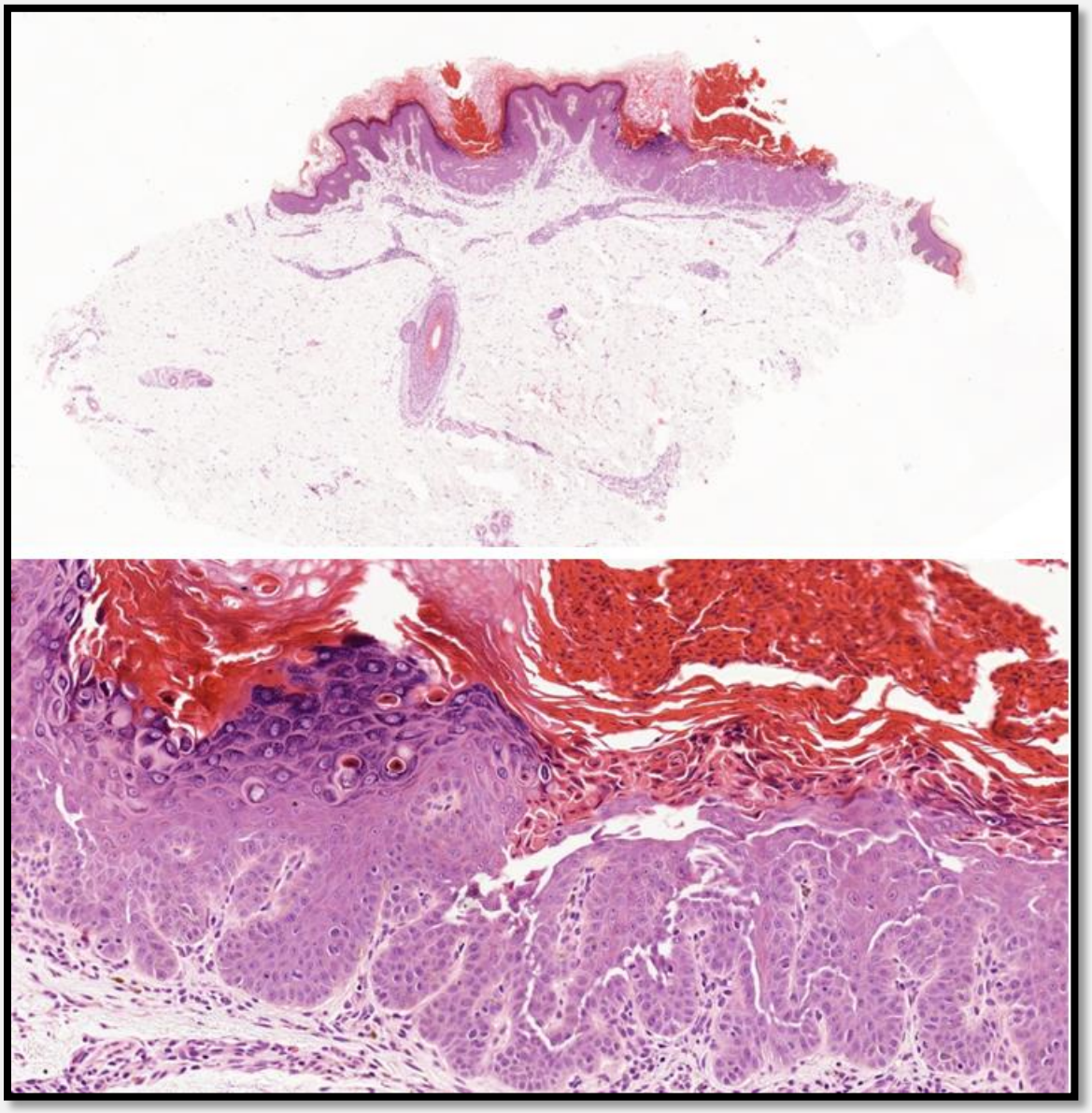
Reference:

1. Barnhill, R., Crowson, A. N., Magro, C., & Piepkorn, M. (2010). Dermatopathology. McGraw Hill Professional.
2. Stacey E. Mills, eds. Sternberg's diagnostic surgical pathology. Lippincott Williams & Wilkins, 2010.

Case 16

32-year-old female, erythematous scaly lesions over scalp, forehead and back of ear. Family history of similar skin lesions. Skin biopsy

Targeted Diagnosis: **Darier's disease (keratosis follicularis)**



Case 16

Submitted Diagnoses by Participating Institutions	Number
Darier's Disease/ Keratosis follicularis/ Acantholytic dermatosis suggestive of Darier's disease	14
Porokeratosis	4
Pitryasis rubra pilaris	1
Epidermal naevus.	1

Educational notes:

1. The skin shows mild acanthosis with focal acantholysis in the spinous layer and marked hyperkeratosis and parakeratosis in the overlying corneal layer. Characteristic dyskeratotic cells, the corps ronds and grains, are evident.
2. Darier's disease (keratosis follicularis) is an autosomal dominant disorder with mutations in the ATP2A2 gene coding a calcium pump.
3. Histologically, Darier's disease is characterized by acantholytic dyskeratosis. There are two types of dyskeratotic cells: the corps ronds (large cells in the spinous layer with round nucleus, perinuclear halo and eosinophilic cytoplasm) and the corps grains (small cells in the granular or corneal layer with elongated pyknotic nuclei and shrunken eosinophilic cytoplasm). Direct immunofluorescence test is negative.
4. Transient acantholytic dermatosis (Grover's disease) is a differential diagnosis. The clinical context with mixed acantholytic patterns (Darier's pattern, Hailey–Hailey-like pattern, pemphigus pattern or spongiotic pattern) within a specimen distinguishes this from Darier's disease.
5. Porokeratosis is characterized by cornoid lamellae which are parakeratotic columns with an absent or decreased granular layer and scattered dyskeratotic cells in the spinous layer layer beneath them. Acantholysis is not observed.

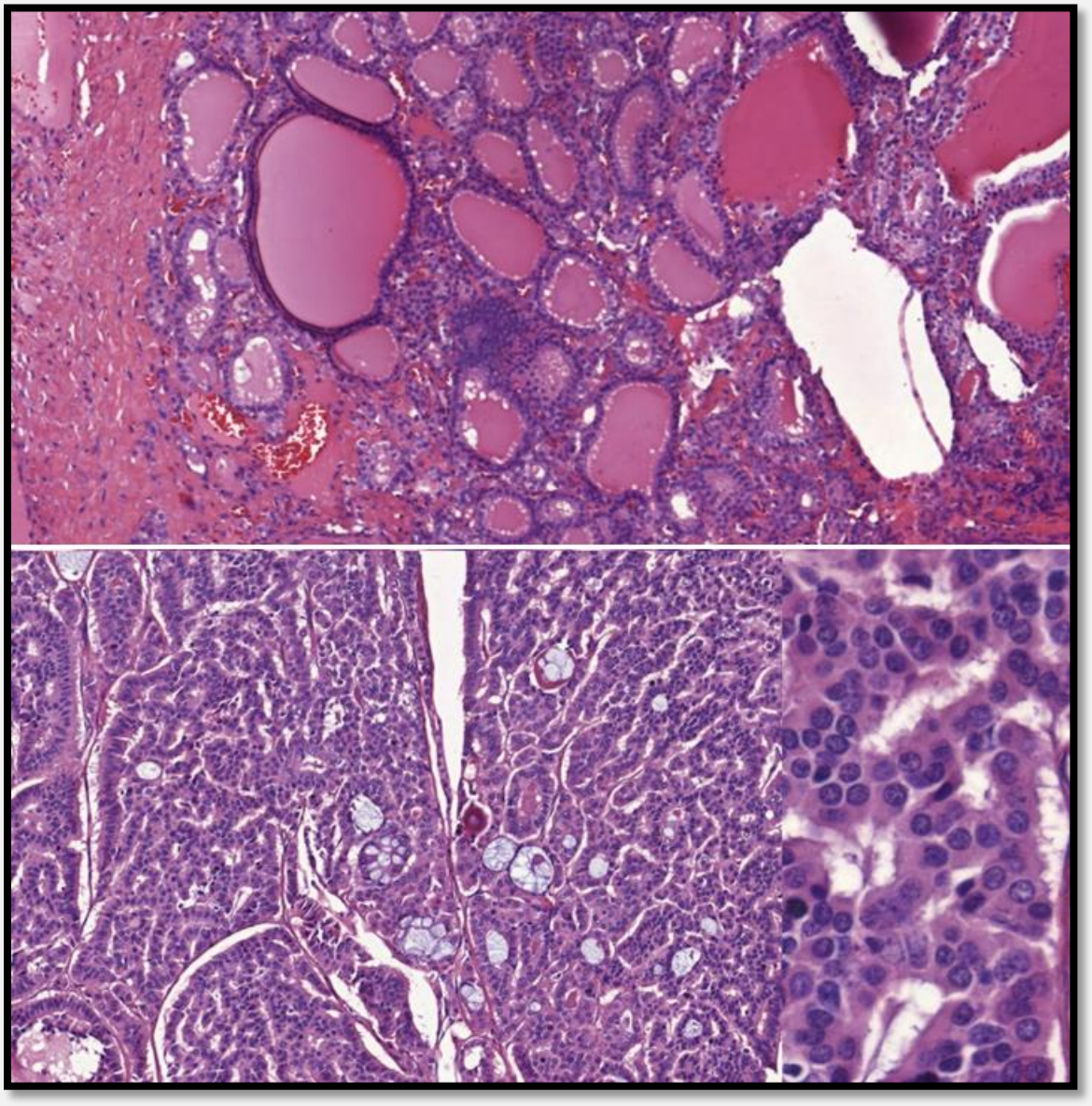
Reference:

1. Busam, K. J. (Ed.). (2016). Dermatopathology 2nd ed. Elsevier Health Sciences.

Case 17

25-year-old female, twisted right ovarian cyst. One representative section.

Targeted Diagnosis: **Strumal carcinoid**



Case 17

Submitted Diagnoses by Participating Institutions	Number
Strumal carcinoid/ Struma ovarii with carcinoid/ Strumal carcinoid associated with struma ovarii	15
Papillary thyroid carcinoma arising from struma ovarii/ Follicular variant of papillary carcinoma arising from struma ovarii	3
Poorly differentiated papillary/insular variant of papillary carcinoma.	1
Struma ovarii	1

Educational notes:

1. The cyst wall contains thyroid tissue with colloid-containing follicles. In addition, there are trabeculae and cords of columnar to cuboidal cells with uniform round nuclei displaying salt-and-pepper chromatin pattern. A few scattered glands with intraluminal mucin and bona fide intestinal-type mucinous glands are observed.
2. Strumal carcinoid is a combination of insular or trabecular carcinoid and struma ovarii. The carcinoid and struma components are admixed or discretely separated. In strumal carcinoids, mucinous glands are fairly common findings (about 40%). Immunohistochemically, the carcinoid component is positive for neuroendocrine markers whereas the strumal component is positive for TTF-1 and CK7. Strumal carcinoids are usually benign.
3. Struma-derived thyroid-type carcinomas (papillary carcinoma and follicular carcinomas) are very rare in strumal carcinoids. They are more commonly found in struma ovarii, occupying the entire or forming a predominant portion of the tumor mass. Nonetheless, it remains unclear whether to apply similar criteria for eutopic thyroid to diagnose struma-derived thyroid-type carcinomas. The outcome of struma-derived thyroid-type carcinomas is generally favorable.

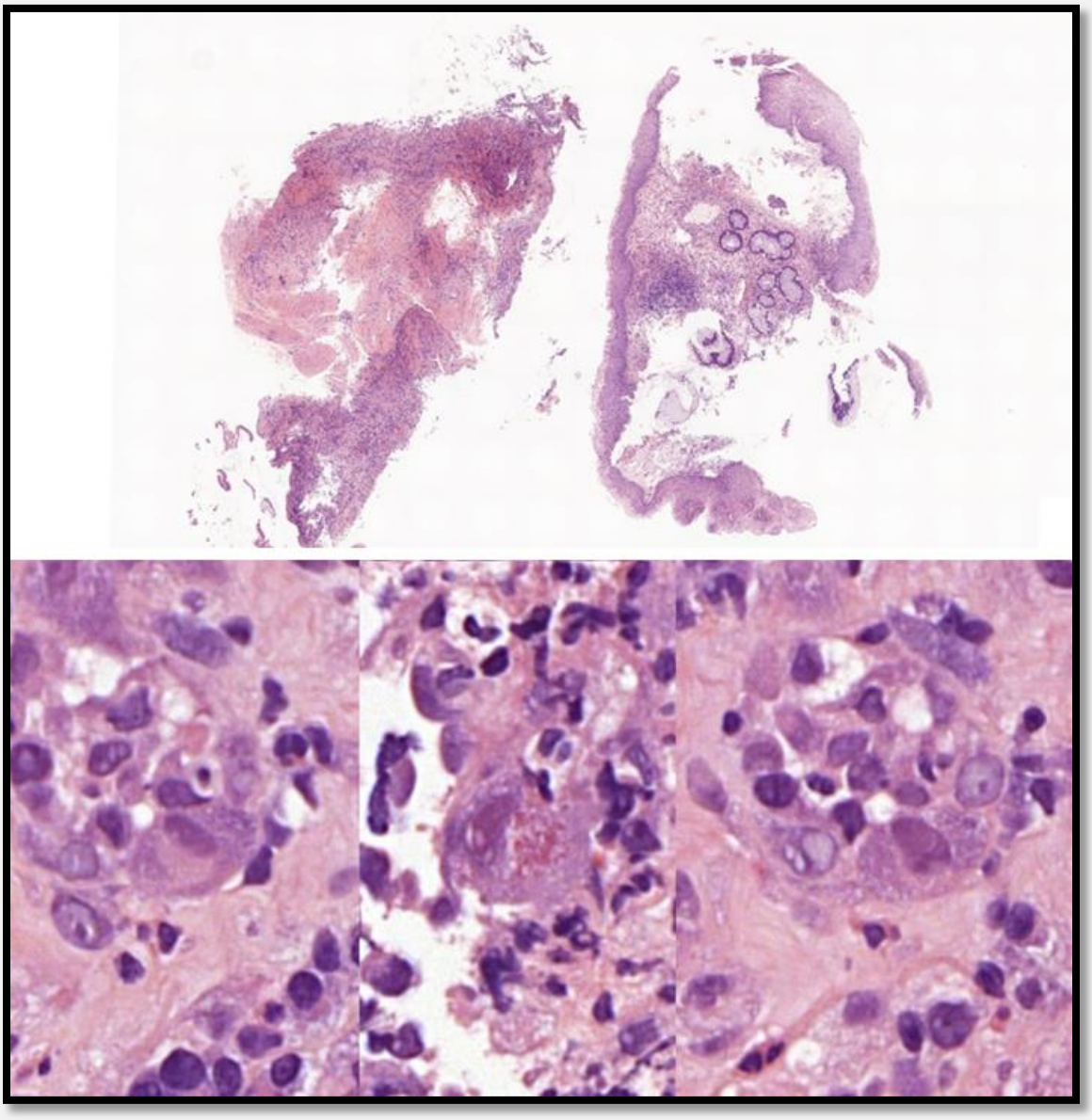
Reference:

1. World Health Organization. (2014). WHO classification of tumours of the female reproductive organs. Robert J. Kurman (Ed.). Internat. Agency for Research on Cancer.

Case 18

69-year-old male, per rectal bleeding, colonic biopsy.

Targeted Diagnosis: **Cytomegalovirus colitis**



Case 18

Submitted Diagnoses by Participating Institutions	Number
CMV colitis/ Cytomegalovirus colitis/ Viral infection suggestive of CMV/ CMV proctitis	14
Chronic active proctitis with viral infection. Differential diagnosis CMV or HSV. Require special stain for confirmation./ Viral proctitis, Cytomegalovirus or Herpes simplex virus	2
Benign ulcer, possible amoebic colitis.	1
Atypical subepithelial glands suspicious of well differentiated adenocarcinoma with CMV proctitis	1
Anal Intraepithelial Neoplasia (AIN) II and Ulcerated tissue - for infective screening (ancillary test : PASS and CMV staining)	1
AIN 2	1

Educational notes:

1. There are two fragments of tissue; the colonic tissue fragment is extensively ulcerated with neutrophilic infiltrates. The lamina propria contains mixed lymphocytic and plasma cell infiltrates. A few enlarged cells display characteristic nuclear and cytoplasmic inclusion bodies that have a distinctive magenta tinctorial quality. The other fragment is covered by stratified squamous epithelium with reactive changes. The lamina propria also contains mixed lymphocytic and plasma cell infiltrates.
2. The acute colitis pattern features cryptitis, crypt abscesses, erosions, and ulcerations in the absence of chronicity. Although non-specific, this pattern of injury is commonly caused by (1) acute viral and bacterial infections, (2) medications and (3) emerging or partially treated inflammatory bowel disease.
3. Recognition of viral cytopathic effect of cytomegalovirus (CMV), i.e. cytomegaly with characteristic nuclear and cytoplasmic inclusions, is the key for this diagnosis. Endothelial cells, macrophages, and stromal cells are mostly affected by CMV. Immunohistochemistry against CMV can be an aid in densely inflamed and ulcerated biopsies. Apart from CMV, herpes simplex virus and adenovirus are likely to be encountered in routine preparation. In herpes simplex virus, multinucleated cells with nuclear molding and chromatin margination are observed. Epithelial cells infected by adenovirus show irregular basal amphophilic nuclei associated with vacuolated cytoplasm.

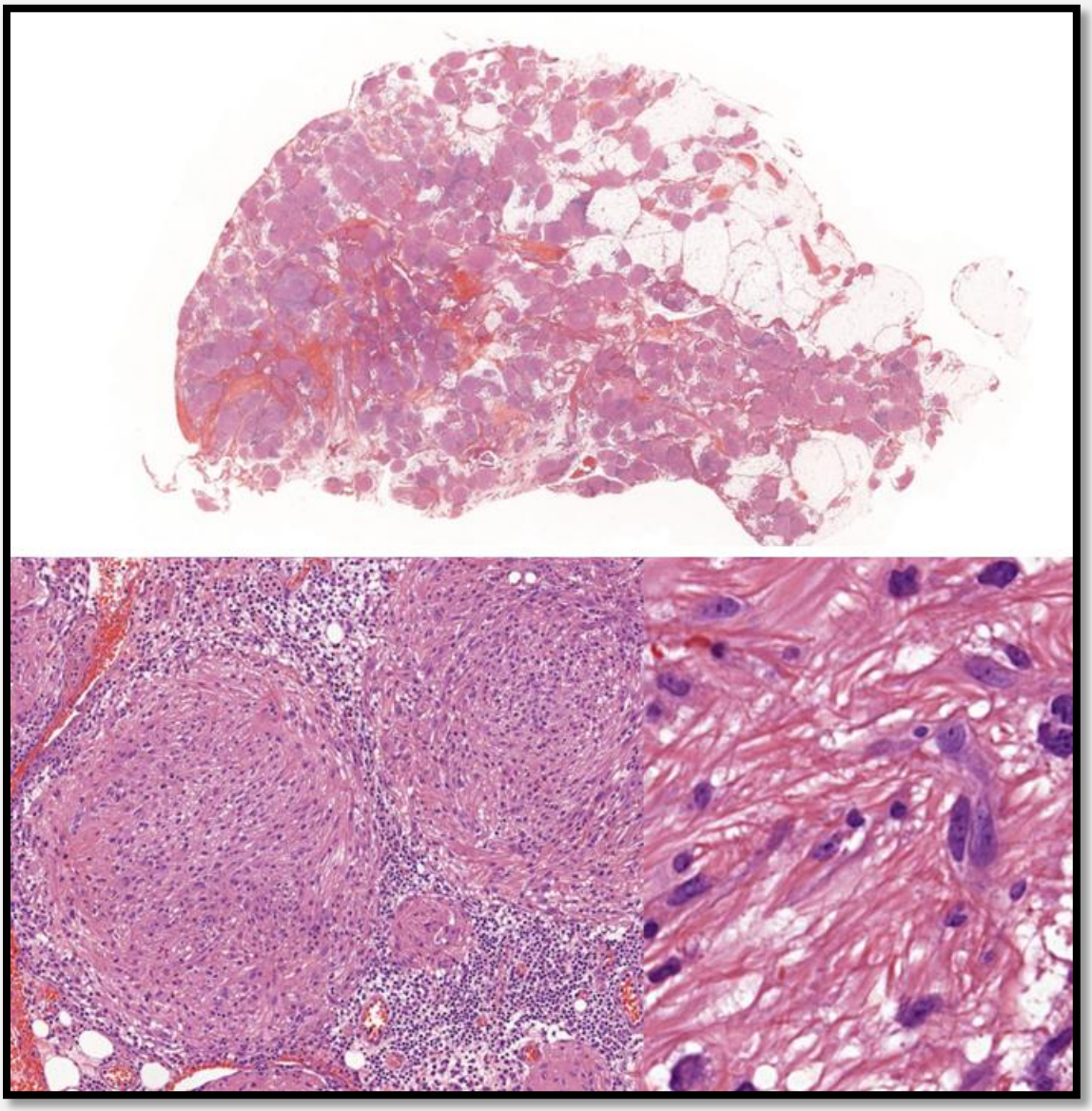
Reference:

1. Talbot, I., Price, A., & Salto-Tellez, M. (2006). Biopsy pathology in colorectal disease. CRC Press.
2. Arnold, C. A., Lam-Himlin, D. M., & Montgomery, E. A. (2015). Atlas of Gastrointestinal Pathology: A Pattern Based Approach to Non-neoplastic Biopsies;[includes Interactive Ebook with Complete Content]. Wolters Kluwer.

Case 19

12-year-old female, unilateral ovarian tumor and peritoneal nodule. One representative section from peritoneal nodule.

Targeted Diagnosis: **Gliomatosis peritonei**



Case 19

Submitted Diagnoses by Participating Institutions	Number
Gliomatosis peritonei/ peritoneal gliomatosis	19
Leiomyomatosis peritonealis	1

Educational notes:

1. There are miliary nodules composed of mature glial tissue with fibrillary background associated with lymphocytic infiltrates in the adipose tissue. These are peritoneal implants (gliomatosis peritonei) usually associated with mature or immature teratomas.
2. Teratomas and implants are graded according to the aggregate amount of immature neuroepithelium on any single slide. Peritoneal implants composed entirely gliomatosis peritonei are graded as grade 0. Presence of gliomatosis peritonei is nonetheless associated with excellent clinical outcome.
3. Generous sampling of primary ovarian teratomas as well as implants is important as not to under sample the immature components.

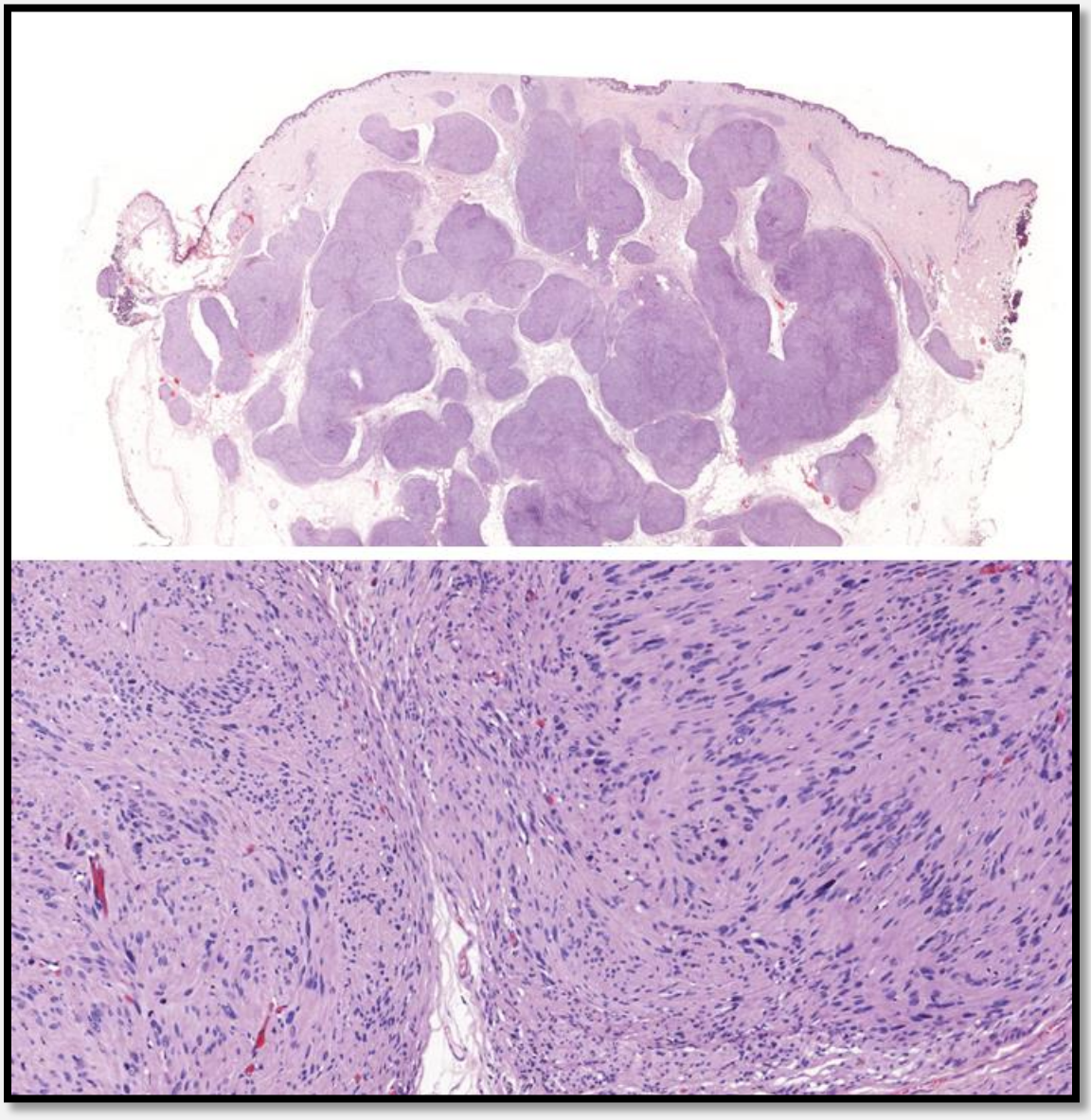
Reference:

1. World Health Organization. (2014). WHO classification of tumours of the female reproductive organs. Robert J. Kurman (Ed.). Internat. Agency for Research on Cancer.
2. Clement, P. B., & Young, R. H. (2014). Atlas of gynecologic surgical pathology 3rd edition. Philadelphia, Pa, USA: Saunders.

Case 20

50-year-old female, back lump. Excision biopsy.

Targeted Diagnosis: **Plexiform schwannoma**



Case 20

Submitted Diagnoses by Participating Institutions	Number
Plexiform schwannoma	15
Schwannoma	5

Educational notes:

1. This tumor shows plexiform architecture in the dermis, composed of nodules with peripheral thin layers of fibrous capsule. The nodules are composed of spindle cells with focal degenerative nuclear atypia. Nuclear palisading forming Verocay bodies is evident.
2. Plexiform schwannoma is a unique variant of schwannoma. It should be distinguished from plexiform neurofibroma as the latter is typically associated with neurofibromatosis type 1.
3. Although plexiform schwannomas are commonly solitary, sporadically occurring tumors, presence of multiple lesions has weak association with neurofibromatosis type 2 and schwannomatosis.

Reference:

1. World Health Organization. (2016). WHO classification of tumours of the central nervous system. Louis DN (Ed.). Internat. Agency for Research on Cancer.