International Academy of Pathology
Malaysian Division

FINAL REPORT

QUALITY ASSURANCE PROGRAM
GENERAL DIAGNOSTIC HISTOPATHOLOGY
CYCLE 02/2020

NOTES FROM THE COORDINATOR

1. For this cycle 02/2020, a total of 24 institutions responded online by the closing date of 15 November 2020.

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 02/2020 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. Wan Syahira Ellani, Dr. Adam Malik, Dr. Suhaila Abdullah, Dr Hairulhasliza Harun, Dr. Chew Bee See, Dr. Yusri Yusuf and Dr. Nurul Akmar Misron.

Prepared by,

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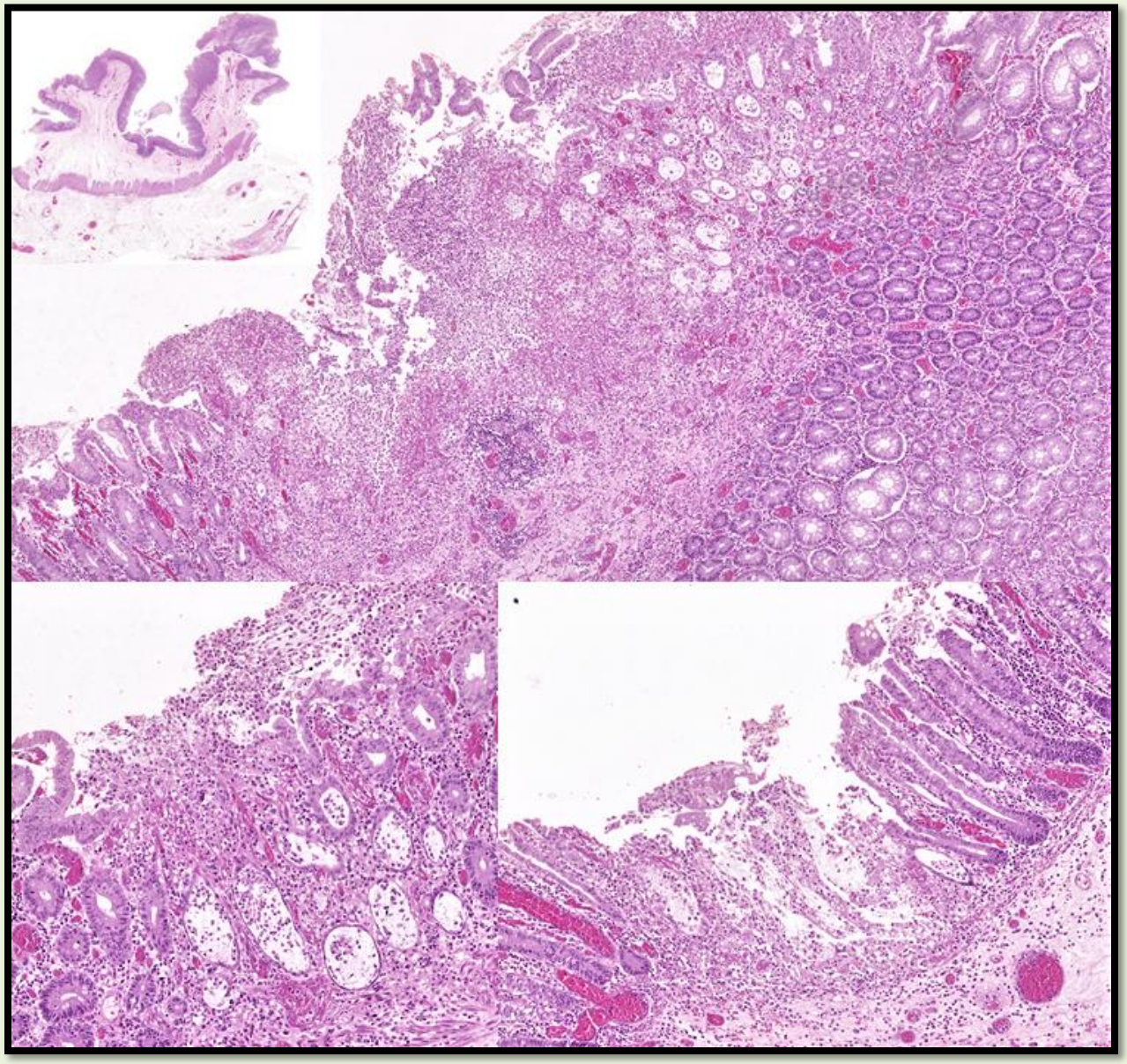
Coordinator for IAP-MD QAP

Case 11

Case 11: A 58-year-old male presented with abdominal pain and distension for a week. He had underlying smear positive pulmonary tuberculosis on intensive phase of treatment. One representative section.

Targeted Diagnosis: **Acute colitis with pseudomembranous pattern**



Case 11

Submitted Diagnoses by Participating Institutions	Number	
Pseudomembranous colitis	19	Acceptable
Ischaemic colitis with differential of pseudomembranous colitis	1	Acceptable
Active colitis with ulceration, possible infective cause. Need special stain ie PAS for confirmatory	1	Acceptable
Amoebic colitis	3	

Educational notes:

1. This segment of colon shows acute colitis with mucosal necrosis involving the deeper crypts. This is associated with pseudomembrane formed at surface composed of fibrin, neutrophils and cellular debris.
2. There are several causes accounting for acute colitis with pseudomembranous pattern. The well recognized etiology includes post antibiotic *C. difficile* toxin. Nonetheless "pseudomembranous colitis" is not synonymous to *C. difficile* colitis as ischemia and enterohemorrhagic *E. coli* and *Shigella* infections could result in similar histological features.
3. Distinction between ischemic colitis and *C. difficile* colitis is impossible histologically even though lamina propria hyalinization is regarded as a feature favoring ischemia. Gross findings of the resected colon provide better clue as *C. difficile* colitis involves the colon continuously whereas ischemic colitis involves the colon segmentally especially the watershed territories of blood supply, i.e. the splenic flexure (Griffiths' point) and rectosigmoid junction (Sudeck's point).
4. For infectious colitis causing a pseudomembranous pattern, it depends on stool studies for diagnosis.

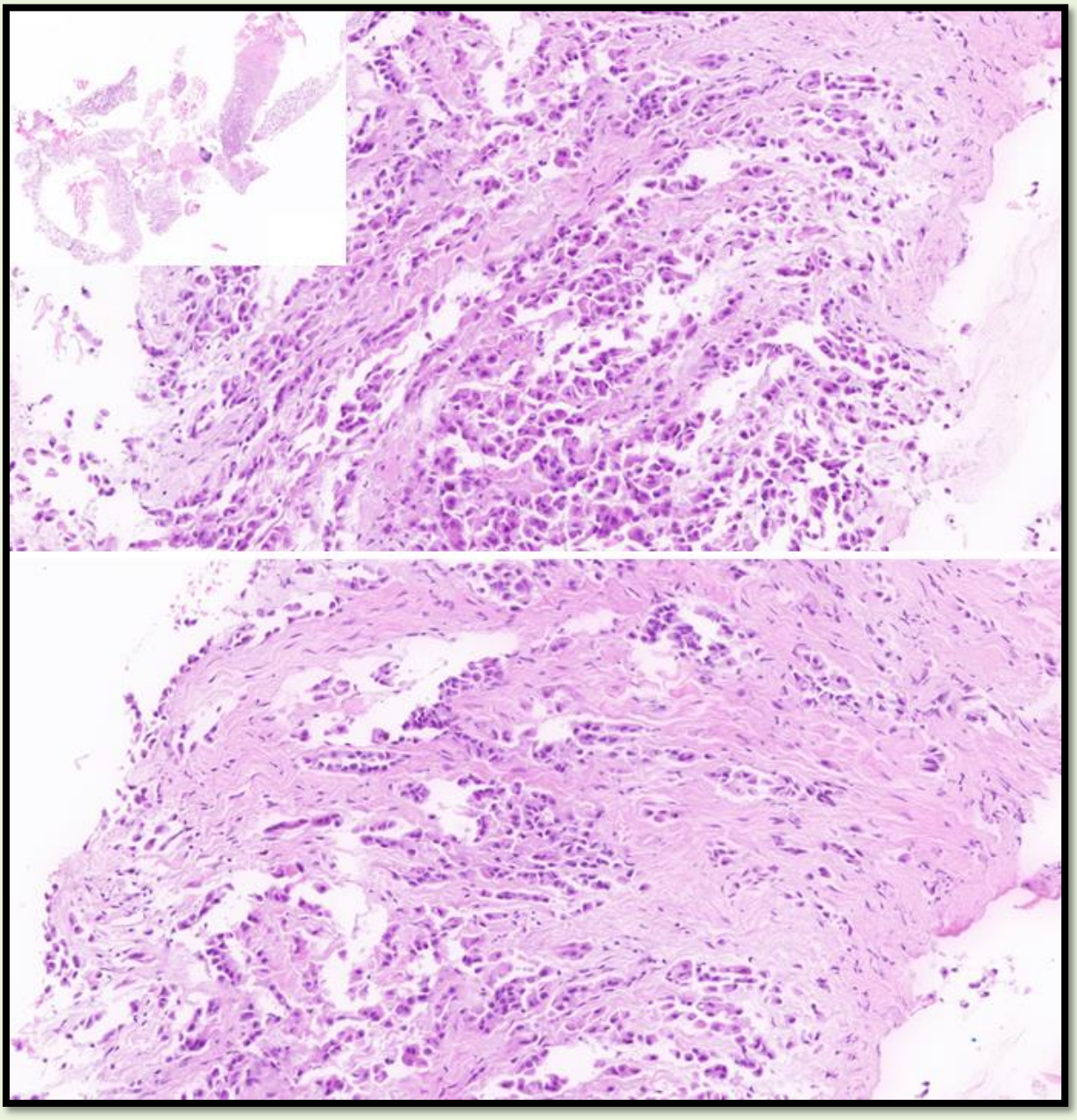
Reference:

1. Arnold, C., Lam-Himlin, D., & Montgomery, E. A. (2014). Atlas of Gastrointestinal Pathology: A Pattern Based Approach to Non-Neoplastic Biopsies. Lippincott Williams & Wilkin.
2. Odze, Robert D., and John R. Goldblum (2015). Odze and Goldblum Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas. Elsevier Health Sciences.

Case 12

Case 12: A 50-year-old male. CT scan showed circumferential nodular pleural thickening. One representative section.

Targeted Diagnosis: **Epithelioid mesothelioma**



Case 12

Submitted Diagnoses by Participating Institutions	Number	
Mesothelioma	5	Acceptable
Mesothelioma. Differential diagnosis is metastatic adenocarcinoma. For immunohistochemistry to confirm diagnosis/ Metastatic adenocarcinoma TRO mesothelioma	7	Acceptable
Malignant lesion, differentials include Mesothelioma, Adenocarcinoma and Malignant Melanoma. Need IHC for confirmatory/ Malignant melanoma. Differential diagnosis includes malignant mesothelioma and metastatic carcinoma/ Metastatic Adenocarcinoma most likely Mucinous Adenocarcinoma. Need few IHC stain to know the primary (lung?) and exclude mesothelioma and melanoma (pigment present)	9	Acceptable
Metastatic melanoma. Differential of malignant mesothelioma	1	Acceptable
Metastatic malignant neoplasm, differential diagnosis include melanoma or carcinoma (IHC needed)	1	
Metastatic melanoma	1	

Educational notes:

1. The biopsy shows fragments of fibro-muscular tissue. Infiltration by discohesive clusters of epithelioid malignant cells displaying pleomorphic hyperchromatic nuclei and moderate eosinophilic cytoplasm is evident. Given the CT findings of circumferential nodular pleural thickening, epithelioid mesothelioma is highly considered, which is further confirmed by immunohistochemistry for mesothelial markers.
2. Demonstration of tissue invasion separates reactive mesothelial hyperplasia from epithelioid mesothelioma. In the presence of tumor mass, tissue invasion is not required for the diagnosis of epithelioid mesothelioma.
3. Pleural epithelioid mesothelioma needs to be differentiated from metastatic carcinoma. This is aided by a panel of immunohistochemical markers. International Mesothelioma Interest Group (IMIG) recommends that at least 2 mesothelial and 2 carcinoma markers to be included; in addition, cytokeratin (a broad spectrum anticytokeratin antibody) should be included as virtually all mesotheliomas are cytokeratin positive. Keratin-negative malignant epithelioid neoplasm raises the possibility of malignant melanoma, epithelioid hemangioendothelioma, angiosarcoma or lymphoma in a case of pleural thickening. IMIG recommends calretinin, cytokeratin 5 or 5/6, WT1 and podoplanin (D2-40) as best positive mesothelioma markers, whereas claudin 4, MOC31, and BER-EP4 as the best overall carcinoma markers. TTF-1 and napsin A are useful markers to add if an adenocarcinoma of pulmonary origin is considered. p40 (or p63) will aid in differentiating squamous cell carcinoma from epithelioid mesothelioma.

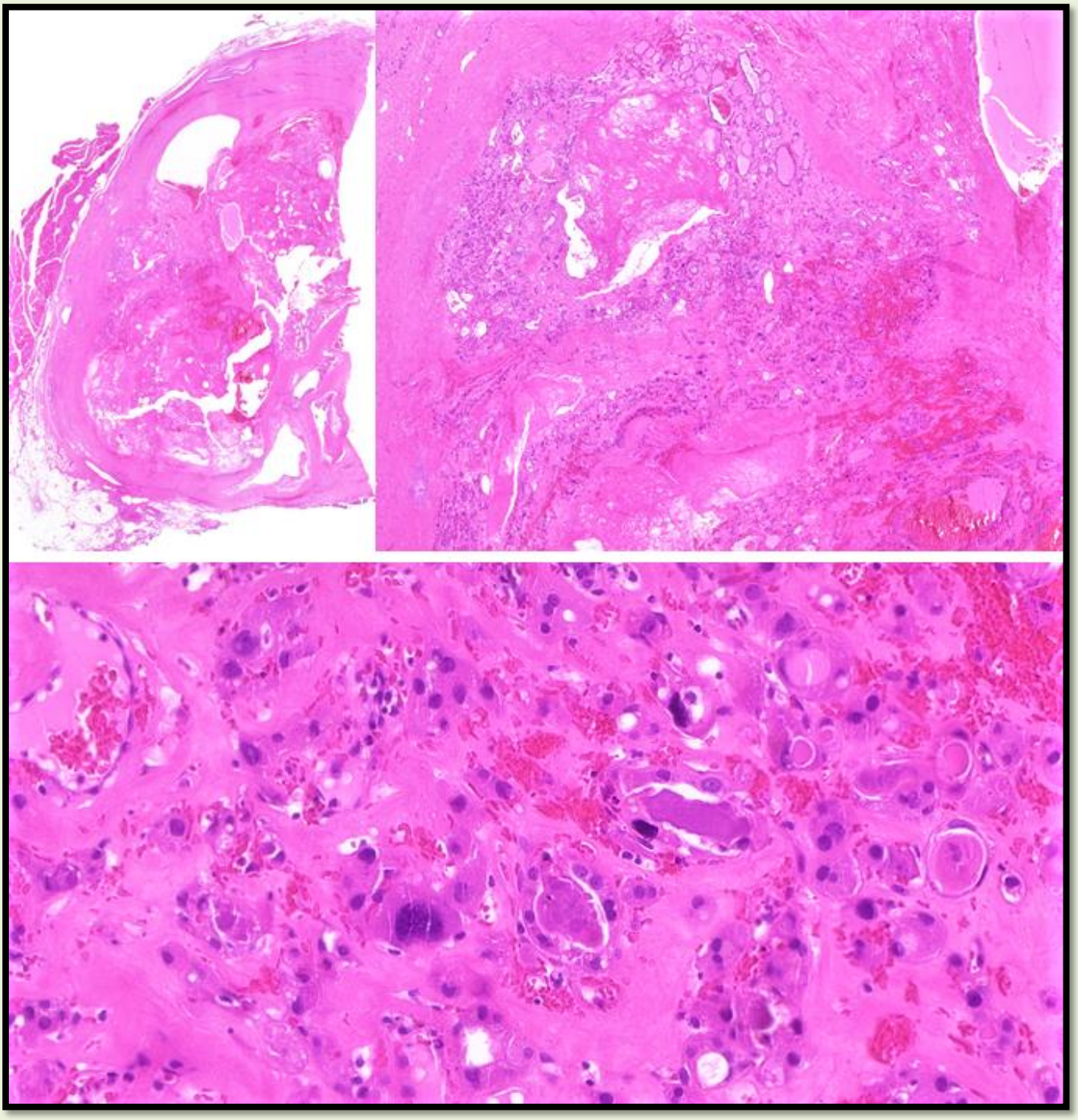
Reference

1. Husain, Aliya Noor, et al. "Guidelines for pathologic diagnosis of malignant mesothelioma 2017 update of the consensus statement from the International Mesothelioma Interest Group." Archives of pathology & laboratory medicine 142.1 (2018): 89-108.

Case 13

Case 13: A 56-year-old female had a previous history of radio-iodine therapy for hyperthyroidism. Thyroidectomy was performed. One representative section.

Targeted Diagnosis: **Radiation thyroiditis**



Case 13

Submitted Diagnoses by Participating Institutions	Number	
Radiation thyroiditis/ radioactive Iodine -induced changes/ Post-Radioiodine changes	22	Acceptable
Nodular Hyperplasia with radiation effect.	2	Acceptable

Educational notes:

1. The thyroid gland shows extensive fibrosis, fibrinoid necrosis and hemorrhage. Scattered atrophic follicles and large bizarre epithelial and stromal cells displaying hyperchromatic and pleomorphic nuclear changes are observed. Correlation with the previous history of radio-iodine therapy, these features are those of chronic stage of radiation thyroiditis.
2. Radiation thyroiditis occurs following external radiation or iodine-131 treatment for Graves disease. In acute stage several weeks after exposure, congestion, edema, acute inflammation and follicular disruption are observed. There may be severe degenerative changes associated with cytoplasmic vacuolization, necrosis and desquamation of epithelial cells. Vascular fibrinoid necrosis, thrombi and hemorrhage may be seen.
3. In chronic stage, the thyroid gland is characterized by atrophic follicles, fibrosis, mild lymphocytic infiltration, and squamous or oncocytic metaplasia. Large bizarre cells with hyperchromatism and pleomorphism are observed, which should not be mistaken as malignancy. Vascular changes such as intimal thickening and fibrosis may be noted.
4. In addition, hyperplastic nodules, either single or multiple, with cystic degeneration may occur. Neoplasm such as papillary carcinoma, follicular adenoma and follicular carcinoma may occur in post-irradiated thyroid.

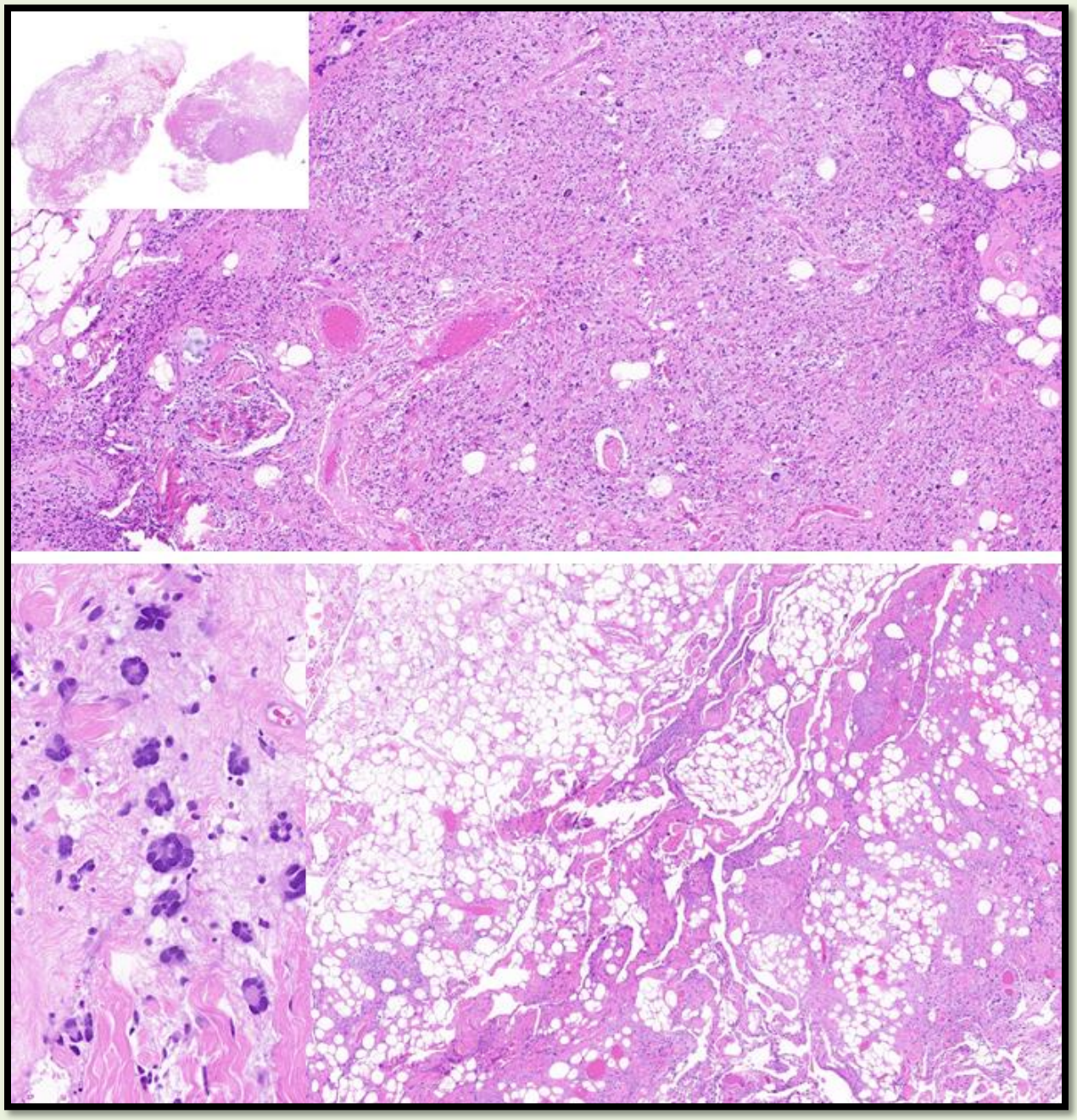
Reference

1. Douglas R. Gnepp and Justin A. Bishop Gnepp's Diagnostic Surgical Pathology of the Head and Neck. 3rd edition. Elsevier, 2020.

Case 14

Case 14: A 75-year-old male had a 3cm-left forearm swelling for a year. One representative section.

Targeted Diagnosis: **Pleomorphic lipoma**



Case 14

Submitted Diagnoses by Participating Institutions	Number	
Pleomorphic/Spindle cell lipoma/ Pleomorphic Lipoma. CD34 stain is needed to exclude Atypical Lipomatous Tumour	22	Acceptable
Atypical lipomatous tumour	2	

Educational notes:

1. This lipomatous lesion is composed of a triad of bland-spindle cells, mature adipocytes and ropy collagen bundles. Pleomorphic spindle cells and numerous multinucleated floret-like giant cells are noted showing flower-petal arrangement of hyperchromatic nuclei. These features are those of pleomorphic lipoma.
2. Pleomorphic lipoma and spindle cell lipoma represent different morphological spectrum of the same benign lipomatous neoplasm. Compared to spindle cell lipoma, pleomorphic lipoma shows additional pleomorphic spindle cells and multinucleated floret-like giant cells.
3. The differential diagnosis of pleomorphic lipoma includes atypical spindle cell/pleomorphic lipomatous tumor (AS/PLT), and atypical lipomatous tumor/ well differentiated liposarcoma (ATL/WDLPS).
4. AS/PLT is a new benign entity characterized by ill-defined tumor margin showing pleomorphic lipoma-like areas. Histologically, AS/PLT differs from pleomorphic lipoma by presence of pleomorphic multinucleated giant cells and pleomorphic lipoblasts.
5. ATL/WDLPS is a locally aggressive adipocytic tumor characterized by presence of focal bizarre stromal cells exhibiting marked nuclear hyperchromasia, which can be identified within fibrous septa or blood vessel walls. Lipoblasts may vary from none to many. Differs from pleomorphic lipoma, ropy collagen bundles and mast cells are usually not observed in ATL/WDLPS. ATL/WDLPS shows MDM2 (and/or CDK4) amplification, which is not observed in pleomorphic lipoma or AS/PLT.
6. Of note, mere presence of lipoblasts is less important than the histological background where lipoblasts are encountered in making a diagnosis of adipocytic tumors. Pleomorphic lipoma is one of those benign adipocytic tumors containing lipoblasts in as many as 50% of cases. On the other hand, ATL/WDLPS may contain none.

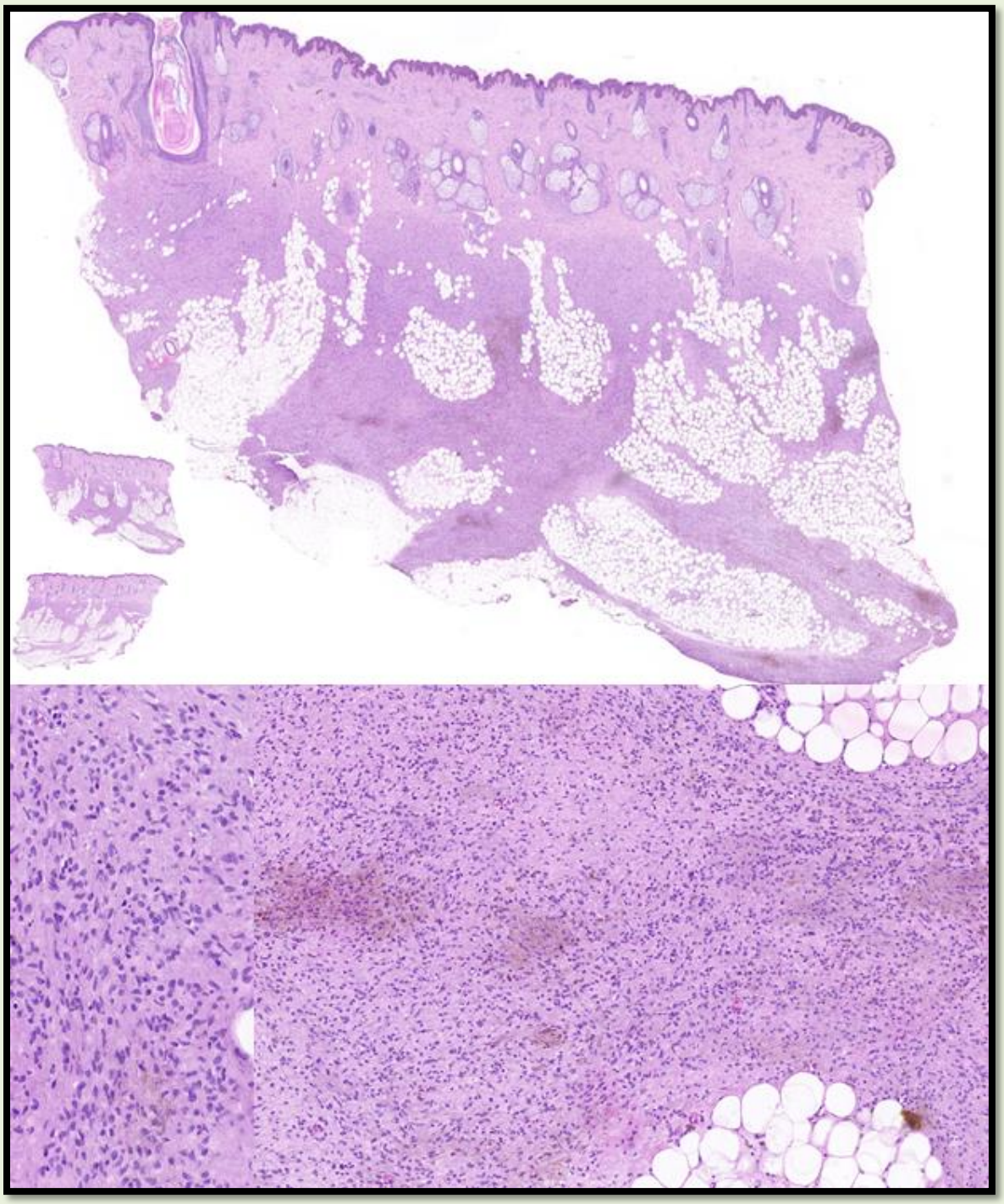
Reference

1. WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours. Lyon (France): International Agency for Research on Cancer; 2020. (WHO classification of tumours series, 5th ed.; vol. 3).
2. Creytens, David, et al. ""Atypical" Pleomorphic Lipomatous Tumor." The American Journal of Surgical Pathology 41.11 (2017): 1443-1455.

Case 15

Case 15: A 23-year-old female. Left facial skin lesion was excised. One representative section.

Targeted Diagnosis: **Diffuse pigmented neurofibroma/ congenital melanocytic nevus**



Case 15

Submitted Diagnoses by Participating Institutions	Number	
Melanotic neurofibroma/ Pigmented neurofibroma/ Diffuse, pigmented neurofibroma/	10	Acceptable
Benign pigmented spindle cell tumour, suggestive of pigmented neurofibroma. IHC to exclude dermatofibrosarcoma protruberans and melanocytic tumour/ Spindle cell lesion. Differential diagnosis includes deep penetrating nevi, diffuse neurofibroma, fibromatosis, DFSP, dermatofibroma	6	Acceptable
Congenital lipomatous melanocytic naevus	1	Acceptable
Benign Deep Dermal and Subcutaneous Lesion. Differential could be Dermal Melanocytosis, Dermal Melanocyte Hamartoma, Cutaneous Neurocrictic Hamartoma etc.	1	Acceptable
Congenital blue naevus/ blue nevus/ cellular blue nevus	3	
Intradermal melanocytic naevus	1	
Pigmented dermatofibrosarcoma protuberans (Bednar tumour)	1	
morphea/scleroderma	1	

Educational notes:

1. The skin shows an infiltrative lesion located in the deep dermis and subcutis spreading along the fibrous septa and into the fat, giving rise to honey-comb pattern in areas. The lesion is composed of bland-looking, loosely arranged, oval-shaped spindle cells. Fine granular melanin pigments are noted in foci. There is no storiform architecture, nuclear atypia or mitosis.
2. Further history provided that the lesion was clinically diagnosed as congenital melanocytic nevus. Histologically, the differential diagnosis lies between diffuse pigmented neurofibroma and congenital neuroid melanocytic nevus as these two entities displays overlapping histological features with deep infiltration of spindle cells with neuroid features. Lack of junctional or superficial nevoid component would favor diffuse pigmented neurofibroma over congenital neuroid melanocytic nevus.
3. Although honey-comb pattern is observed in this lesion, this lesion is differentiated from Bednar tumor (pigmented dermatofibrosarcoma protuberans) as this lesion lacks the repetitive storiform pattern. S100 protein and CD34 immunohistochemistry would help this distinction as Bednar tumor is CD34-positive but S100 protein-negative.
4. This lesion is differentiated from blue nevi and related lesions as these lesions are characterized by the presence of dendritic melanocytes. Dendritic melanocytes are bipolar or stellate with lengthy dendritic processes. Cellular blue nevus shows cellular foci of round, oval, or fusiform cells that constitute at least one-third to one-half of the tumor in addition to the dendritic melanocytes. The overall architecture is multilobular or plexiform.

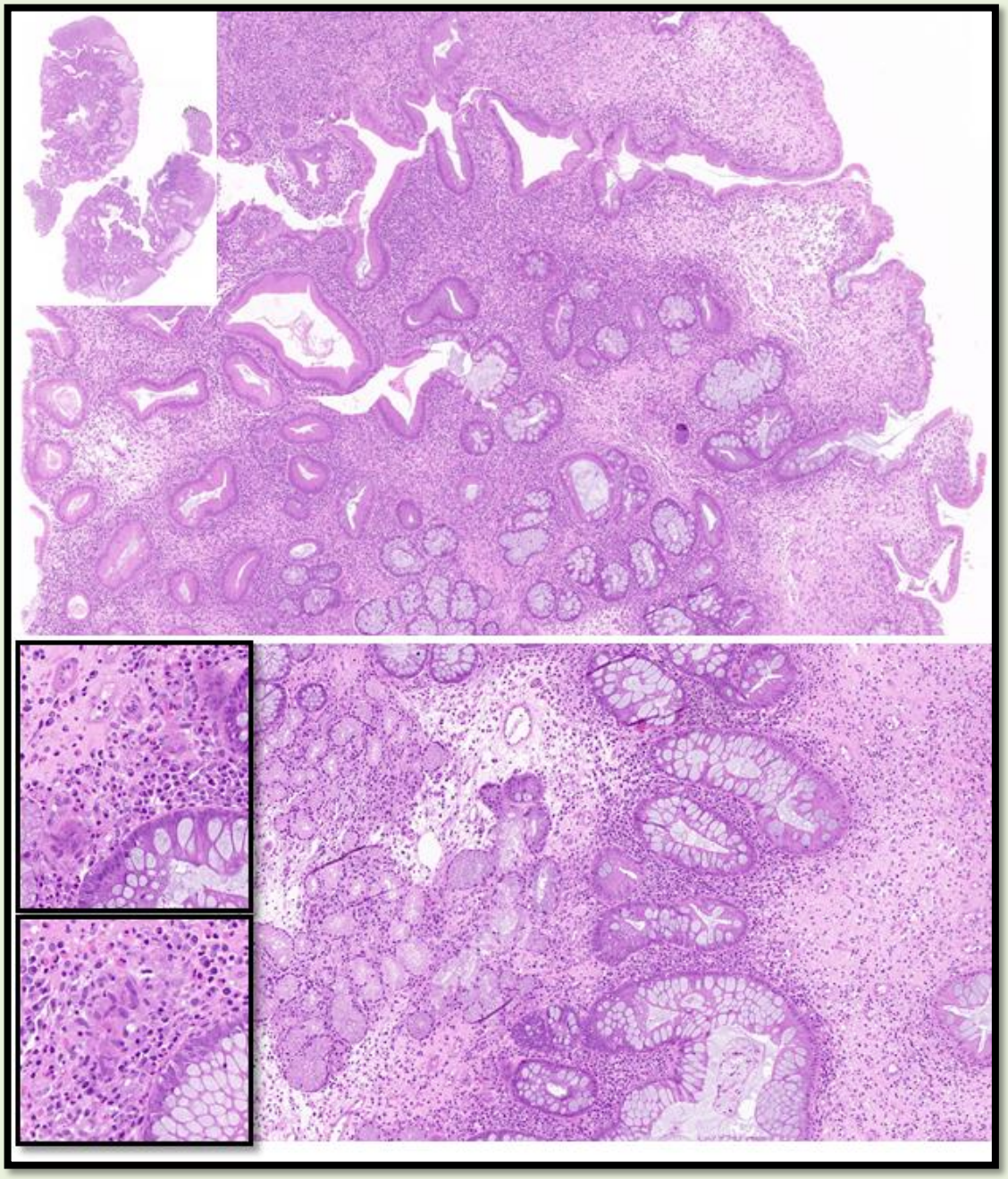
Reference

1. Enzinger and Weiss's Soft Tissue Tumors.7th ed. JR Goldblum, AL Folpe, and SW Weiss, eds. Philadelphia, PA: Elsevier, 2020
2. Barnhill, Raymond L., et al. Dermatopathology. 4th edition. McGraw Hill Professional, 2020

Case 16

A 52-year-old male presented with diarrhea and loose stools for 5 months. Colonoscopy and polypectomy were performed. One representative section.

Targeted Diagnosis: **Inflammatory pseudopolyp in the background inflammatory bowel disease (IBD).**



Case 16

Submitted Diagnoses by Participating Institutions	Number	
Inflammatory pseudopolyp with underlying IBD/ Inflammatory pseudopolyp with chronicity changes/Pseudopolyp with active colitis and chronicity features, consistent with IBD/ Inflammatory polyp tro IBD	5	Acceptable
Inflammatory polyp TRO IBD or CMV Colitis. Kindly do IHC. / Ulcer with acute on chronic inflammation and CMV infection; features suggestive of inflammatory bowel disease/ Inflammatory pseudopolyp with features of chronic active colitis and cmv colitis consistent with inflammatory bowel disease favoring Crohns.	3	Acceptable
Inflammatory polyp with gastric/ pyloric gland/ antral type metaplasia/ gastric heterotopia	4	Acceptable
Inflammatory polyp/ Benign polyp. Differentials: 1. Inflammatory pseudopolyp, 2. Hyperplastic polyp	5	
Juvenile polyp/ Retention polyp/ inflammatory polyp vs juvenile polyp	3	
Hamartomatous polyp	1	
Sessile serrated adenoma/ sessile serrated lesion	2	
Malakoplakia	1	

Educational notes:

1. This polypoid colonic tissue fragment shows active inflammation with surface erosion and lamina propria expansion containing areas of dense mixed acute and chronic inflammatory infiltrates. Marked chronic changes such as focal villiform mucosal surface, moderate crypt distortion with variably dilated and irregular crypts, pyloric gland metaplasia and dense lymphoplasmacytic infiltrates in the lamina propria are noted. A few pericryptal microgranulomas are observed. These changes are consistent with inflammatory pseudopolyp in the background inflammatory bowel disease (IBD), especially Crohn disease.
2. This biopsy shows chronic colitis pattern with pyloric gland metaplasia (always abnormal in colon indicating chronic mucosal injury), crypt distortion, villiform mucosal surface and dense lamina propria lymphoplasmacytic infiltrates. Presence of microgranuloma (at least five epithelioid macrophages) unrelated to crypt injury (non-cryptolytic granulomas) in the background of chronic colitis is very reliable to distinguish Crohn disease from ulcerative colitis. Nonetheless, granulomas per se are not diagnostic of Crohn disease and they occur in tuberculosis and, rarely, in other infective colitides.
3. Inflammatory pseudopolyps are commonly found in patients with inflammatory bowel disease. They occur in other colitides as well as sites of ulcers and anastomoses.

Reference:

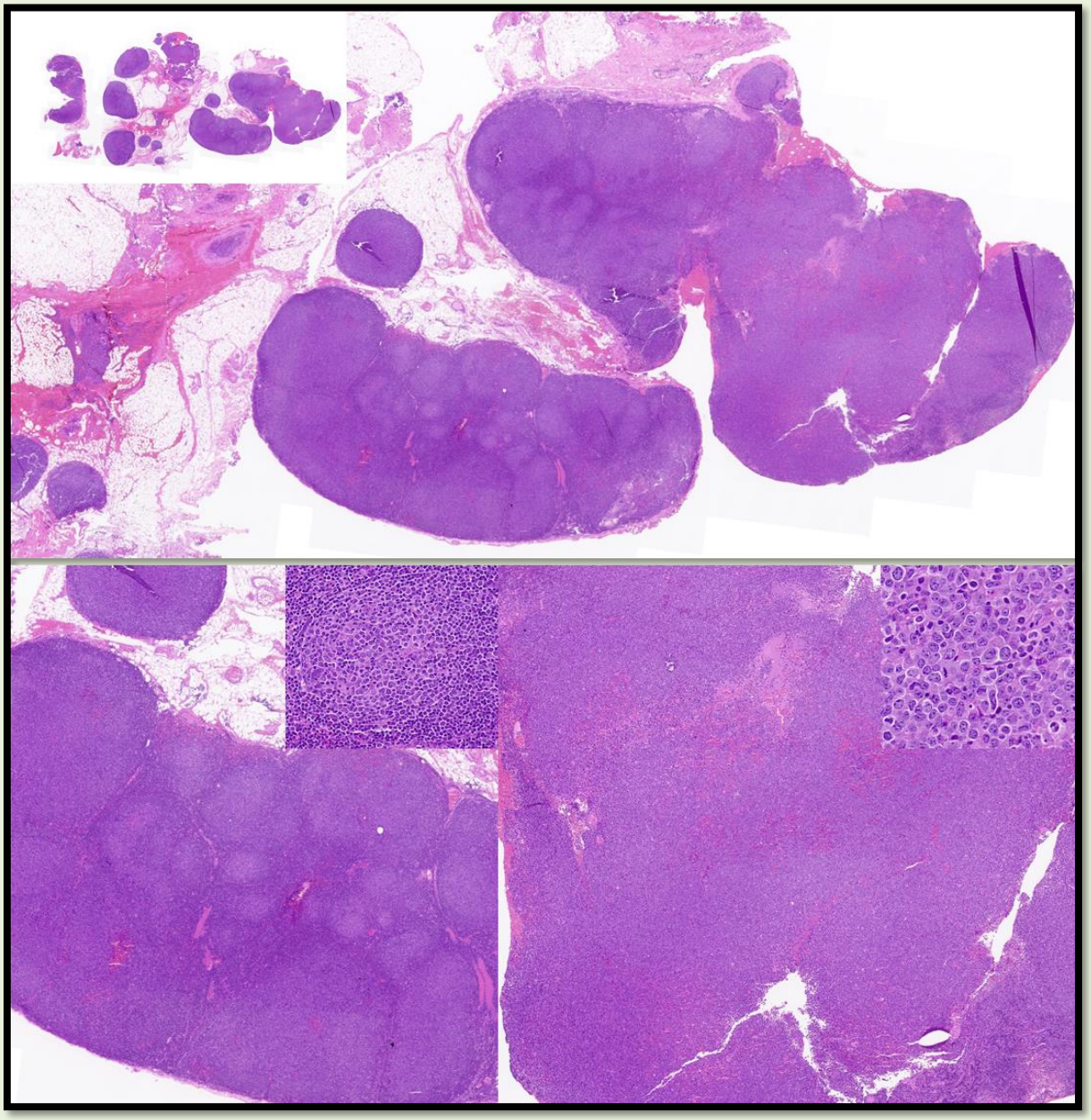
1. Feakins, Roger M. "Inflammatory bowel disease biopsies: updated British Society of Gastroenterology reporting guidelines." Journal of clinical pathology 66.12 (2013): 1005-1026.
2. Arnold, C., Lam-Himlin, D., & Montgomery, E. A. (2014). Atlas of Gastrointestinal Pathology: A Pattern Based Approach to Non-Neoplastic Biopsies. Lippincott Williams & Wilkin.

Case 17

Case 17: A 46-year-old male presented with an enlarged left posterior cervical lymph node. One representative section.

Targeted Diagnosis:

1. **Diffuse large B cell lymphoma 20% and**
2. **Follicular lymphoma, follicular pattern, grade 3B**



Case 17

Submitted Diagnoses by Participating Institutions	Number	
Follicular lymphoma, (Grade 3B or Grade 3A) with diffuse large cell lymphoma/ High-grade follicular lymphoma with areas of diffuse large B cell lymphoma (DLBCL) transformation. / Diffuse large cell lymphoma arising from follicular lymphoma. Further immunohistochemical studies are required for diagnosis/ Lymphoma. Base on morphology Follicular Lymphoma is suspected. CD21/CD23 are needed to excluded DLBCL component. Other differential could be anaplastic T cell lymphoma./ High grade Non Hodkin lymphoma, with follicular pattern and large cell transformation	17	Acceptable
Follicular lymphoma grade 3A with follicular and diffuse pattern (IHC needed)	1	Acceptable
Follicular lymphoma/ Follicular lymphoma, grade 1B/ Non Hodgkin lymphoma suggestive of follicular lymphoma	4	
Non-Hodgkin Lymphoma (IHC for further subtyping)	1	
Malignant infiltration, differential include Non-Hodgkin Lymphoma and Undifferentiated Carcinoma. Need IHC for confirmatory.	1	

Educational notes:

1. Multiple lymph nodes are involved by follicular lymphoma (grade 3b) displaying closely packed, ill-defined neoplastic follicles containing mostly exclusively of centroblasts. Most of the lymph nodes show follicular pattern. There is a diffuse area (about 20%) exclusively composed of sheets of centroblasts, consistent with diffuse large B cell lymphoma. Relevant immunohistochemistry confirms the diagnosis.
2. Neoplastic follicles of follicular lymphoma are characterized by loss of zoning and composed of randomly distributed centrocytes and centroblasts or exclusively centroblasts in grade 3b. They have attenuated mantle zones. Immunohistochemically, the neoplastic follicles are positive for B-cell-associated antigens (CD20, CD79a) and usually positive for BCL2, BCL6, and CD10 and negative for CD5 and CD43.
3. Follicular lymphoma is graded by counting the absolute number of centroblasts in 10 neoplastic follicles. Nonetheless, diffuse area can be observed in follicular lymphoma. A diffuse area is defined as an area completely lacking follicles as evidenced by the absence of follicular dendritic cell meshwork (CD21+/CD23+). If that diffuse area shows grade 3 cytology (i.e. more than 15 centroblasts per HPF), that area is designated as diffuse large B cell lymphoma. If it shows grade 1-2 cytology (0-15 centroblasts per HPF), that area constitutes the diffuse area of follicular lymphoma, even though the follicular lymphoma can be grade 3 (which is based on assessment of neoplastic follicles).
4. 25 - 35% of patients with follicular lymphoma show transformation or so-called progression to diffuse large B cell lymphoma.

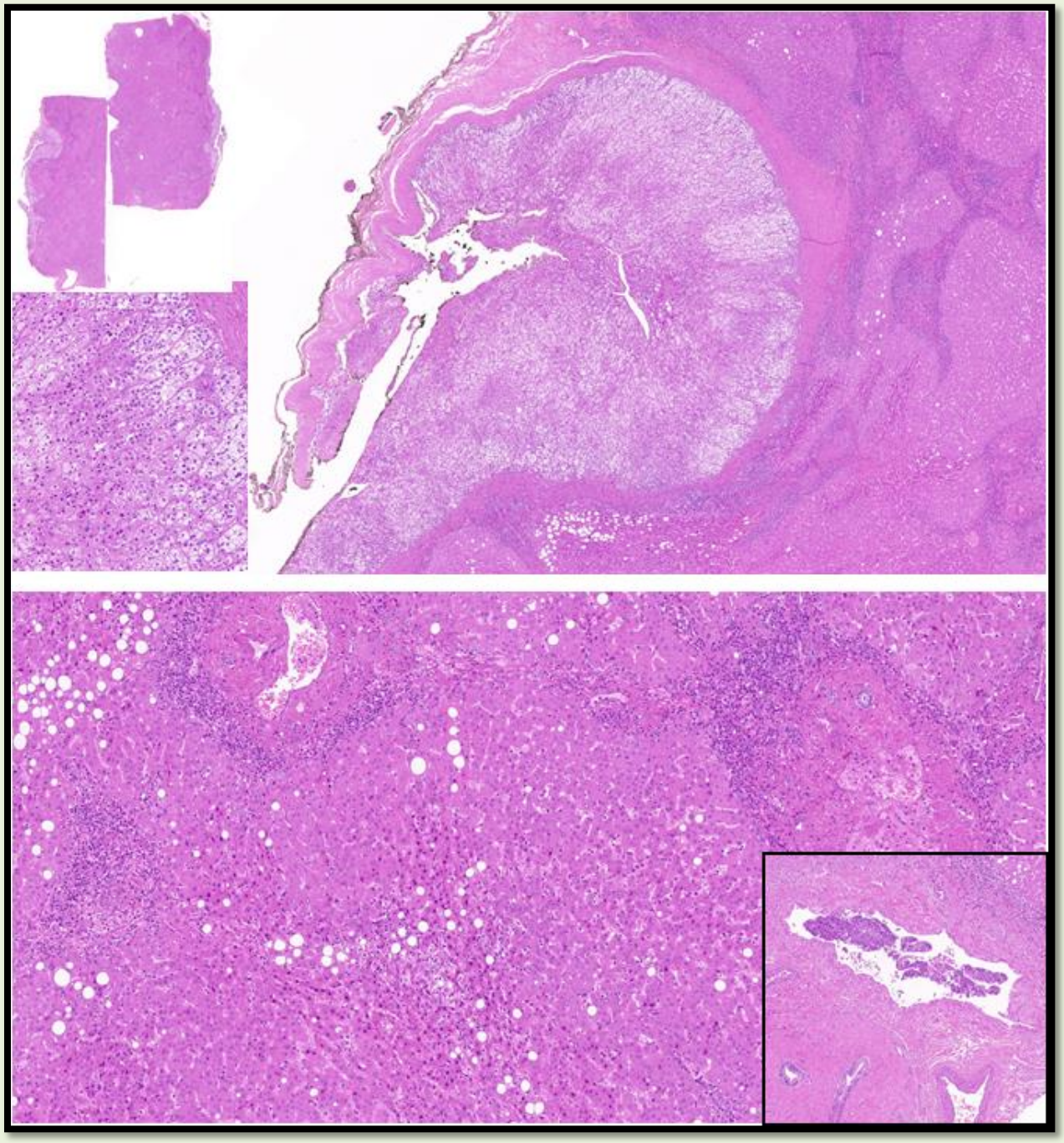
Reference

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J (Eds): WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (Revised 4th edition). IARC: Lyon 2017.

Case 18

Case 18: A 69-year-old male had underlying hepatitis C and hepatocellular carcinoma. On laparotomy, a yellowish patch was noted on the liver surface. One representative section.

Targeted Diagnosis: **Adrenal rest, liver cirrhosis and tumor emboli**



Case 18

Submitted Diagnoses by Participating Institutions	Number	
Adrenocortical heterotropia with tumour emboli and background of cirrhotic liver/ Adrenal gland ectopia, tumour emboli (hepatocellular carcinoma) with cirrhotic liver nodule	7	Acceptable
Hepatic adrenal cortical rest in the background of liver cirrhosis with steatohepatitis/ Hepatic adrenal rest tumor with background of liver cirrhosis/ Adrenal heteropia with background of cirrhotic liver/ Adrenal Gland with congenital fused capsule. The liver shows evidence of cirrhosis with small cell dysplasia.	7	Acceptable
Tumour emboli of hepatocellular carcinoma and ectopic adrenal tissue	2	Acceptable
Adrenal rest in the liver in the background of chronic hepatitis changes	2	Acceptable
Adrenal heterotopia/ Adrenal cortical rest/ Hepatic adrenal rest tumour.	5	Acceptable
Ectopic pancreatic tissue, tumour emboli with background cirrhosis	1	

Educational notes:

1. Adrenal rest is located in the hepatic capsule. The adrenal rest is composed predominantly of zona fasciculata. There are trabeculae of large clear cells with bubbly cytoplasm. The liver shows cirrhosis with marked chronic periportal inflammation and fatty change (5%), consistent with chronic hepatitis C. There are two foci of tumor emboli.
2. Adrenal tissue found in the liver can represent adrenal-hepatic fusion, adrenal-hepatic adhesion, or adrenal rest (tumors). In fusion, both adrenal and hepatic parenchymal cells intermingle. In adhesion, the adrenal gland is attached to the liver with the presence of capsule between the twos. For adrenal rest (tumors), the heterotopic adrenal cortical tissue is separated from the right adrenal glands and is located within the capsule of the liver.
3. Location of the adrenal rest in the liver capsule is important to differentiate it from lipid-rich hepatocellular carcinoma, metastatic renal cell carcinoma, and angiomyolipoma. Immunoprofile of adrenal rest showing positivity towards Melan-A, inhibin, synaptophysin, and CD56 maybe helpful in challenging cases.

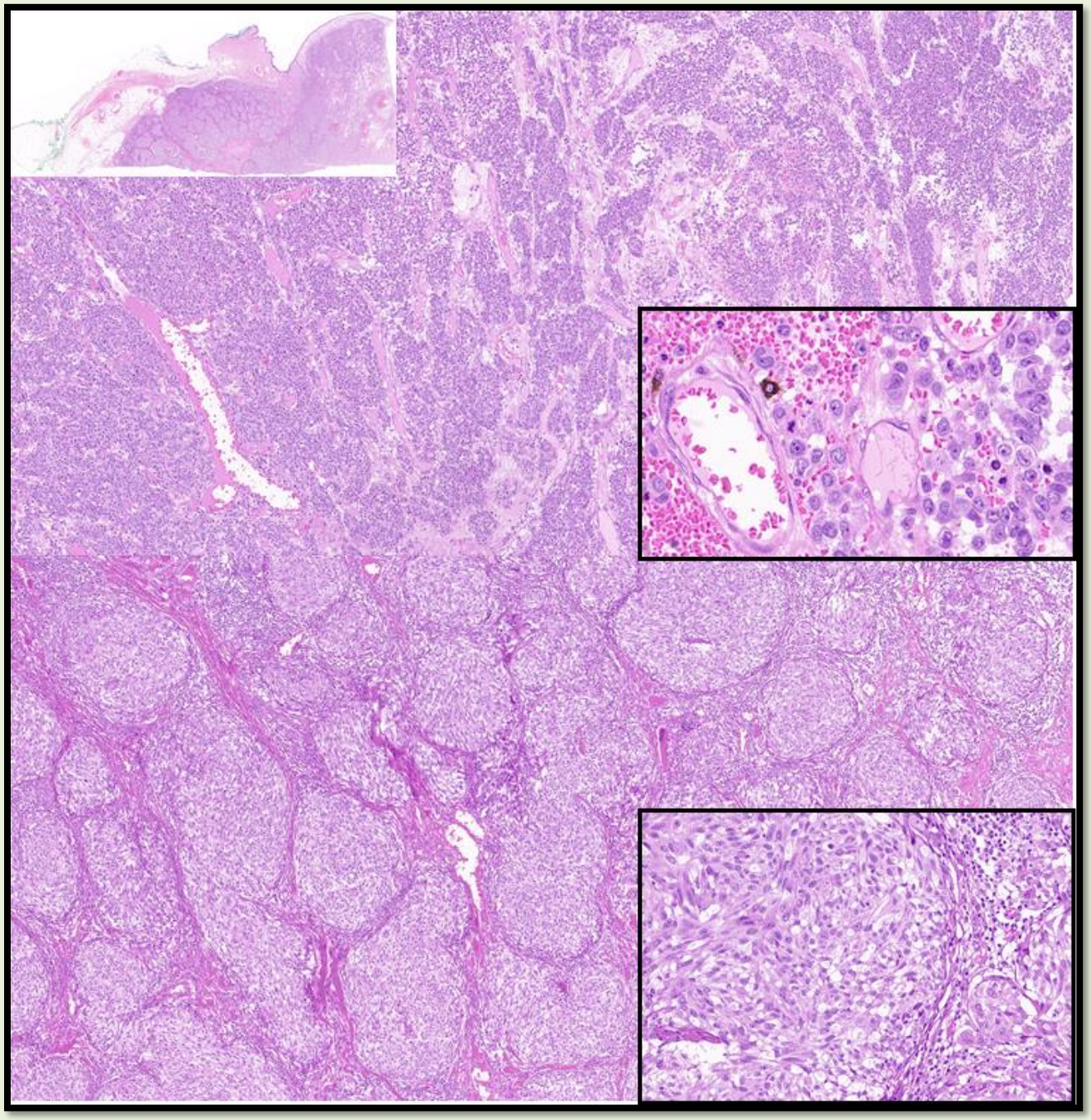
Reference

1. Mounajjed, Taofic, Vishal S. Chandan, and Michael S. Torbenson, eds. Surgical pathology of liver tumors. Springer, 2015.
2. Sugiyama, Tomoko, et al. "Hepatic adrenal rest tumor: Diagnostic pitfall and proposed algorithms to prevent misdiagnosis as lipid - rich hepatocellular carcinoma." Pathology International 65.2 (2015).

Case 19

Case 19: A 64-year-old lady presented a right breast mass for 4 months. The excised tumor was negative for CK AE1/AE3. One representative section.

Targeted Diagnosis: **Melanoma**



Case 19

Submitted Diagnoses by Participating Institutions	Number	
Malignant Melanoma. Need IHC for confirmatory/Malignant melanoma, mixed desmoplastic and conventional types	5	Acceptable
High grade malignant tumour. Differential diagnosis: Malignant melanoma or Neuroendocrine carcinoma/Rhabdomyosarcoma/ Metaplastic carcinoma/ clear cell sarcoma/ Malignant spindle & epithelioid tumour TRO melanoma, sarcoma. IHC HMB45, S100 & Melan A	7	Acceptable
Sarcoma of the breast/ Malignant mesenchymal tumour. Differential diagnosis includes inflammatory myofibroblastic tumour with malignant behavior/ metaplastic carcinoma	3	Acceptable
High grade malignant tumour. Differential diagnosis: sarcoma, metaplastic carcinoma, dysgerminoma, lymphoma/ High grade epithelioid tumour. Differentials include epithelioid hemangioendothelioma/metastatic paraganglioma/ Myofibroblastic sarcoma, Leiomyosarcoma, Angiosarcoma	3	Acceptable
Metaplastic carcinoma/ Medullary carcinoma	2	
Rhabdomyosarcoma- Alveolar and pleomorphic subtype/ Rhabdomyosarcoma	2	
Myofibroblastoma	2	

Educational notes:

1. There are sheets of mitotically active malignant cells in the deep dermis and subcutaneous tissue with a Grenz zone separated from the overlying epidermis. The malignant cells assume two different morphologies. The epithelioid discohesive malignant cells show marked nuclear pleomorphism with macronucleoli and occasional nuclear pseudoinclusions. The spindle malignant cells arrange in nodular compact nests. Rare malignant cells contain brown cytoplasmic pigments. This morphology variety raises the possibility of melanoma, which is confirmed with relevant immunohistochemistry.
2. Many differential diagnoses including carcinoma, melanoma, sarcomas are considered, requiring comprehensive immunohistochemistry. Given the spindle cell morphology component, metaplastic carcinoma and melanoma are prime consideration. Negativity towards a panel of keratins, EMA and p63 helps to rule out metaplastic carcinoma. At least two melanoma markers such as HMB45, melan-A, and S-100 protein should be performed to ascertain melanoma. A caveat is that ductal carcinoma of the breast can be positive for S100 protein.
3. Melanomas in the breast can be metastatic melanomas to the breast from other cutaneous locations. They can also be primary cutaneous melanomas of the skin overlying the breast and rarely are primary noncutaneous melanomas of the breast parenchyma.

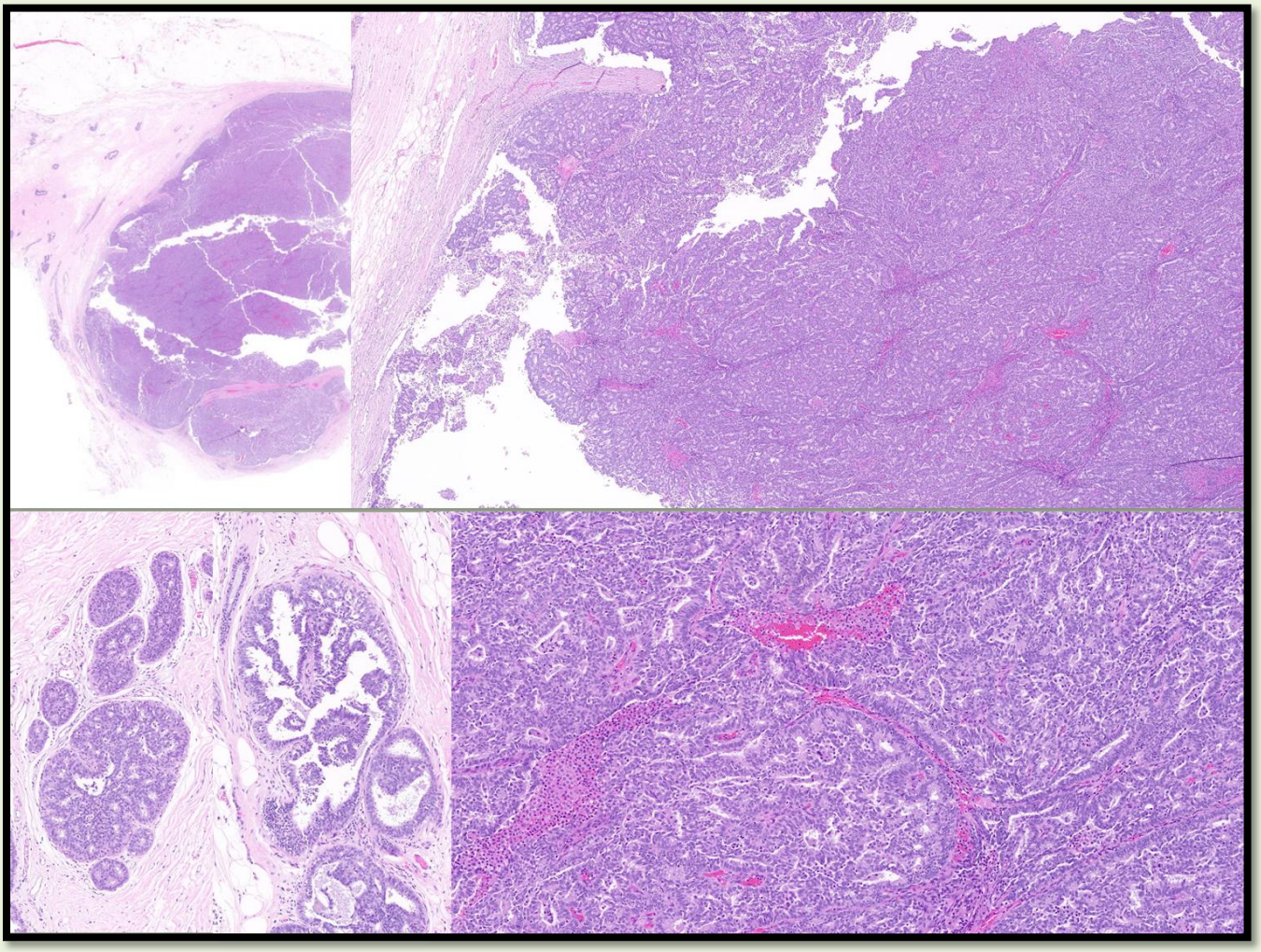
Reference

1. Dabbs, D. J. (2016). Breast Pathology. Elsevier Health Sciences.
2. Koh, Jiwon, et al. "Primary malignant melanoma of the breast: A report of two cases." Journal of pathology and translational medicine 53.2 (2019): 119.

Case 20

Case 20: A 60-year-old lady presented with a right circumscribed mass on the mammogram. Tru-cut biopsy: indeterminate. One representative section.

Targeted Diagnosis: **Encapsulated papillary carcinoma with ductal carcinoma in situ, intermediate grade**



Case 20

Submitted Diagnoses by Participating Institutions	Number	
Encapsulated papillary carcinoma with ductal carcinoma in situ	1	Acceptable
Encapsulated papillary carcinoma/ encysted papillary carcinoma of the breast/ Encapsulated papillary carcinoma. Comment: Would like to do p63 immunohistochemical study and further sections to look for invasion	14	Acceptable
Encapsulated papillary carcinoma with usual ductal hyperplasia	1	Acceptable
Papillary neoplasm, favors encapsulated papillary carcinoma	2	Acceptable
Papillary neoplasm. Differentials of encapsulated papillary carcinoma or solid papillary carcinoma, in situ or papillary ductal carcinoma in situ	2	Acceptable
Solid papillary carcinoma to do IHC TRO invasive carcinoma. IHC: P63, CK56, ER,PR/ Solid papillary carcinoma	2	Acceptable
Papillary carcinoma	1	
Invasive papillary carcinoma	1	

Educational notes:

1. This is a papillary neoplasm surrounded by fibrous capsule without invasion. There are slender fibrovasular papillae. Intermediate grade neoplastic epithelial cells arranged in cribriform pattern tightly fill the gaps between the papillae. These features are characteristic of encapsulated papillary carcinoma (EPC). Adjacent ducts show intermediate grade ductal carcinoma in situ (DCIS) of cribriform and papillary types.
2. EPC lacks myoepithelial cells throughout as well as the periphery of the lesion. As such, frank invasion is defined by infiltrative permeation through the fibrous capsule. EPC without frank invasion is staged as pTis and graded according to nuclear grade.
3. EPC differs from solid papillary carcinoma (SPC) as the papillae in SPC are delicate and inconspicuous. SPC appears as expansive nodules with a solid growth pattern. SPC is also usually positive for chromogranin A and synaptophysin.
4. EPC differs from papillary DCIS as papillary DCIS usually occurs as multiple small lesions with presence of myoepithelial cells at the periphery. Nonetheless, papillary DCIS often coexists with EPC especially at the retroareolar region.

Reference

1. WHO Classification of Tumours Editorial Board. Breast tumours. Lyon (France): International Agency for Research on Cancer; 2019. (WHO classification of tumours series, 5th ed.; vol. 2).

©E.S. Ch'ng, International Academy of Pathology, Malaysian Division Secretariat, Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia, December 2020.