International Academy of Pathology
Malaysian Division

FINAL REPORT

QUALITY ASSURANCE PROGRAM
GENERAL DIAGNOSTIC HISTOPATHOLOGY
CYCLE 02/2021

NOTES FROM THE COORDINATOR

1. For this cycle 02/2021, a total of 27 institutions responded online by the closing date of 15 November 2021.

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 02/2021 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. Fazilah Hassan, Dr. Suhaila Abdullah, Dr. Nurul Akmar Misron, Dr. Zahrah Tawil, and Dr. Mariani Hashim.

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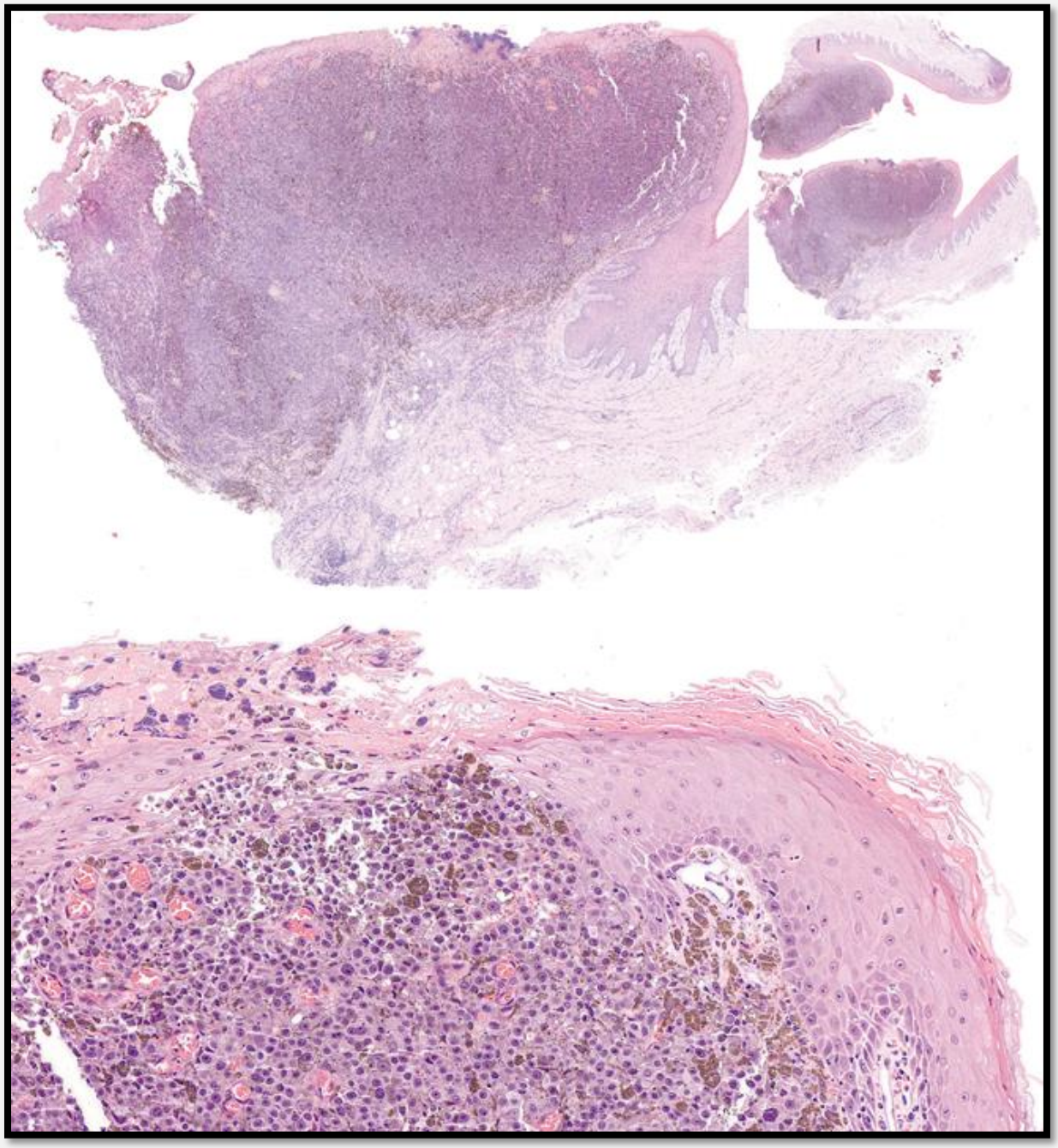
Coordinators for IAP-MD QAP

Case 1

Case 1: An 86-year-old lady presented with a hyperpigmented lesion on the right palate. One representative section.

Targeted Diagnosis: **Mucosal melanoma**



Case 1

Submitted Diagnoses by Participating Institutions	Number	
Nodular melanoma, nodular melanoma, mucosal melanoma, melanoma	27	Acceptable

Educational notes:

1. There is an ulcerating nodular melanoma in the mucosa composed of sheets of epithelioid malignant cells with large vesicular nuclei harboring prominent nucleoli. Melanin pigments are evident.
2. Oral mucosa melanomas are rare. They typically present at an advanced stage with a vertical growth pattern. One third of oral mucosa melanomas arise from pre-existing melanocytic lesions; the hard palate and maxillary gingiva are the most involved sites. Their cellular morphology varies, ranging from epithelioid cells as in this case, to spindled, plasmacytoid or mixed appearance. Most cases show predominantly solid arrangement, although other architectural patterns such as alveolar, organoid and pagetoid formation can be seen. Most primary oral melanomas are heavily pigmented, but some are amelanotic and immunohistochemistry can be helpful to confirm the diagnosis.
3. The presence of an in-situ component or a radial growth phase is an important feature in distinguishing primary oral melanomas from metastatic melanomas. However, advanced tumors may lack an in-situ component. Other features that favor primary oral origin include pigmented lesions involving the palate and gingiva with mucosal ulceration and extension along the minor salivary glands. In contrast, involvement of base of tongue with intact overlying mucosa along with palatal and gingival sparing is commonly seen in metastatic melanomas.
4. Oral mucosal melanomas have a median survival of 2 years. Prognostic factors for cutaneous melanomas such as Clark level of invasion and Breslow thickness do not apply in oral mucosal melanomas.

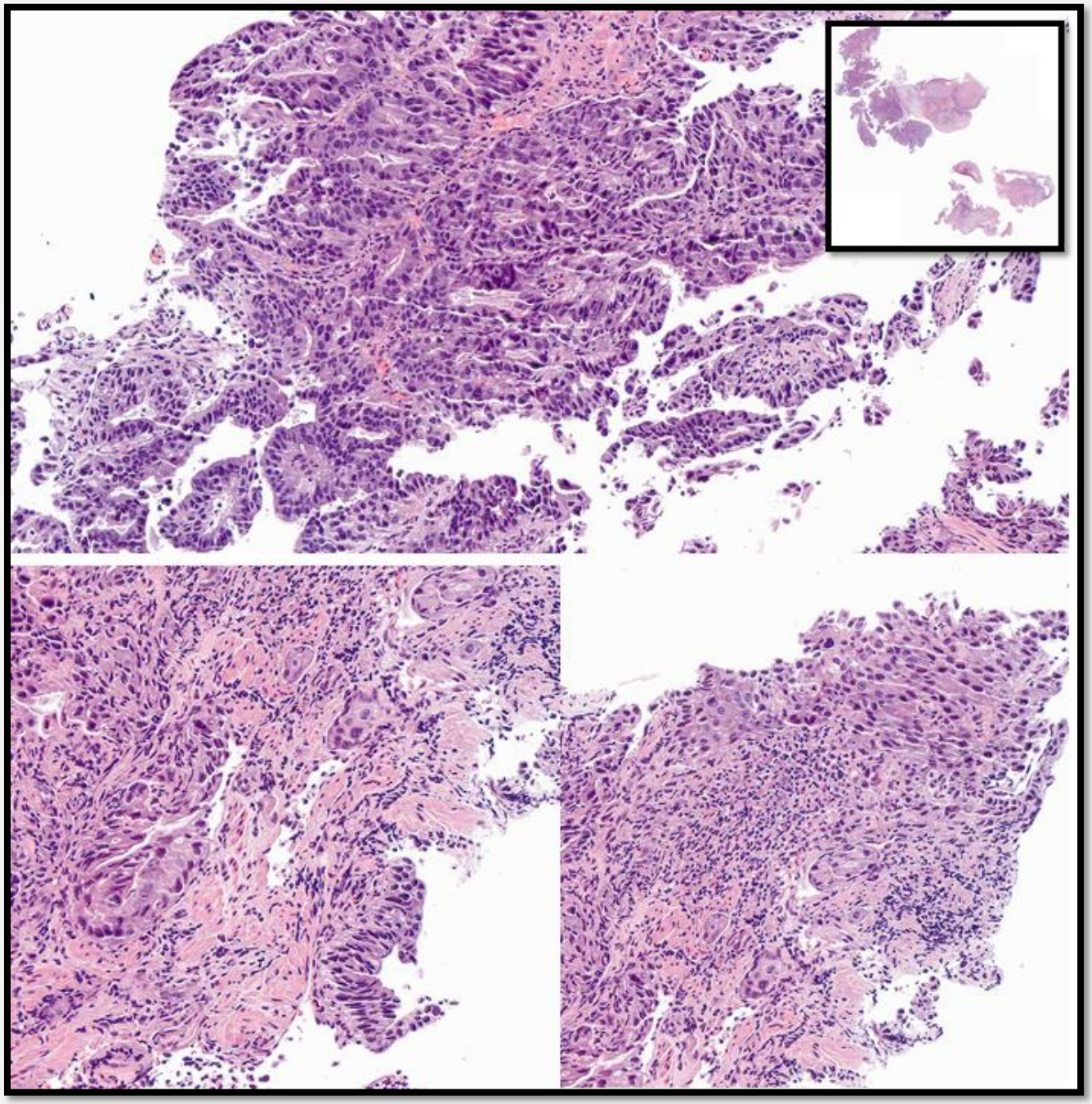
Reference:

1. Mihajlovic M, Vlajkovic S, Jovanovic P, Stefanovic V. Primary mucosal melanomas: a comprehensive review. Int J Clin Exp Pathol. 2012;5(8):739-753.
2. de-Andrade BA, Toral-Rizo VH, León JE, et al. Primary oral melanoma: a histopathological and immunohistochemical study of 22 cases of Latin America. Med Oral Patol Oral Cir Bucal. 2012;17(3):e383-e388. Published 2012 May 1. doi:10.4317/medoral.17588
3. El-Naggar A.K., Chan J.K.C., Grandis J.R., Takata T., Slootweg P.J. (Eds): WHO Classification of Head and Neck Tumours (4th edition). IARC: Lyon 2017.

Case 2

Case 2: A 63-year-old man presented with dysphagia. Biopsy of the lower esophagus was performed. One representative section.

Targeted Diagnosis: **Focal intramucosal adenocarcinoma arising in Barret dysplasia, high grade**



Case 2

Submitted Diagnoses by Participating Institutions	Number	
Adenocarcinoma in background Barret's esophagus	15	Acceptable
Adenocarcinoma in background Barret's esophagus with squamous/glandular dysplasia	5	Acceptable
Adenocarcinoma	3	Acceptable
Adenosquamous carcinoma	3	Acceptable
Poorly differentiated carcinoma	1	

Educational notes:

1. The biopsy shows squamocolumnar mucosal tissue fragments with evidence of intestinal metaplasia, consistent with Barret esophagus. There is widespread high-grade dysplasia of the glandular epithelium displaying marked nuclear pleomorphism and hyperchromatism, full thickness nuclear stratification and loss of nuclear polarity. Areas of confluent glands with a solid growth pattern are indicative of intramuscosal adenocarcinoma.
2. Glandular dysplasia with marked architectural distortion in Barret esophagus requires distinction between high-grade Barret dysplasia and intramucosal adenocarcinoma. Intramucosal adenocarcinomas are adenocarcinomas that display lamina propria invasion but remain within the boundary of muscularis mucosae (stage pT1a). Histologically, intramucosal adenocarcinoma is distinguished from high-grade Barret dysplasia based on presence of a solid growth pattern, individual cells infiltrating the lamina propria or an anastomosing never-ending glandular pattern. Of note, back-to-back glandular formation and cribriforming are features that fall within the realms of high-grade Barret dysplasia.
3. When dysplastic glands invade in the interspaces between fibers of smooth muscles as focally observed in this case, this finding should not be over-staged as muscularis propria invasion. As duplicated and distorted muscularis mucosae is consistently present in Barret esophagus, recognition of invasion into such muscularis mucosae supports the diagnosis of intramucosal adenocarcinoma.
4. Although focal squamous dysplasia is observed, the diagnosis of adenosquamous carcinoma requires admixture of both adenocarcinoma and squamous carcinoma components without a specific ratio according to WHO classification of digestive system tumors. Nonetheless, the Japanese Classification of Esophageal Cancer requires >20% of each component to be present, otherwise the tumor is classified according to the primary component alone.

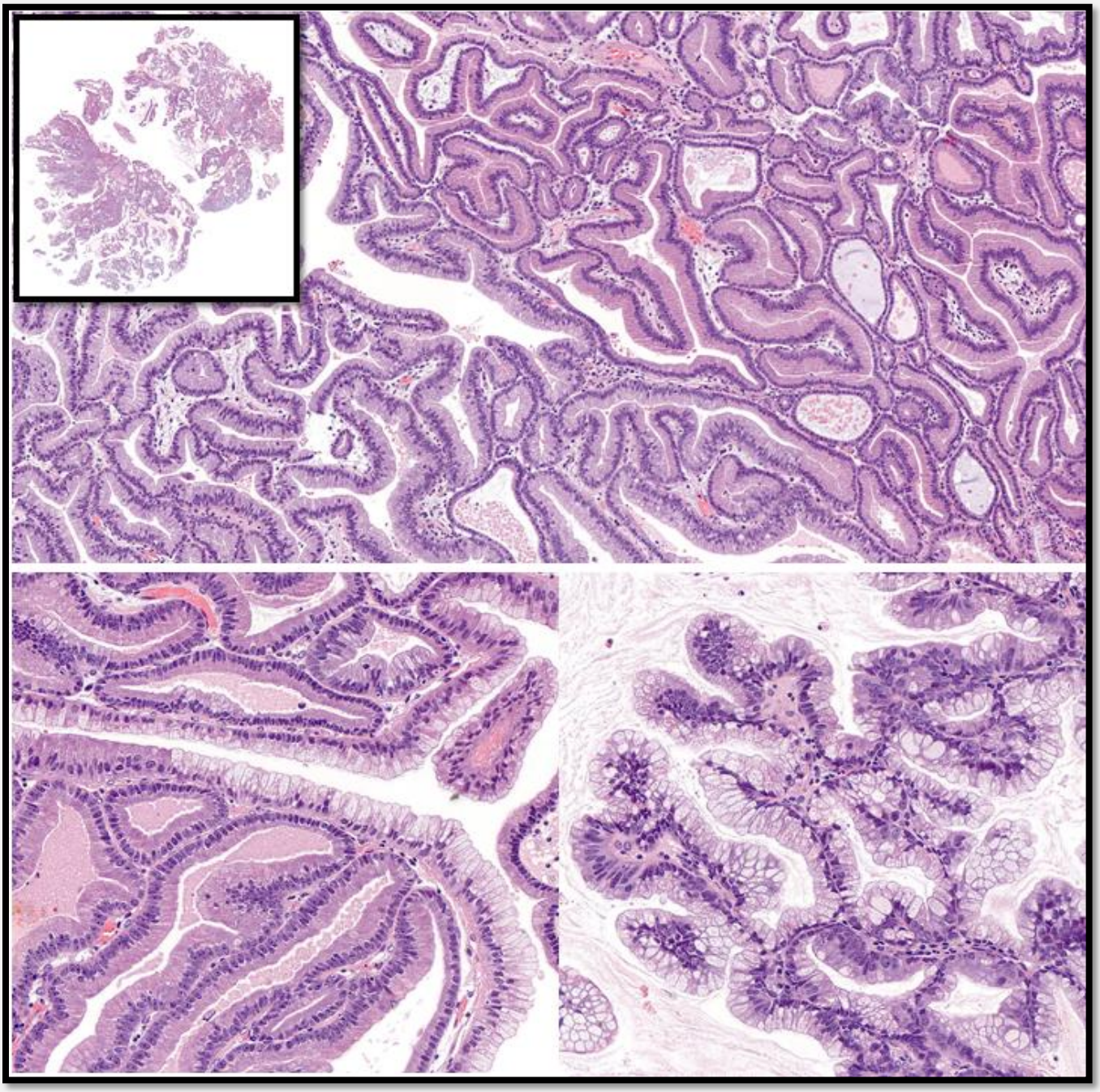
Reference

1. WHO Classification of tumours Editorial Board. Digestive system tumours. Lyon (France): International Agency for Research on Cancer;2019. (WHO Classification of tumours series, 5th ed.; vol1).
2. Yin, Feng & Gonzalo, David & Lai, Jinping & Liu, Xiuli. (2018). Histopathology of Barrett's Esophagus and Early-Stage Esophageal Adenocarcinoma: An Updated Review. Gastrointestinal Disorders. 1. 147-163. 10.3390/gidisord1010011.
3. Robert D. Odze, John R. Goldblum. (2015). Odze and Goldblum surgical pathology of the GI tract, liver, biliary tract, and pancreas. Philadelphia, PA :Saunders/Elsevier.

Case 3

Case 3: A 65-year-old lady presented with right hypochondriac pain and jaundice. Cholecystectomy was performed. One representative section.

Targeted Diagnosis: **Intracholecystic papillary neoplasm (ICPN), low grade dysplasia**



Case 3

Submitted Diagnoses by Participating Institutions	Number	
Intracholecystic papillary neoplasm, low grade/mild dysplasia.	23	Acceptable
Pyloric gland adenoma/ Intracholecystic papillary-tubular neoplasm, low grade	2	Acceptable
Intracholecystic papillary neoplasm, high dysplasia.	2	
Intracholecystic Papillary Mucinous Neoplasm with High Grade Dysplasia	1	

Educational notes:

1. There are polypoid tissue fragments composed of tubule-papillae lined by a layer of columnar epithelium of mixed biliary and foveolar types. The lining epithelium shows low grade dysplasia with basally located nuclei harboring small nucleoli. These features are that of intracholecystic papillary neoplasm, low grade dysplasia.
2. Intracholecystic papillary neoplasm (ICPN) is a preinvasive neoplasm of the gallbladder. It is composed of intraluminal growth of predominantly organized papillary or tubulopapillary architecture with fine fibrovascular stalks. Based on the predominant morphology (>75%) of the lining epithelium, four morphological patterns, i.e., biliary, gastric, intestinal and oncocytic patterns are recognized. However, mixed patterns are also common. There is no clinical implication for subtyping ICPN.
3. Differing from the low-grade lesions, ICPNs with high grade dysplasia are characterized by architectural complexity (e.g., cribriform, compact tubules and solid structure) as well as greater cytological atypia such as loss of nuclear polarity and greater nuclear pleomorphism.
4. Pyloric gland adenoma (also known as intracholecystic papillary-tubular neoplasm, gastric pyloric, simple mucinous type) is composed of lobules of pyloric type or Brunner gland-like glands. The glands are small, round, uniform and tightly packed, displaying tubular configuration with little or no intervening stroma. The cells have abundant apical mucin and, in most cases, display minimal cytological atypia. Pyloric gland adenoma differs from the ICPN, gastric subtype, which is composed of foveolar and pyloric gland components.
5. An associated invasive carcinoma is identified in almost half of all ICPNs. The invasive component is often a tubular adenocarcinoma and may be grossly inapparent or occur away from the main IPCN lesion. Therefore, thorough sampling and careful evaluation are warranted.

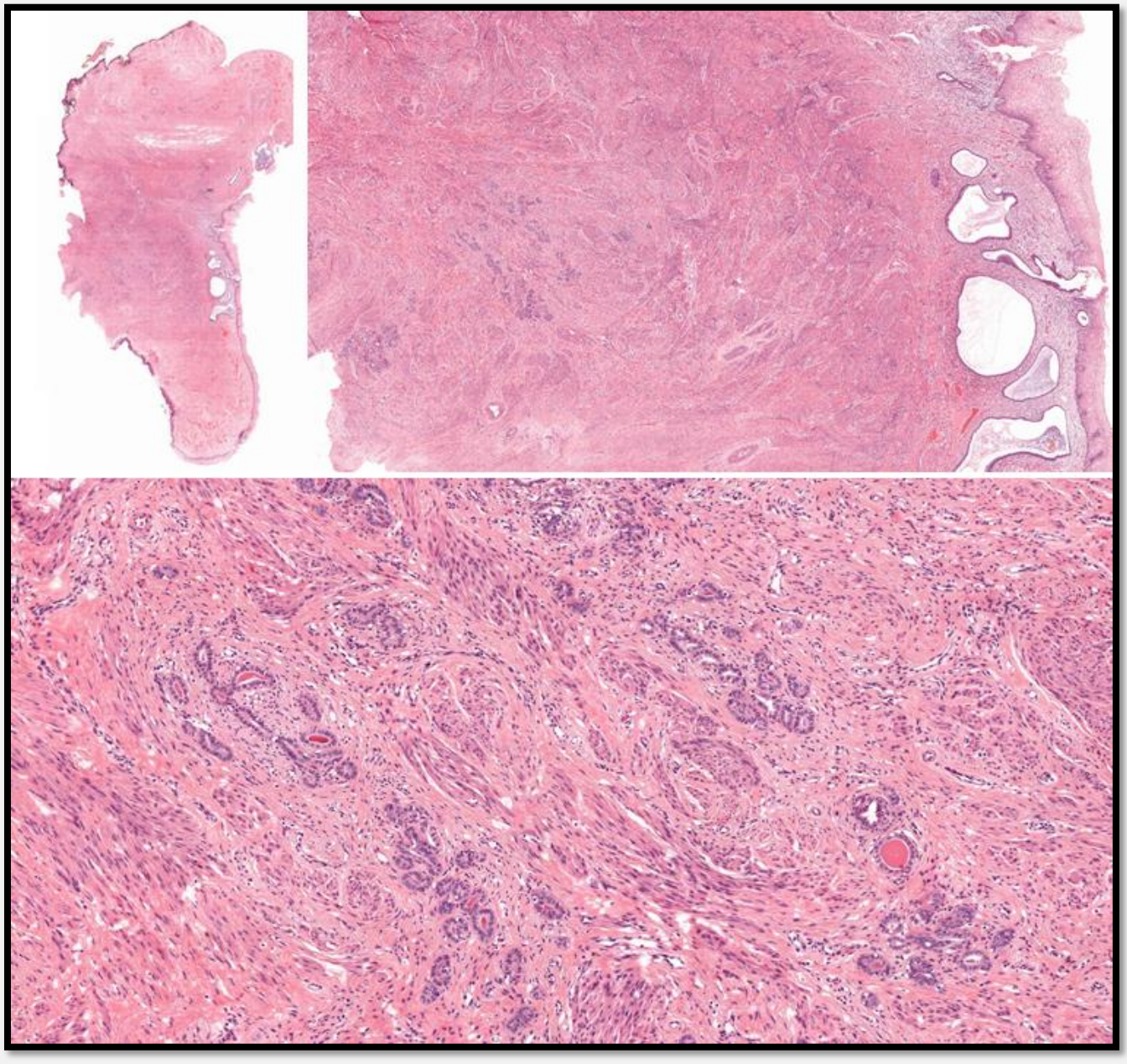
Reference

1. WHO Classification of tumours Editorial Board. Digestive system tumours. Lyon (France): International Agency for Research on Cancer;2019. (WHO Classification of tumours series, 5th ed.; vol1).
2. Yasuni Nakanuma, Yoshikatsu Nomura, Hiroyuki Watanabe, Takuro Terada, Yasunori Sato, Yuko Kakuda, Takashi Sugino, Yoshifumi Ohnishi, Yukiyasu Okamura, Pathological characterization of intracholecystic papillary neoplasm: A recently proposed preinvasive neoplasm of gallbladder,Annals of Diagnostic Pathology,Volume 52,2021

Case 4

Case 4: A 46-year-old lady was diagnosed with adenocarcinoma in situ on pap smear and she underwent cervical cone biopsy. One representative section.

Targeted Diagnosis: **Mesonephric hyperplasia**



Case 4

Submitted Diagnoses by Participating Institutions	Number	
Mesonephric hyperplasia	14	Acceptable
Mesonephric rest/remnant	10	Acceptable
Ectopic thyroid gland with immature squamous metaplasia and chronic non-specific cervicitis	1	
Adenocarcinoma-in-situ with mesonephric remnant / invasive adenocarcinoma	2	

Educational notes:

1. Section from the cervical cone biopsy shows mesonephric hyperplasia characterized by lobules of glands in the deeper part of the cervical wall. These glands are composed of a single layer of cuboidal epithelium without cytological atypia. The covering squamous epithelium and endocervical glands are devoid of dysplasia.
2. Presence of lobules of glands in the deeper part of the cervical wall stimulates infiltrative adenocarcinoma. However, entities such as mesonephric remnants and mesonephric hyperplasia need to be considered. Mesonephric remnants typically involve the deep layer of anterolateral wall of cervix along the path of the mesonephric duct. They may appear infiltrative and extend close to the luminal surface and intermingle with endocervical glands. In contrast, mesonephric hyperplasia has larger and more irregularly distributed glands as compared to mesonephric remnants. In the lobular type, the glands have exaggerated, clustered, lobular arrangement separated by variable amount of stroma. In the diffuse type, mesonephric hyperplasia displays predominantly non-clustered, extensive, and more diffuse proliferation. The least common duct type is characterized by hyperplastic epithelium with papillary tufting, and it may show clefted contours lacking intraluminal secretions.
3. Mesonephric glands are characteristically lined by a layer of simple flat or low cuboidal, non-ciliated cells with distinct basement membranes. They contain PAS-positive, diastase-resistant material. Differing from adenocarcinoma or adenocarcinoma in situ, mesonephric glands lack nuclear atypia. Adenocarcinoma in situ is consistently characterized by nuclear enlargement, coarse chromatin, small single or multiple nucleoli, increased mitotic activity and variable nuclear stratification. An invasive adenocarcinoma shows complex architecture forming labyrinth or maze-like arrangement, and cribriform pattern with single gland profile. Although presence of stromal desmoplasia favors malignancy, distinction from a range of benign conditions showing stromal fibrosis, oedema and dense inflammation is critical.

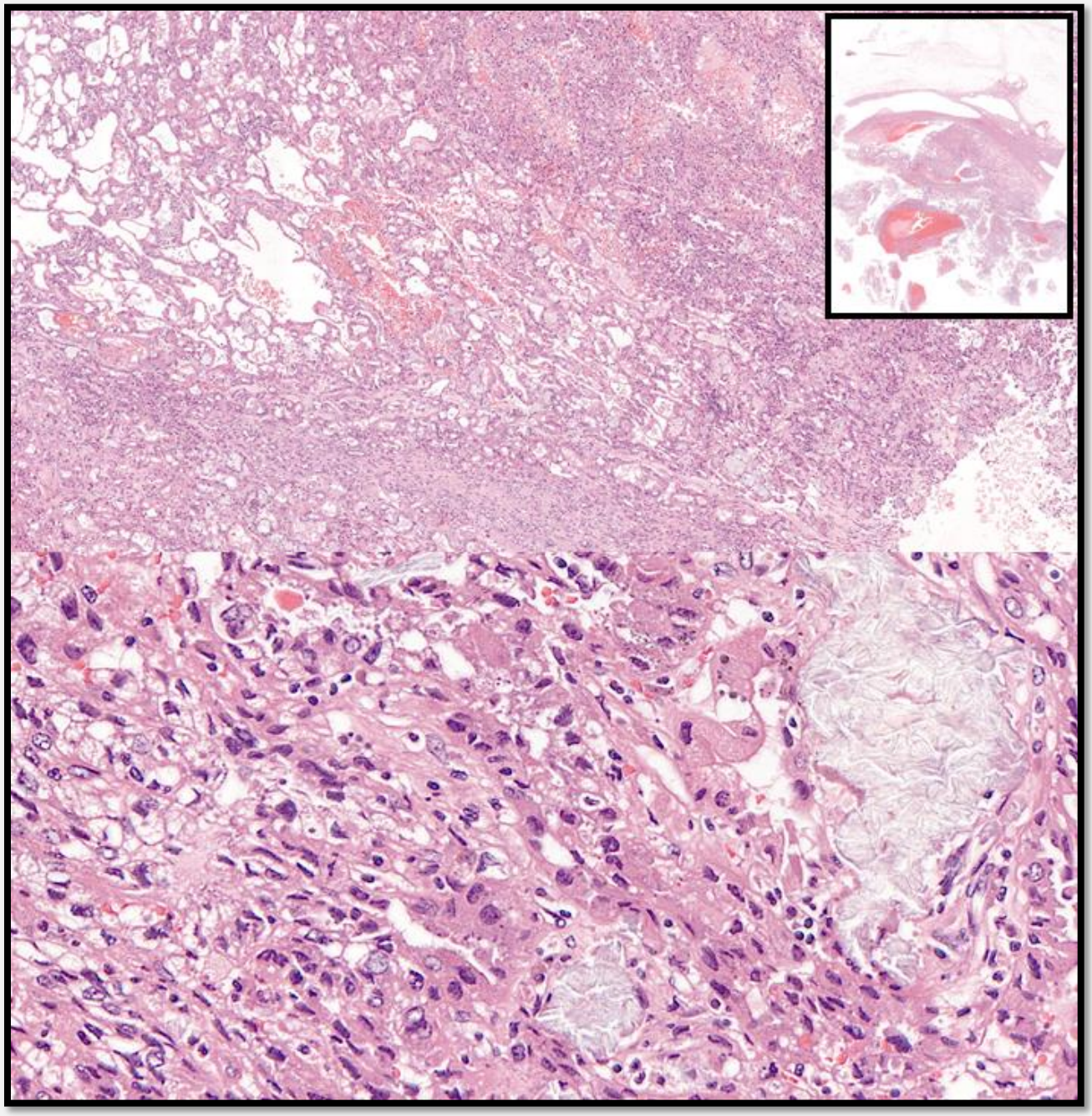
Reference

1. Zaino, R. Glandular Lesions of the Uterine Cervix. Mod Pathol 13, 261–274 (2000).

Case 5

Case 5; A 41-year-old man was noted to have a right renal mass. He had underlying hypertension and was on regular hemodialysis for end stage renal disease. Nephrectomy was performed One representative section.

Targeted Diagnosis: **Acquired cystic kidney disease associated renal cell carcinoma**



Case 5

Submitted Diagnoses by Participating Institutions	Number	
Acquired cystic kidney disease associated renal cell carcinoma	25	Acceptable
Papillary renal cell carcinoma DD: Renal melanoma	1	
Chronic pyelonephritis	1	

Educational notes:

1. Section shows a tumor mass with a variety of growth patterns such as acinar, alveolar and microcystic supported by fine vasculature accompanied by hemorrhage. The tumor cells display abundant eosinophilic granular cytoplasm and high nuclear grade. Crystal depositions are scattered. Those features are those of acquired cystic disease–associated renal cell carcinoma (ACD-RCC).
2. ACD-RCC is a common subtype of renal cell carcinoma occurring in the patients undergoing long-term dialysis. A variety of growth patterns in various combination is common. These include acinar, alveolar, tubular, macroystic, microcystic, papillary and solid patterns. The distinguishing feature is consistent presence of inter- or intra-cystoplasmic lumina imparting a cribriform, microcystic or sieve-like architecture. The tumor cells show abundant eosinophilic, granular cytoplasm and ill-defined cell membrane, sometimes with clear cell cytology. The nuclei are characteristically high grade with prominent nucleoli (Fuhrman grade 3). Polarizable calcium oxalate crystals may be observed within the tumor and parenchyma, although it is not pathognomonic and may be absent.
3. Papillary renal cell carcinoma (PRCC) is composed of papillae formed by delicate fibrovascular cores, a pattern that can be seen in ACD-RCC. However, the presence of cribriform structure such as in this case is the unique pattern to help distinguish ACD- RCC from PRCC or other neoplasms with a predominant papillary structure. The presence of foamy macrophages, psammoma bodies and glassy hyaline globules that can be associated with PRCC are not seen in ACD-RCC. Although foamy cells have been identified within ACD-RCC, immunophenotypic evidence has determined these cells to be neoplastic rather than histiocytic.
4. ACD-RCC typically has indolent clinical behavior. Nonetheless, metastasis could occur in those with sarcomatoid or rhabdoid features and occasionally in those ACD-RCCs with typical features.

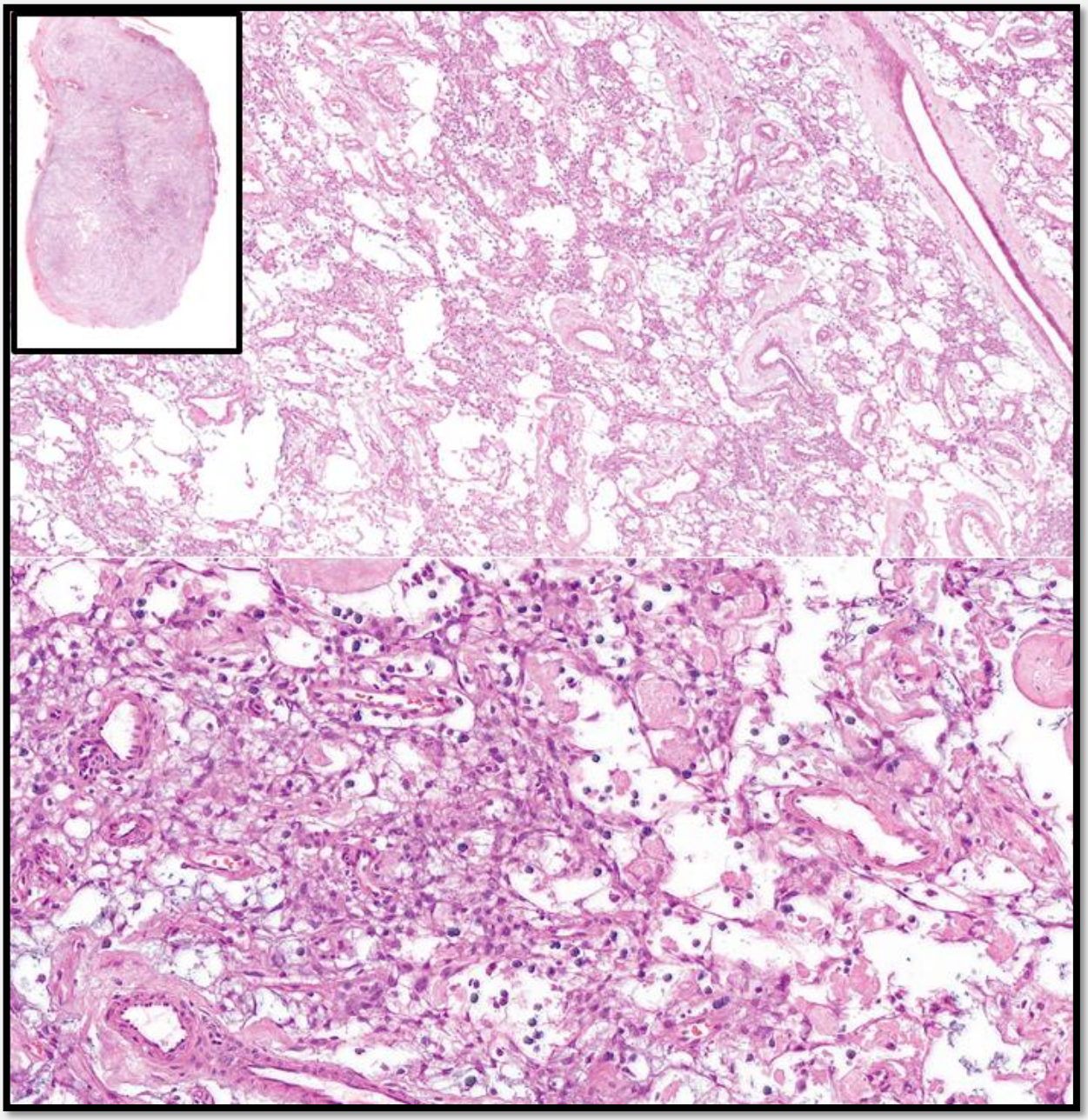
Reference

1. Holger Moch, Peter A. Humphrey, Thomas M. Ulbright, Victor E. Reuter (Eds); WHO Classification of tumours of the urinary system and male genital organs (4th edition). IARC: Lyon 2016
2. Michelle Foshat, Eduardo Eyzaguirre; Acquired Cystic Disease–Associated Renal Cell Carcinoma: Review of Pathogenesis, Morphology, Ancillary Tests, and Clinical Features. Arch Pathol Lab Med 1 April 2017; 141 (4): 600–606. WHO Classification of Tumours Editorial Board. Digestive System Tumours: WHO Classification of Tumours, 5th ed.; IARC: Lyon, France (2019).

Case 6

Case 6: A 59-year-old man presented with an extra-axial left frontal lesion. One representative section.

Targeted Diagnosis: **Meningioma (microcystic and angiomatous) grade 1**



Case 6

Submitted Diagnoses by Participating Institutions	Number	
Meningioma, microcystic, angiomatous WHO grade 1.	24	Acceptable
Clear cell meningioma, WHO grade 2/ Chordoid meningioma/ Meningioma (d/d microcystic, chordoid, secretory)	3	Acceptable

Educational notes:

1. This dura-based tumor is well-circumscribed and composed of tumor cells in loose texture pattern. Majority of the tumor cells show fine long processes encompassing clear spaces giving rise to cobweb-like appearance. Tumor cells with vacuolated cytoplasm and a loose mucinous stroma are also noted. Transition to meningothelial-appearing pattern is focally seen. In addition, this tumor is rich in vasculature with larger vessels showing hyalinization. These features are that of meningioma (microcystic and angiomatous), grade 1
2. Meningiomas exhibit a variety of histological appearances. Most of the histological subtypes are grade 1 except for clear cell and chordoid meningiomas are grade 2, and rhabdoid and papillary meningiomas are grade 3. Grade 2 and grade 3 meningiomas are such designated only if such histological patterns predominate (>50%) in the tumor.
3. Apart from that, common variants of meningiomas are graded 2 or 3 based on diagnostic criteria such as mitotic index, worrisome histological features, and brain invasion even these diagnostic criteria are focally met.
4. Due to a variety of histological appearances of meningiomas, occasionally immunohistochemistry is required to support the diagnosis of meningiomas; somatostatin receptor 2a (SSTR2a) has emerged as the more sensitive and relatively specific marker as compared to the commonly utilized EMA.

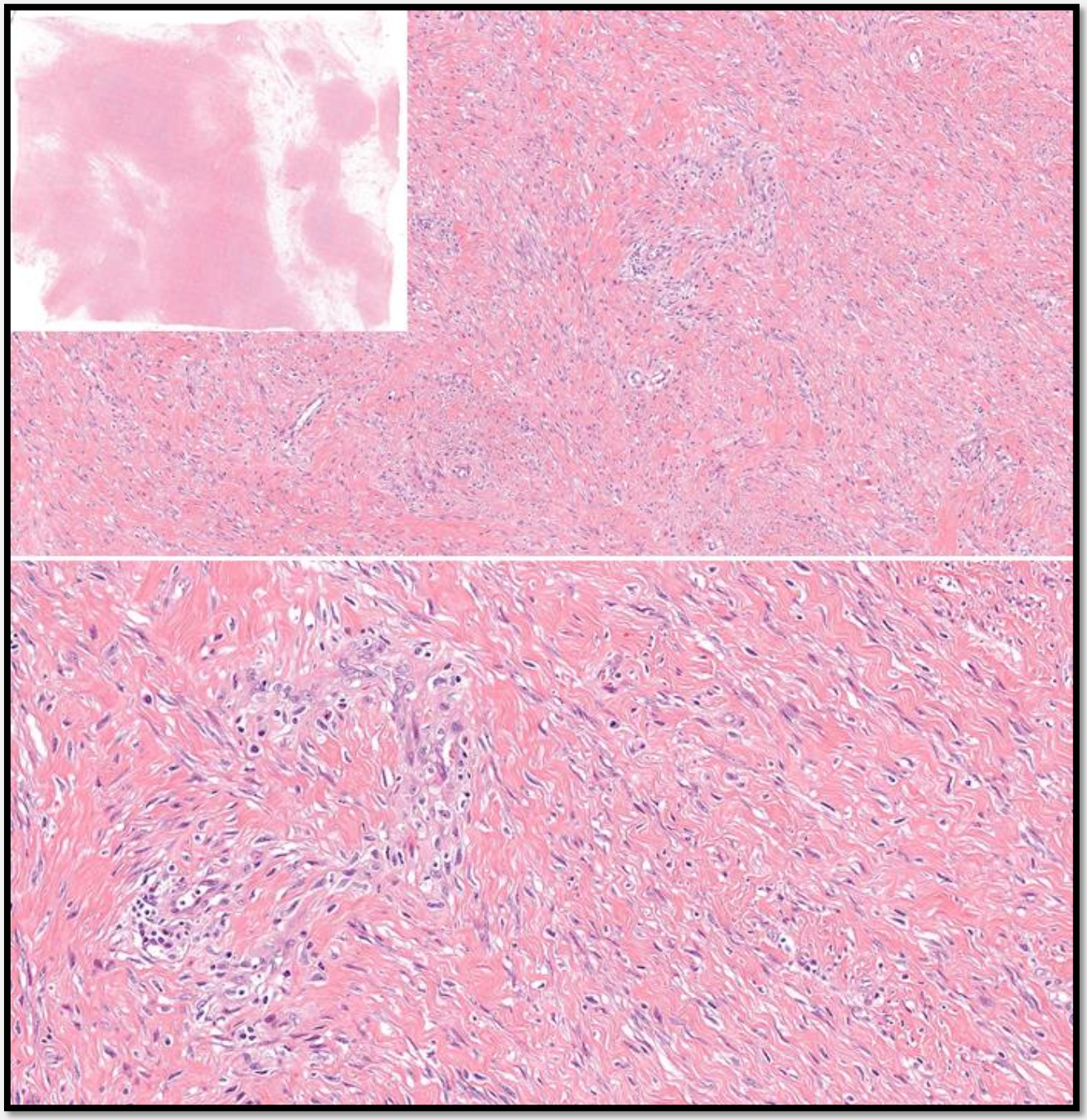
Reference:

1. Perry, A., & Brat, D. J. (2017). Practical Surgical Neuropathology: A Diagnostic Approach E-Book: A Volume in the Pattern Recognition Series. Elsevier Health Sciences

Case 7

Case 7: A 48-year-old man presented with a right testicular mass. One representative section.

Targeted Diagnosis: **Benign myofibroblastic lesion (favoring fibrous pseudotumor with a differential diagnosis of cellular angiofibroma)**



Case 7

Submitted Diagnoses by Participating Institutions	Number	
Fibrous pseudotumor/ Fibrous pseudotumor. further IHC stains	5	Acceptable
Benign spindle cell lesion, differentials include fibrous pseudotumorfibrous tumor, angiofibroma, fibro-thecoma, sclerosing sertoli cell tumor, solitary fibrous tumor, inflammatory myofibroblastic tumor, fibroma	6	Acceptable
Fibroma/ Angiomyxoid fibroma	4	Acceptable
Fibroblastic/myofibroblastic tumor, likely angiofibroma	3	Acceptable
Cellular angiofibroma	2	Acceptable
Sclerosing sertoli cell tumor	3	Acceptable
Benign sex cord stromal tumor/ Differential diagnosis includes sclerosing Sertoli cell tumour and fibroma. Comment: Immunohistochemical stains ie inhibin, beta-catenin required to confirm the diagnosis.	2	Acceptable
Solitary fibrous tumor. STAT6 to confirm.	1	Acceptable
Low grade fibromyxoid sarcoma. (DD Low grade dedifferentiated liposarcoma, sclerosing liposarcoma. Need to exclude benign counterparts such as fibromatosis, neurofibroma. Suggest IHC and molecular study)	1	

Educational notes:

1. There are circumscribed collagenous areas interspersed by loose edematous areas. In the collagenous areas, the spindled cells are bland-looking and spindled in shape without mitotic activity. There are scattered capillaries without hyalinization. This lesion has sparse chronic inflammatory infiltrates. Immunohistochemistry shows that the spindled cells are positive for smooth muscle actin and desmin, and weak positive for CD34. Coupled with immunohistochemical results, this lesion represents a benign myofibroblastic lesion in favor of fibrous pseudotumor over cellular angiofibroma.
2. Morphologically, this intrascrotal myofibroblastic proliferation could represent a spectrum of neoplasms including solitary fibrous tumor, inflammatory myofibroblastic tumor, cellular angiofibroma and fibrous pseudotumor. Lack of branching and dilated vasculature, and lack of prominent lymphoplasmacytic infiltrates make solitary fibrous tumor and inflammatory myofibroblastic tumor less likely respectively. Desirably, STAT6 and ALK immunostaining are required for these diagnoses. Although cellular angiofibroma warrants due consideration, this lesion is not cellular as expected for cellular angiofibroma. In addition, there is no prominent vasculature with hyalinized vessel walls as expected in cellular angiofibroma. As cellular angiofibroma is a member of *RB1*-deleted tumors, loss of Rb protein expression is demonstrable in cellular angiofibroma. Fibrous pseudotumor could appear as “plaque-like”, “inflammatory sclerotic” or “myofibroblastic” as in this case; its nature (ie, reactive vs. neoplastic) remains controversial although it is related to a previous history of trauma, infection, or inflammatory hydrocele.

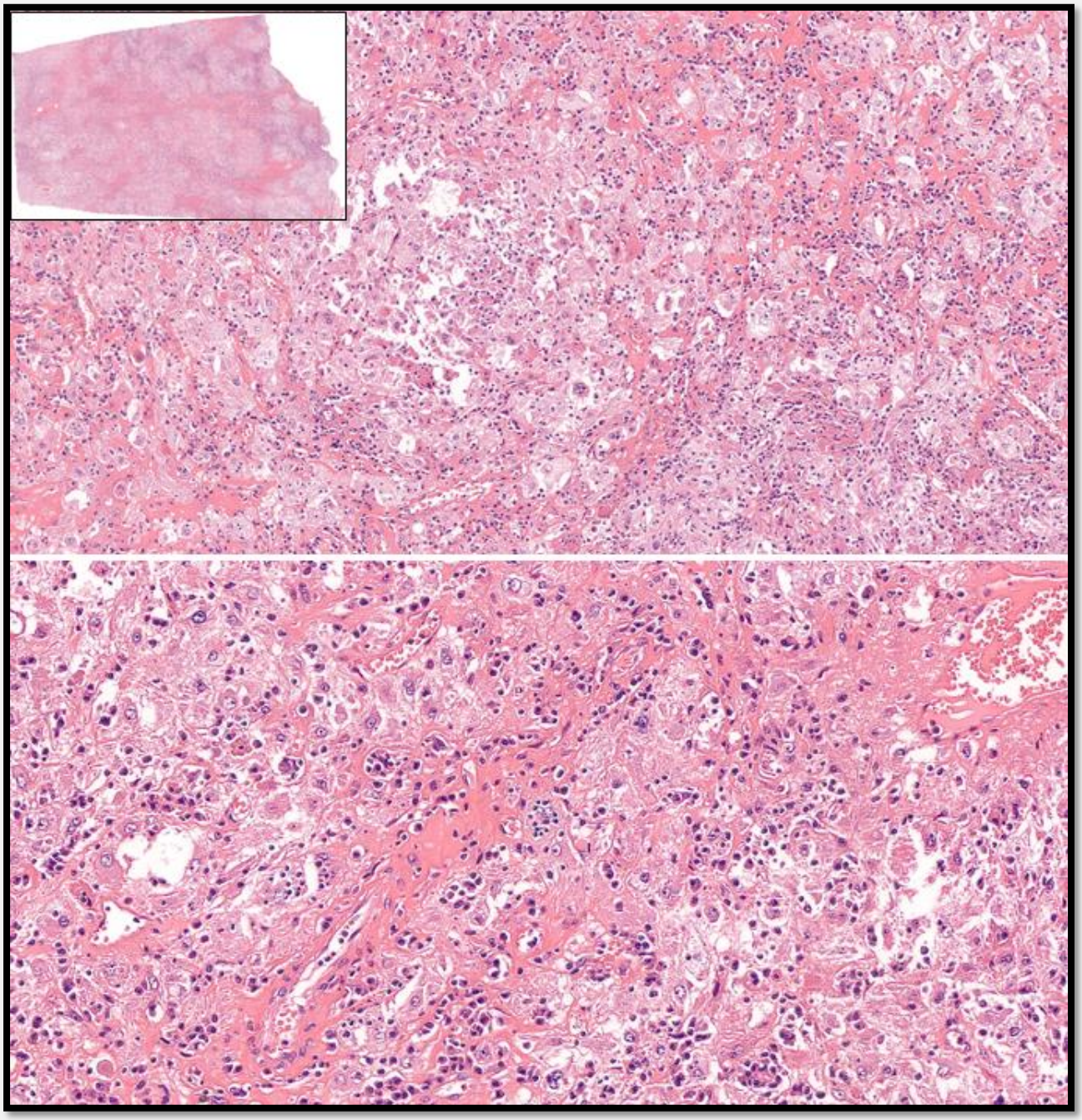
Reference

1. Goldblum, J. R., et al. (2020). Enzinger and Weiss's Soft Tissue Tumors. Elsevier Health Sciences
2. Miyamoto, H., et al. (2010). Paratesticular fibrous pseudotumor: a morphologic and immunohistochemical study of 13 cases. The American journal of surgical pathology, 34(4), 569-574.

Case 8

Case 8: A 43-year-old man presented with a left parietal mass with a radiological differential diagnosis of meningioma. One representative section.

Targeted Diagnosis: **Rosai-Dorfman Disease**



Case 8

Submitted Diagnoses by Participating Institutions	Number	
Rosai Dorfman Disease	22	Acceptable
Plasma cell lesion- plasma cell granuloma with d/d plasmacytoma, plasma-histiocytic disease	1	
Xanthomatous meningioma, Lymphoplasmacytic rich meningioma, rhabdoid meningioma	3	
Pleomorphic xanthoastrocytoma	1	

Educational notes:

1. The tissue is diffusely infiltrated by polygonal cells with abundant eosinophilic granular cytoplasm mixed with scattered lymphocytes and plasma cells. Emperipolesis with intracytoplasmic lymphocytes and plasma cells is evident. These features are consistent with Rosai-Doftman disease (RDD).
2. RDD of the central nervous system corresponds histologically and immunohistochemically to its counterparts occurring elsewhere. It forms dura-based masses stimulating meningioma. Microscopically the mass shows mixed inflammatory infiltrates of histiocytes, lymphocytes and plasma cells. The histiocytes display ample pale or “watery-clear” cytoplasm and possess central large, hypochromatic nuclei with prominent nucleoli. Emperipolesis of intact lymphocytes, plasma cells, neutrophils and occasionally eosinophils is typical. This feature is however not pathognomonic nor required for the diagnosis of RDD; this phenomenon can be focal or encountered in other neoplastic or non-neoplastic histiocytes and even in astrocytes. Extranodal lesions are usually associated with more prominent fibrosis.
3. Dura-based RDD mimics meningioma. Those histiocytes might be mistaken for rhabdoid cells in rhabdoid meningioma, which are plump, displaying eccentric nuclei, open chromatin, prominent nucleoli and eosinophilic globular or fibrillar paranuclear inclusions. Most, but not all, rhabdoid meningiomas also have other histological malignant features such as overtly malignant cytology and elevated mitotic activity. In lymphoplasmacytic-rich or xanthomatous meningioma, presence of conventional meningothelial -appearing pattern with polygonal or spindle shaped cells amidst the background diffuse inflammatory cell infiltrates or xanthomatous change support such diagnoses.
4. Pleomorphic xanthoastrocytoma is an intra-axial tumor whereby the astrocytes show xanthomatous change and may have focal collections of small lymphocytes and plasma cells. However, the tumor cells display nuclear and cytoplasmic pleomorphism. Intranuclear inclusions, nucleolar prominence and granular bodies are frequent features. Frequently there is accompanying diffusely infiltrating, non-pleomorphic astrocytic component.

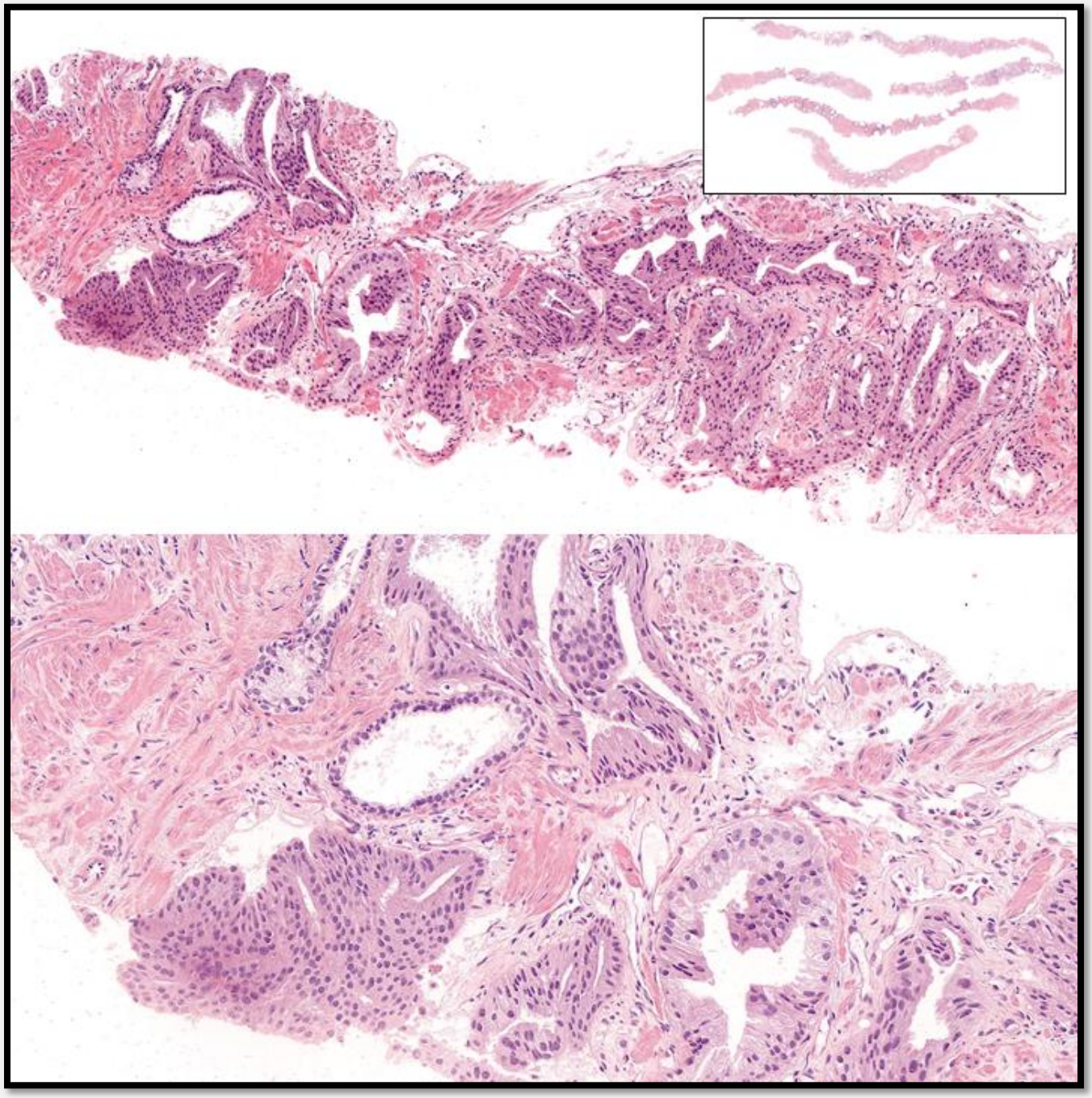
Reference

1. David N. Louis, et. al (Eds): WHO Classification of Tumours of the Central Nervous System (Revised 4th ed). IARC; Lyon 2016.
2. Oussama Abla, et. al. Consensus recommendations for the diagnosis and clinical management of Rosai-Dorfman-Destombes disease. Blood 2018; 131 (26): 2877–2890.

Case 9

Case 9: An 80-year-old man with underlying benign prostate hyperplasia and raised serum PSA level. Biopsy was performed. One representative section.

Targeted Diagnosis: **Prostate acinar adenocarcinoma, pseudohyperplastic variant, Gleason score 6 (3+3), Grade group 1**



Case 9

Submitted Diagnoses by Participating Institutions	Number	
Prostate adenocarcinoma, pseudohyperplastic variant, Gleason 3+3=6/ Adenocarcinoma, Gleason score 6 (3+3), ISUP grade group 1. Background of high grade PIN/ Prostatic acinar adenocarcinoma, Gleason sum 3+4=7	9	Acceptable
High grade PIN ?suspicious focal invasive carcinoma, IHC for HMWCK, p63/ High grade PIN to rule out well differentiated adenocarcinoma.	12	Acceptable
Basal Cell Hyperplasia. Need HMWK, p63, PSA and Ki67	1	
High grade PIN	4	
Atypical intraductal proliferation suspicious for intraductal carcinoma of the prostate (IDC-P), coexisting with basal cell hyperplasia with prominent nucleoli.	1	

Educational notes:

1. There are strips of prostatic tissue displaying foci of crowded atypical glands. These atypical glands are mid to large-sized glands showing amphophilic cytoplasm with undulated architecture and focal papillary infoldings. Presence of benign glands with pale and clear cytoplasm admixed is indicative of infiltrative growth. In addition, these atypical glands show obvious nuclear atypia with nuclear enlargement and prominent nucleoli. Lack of basal cells at these atypical glands are confirmed by HMWCK. These features are that of prostate acinar adenocarcinoma, pseudohyperplastic variant, Gleason score 6 (3+3), Grade group 1.
2. The foci of adenocarcinoma are first recognized based on crowded glands with amphophilic cytoplasm coupled with obvious nuclear atypia. For pseudohyperplastic adenocarcinoma, histological features that are diagnostic of adenocarcinoma (i.e. mucinous fibroplasia, glomerulation and perineural invasion) are rarely observed. Clue to the infiltrative nature of the atypical glands is the presence of admixed benign glands, thus differentiating them from high-grade prostatic intraepithelial neoplasia. Nevertheless, immunohistochemistry for basal cell markers is usually required to confirm absence of basal cell layers in a substantial number of atypical glands to ascertain the diagnosis of pseudohyperplastic adenocarcinoma. Of note, a few glands absent for basal cell layers are not diagnostic of carcinoma, as high grade prostatic intraepithelial neoplasia can have patchy or even negative basal cell layers in occasional glands. In such situation, a diagnosis of “atypical glands suspicious for cancer” may be appropriate.

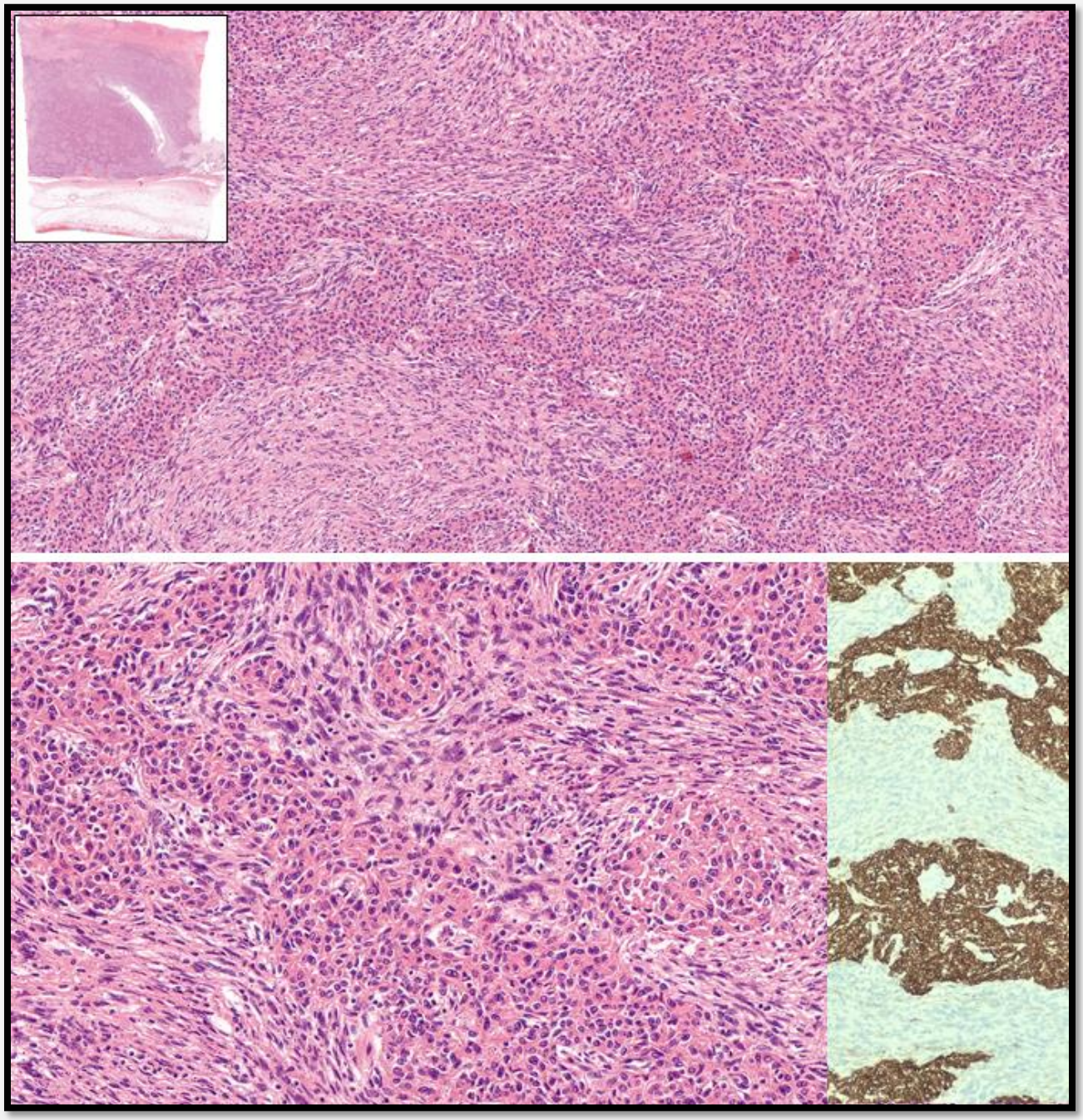
Reference

1. Levi AW, Epstein JI. Pseudohyperplastic prostatic adenocarcinoma on needle biopsy and simple prostatectomy. Am J Surg Pathol. 2000 Aug;24(8):1039-46.
2. Epstein, Jonathan I., and George J. Netto. Differential diagnoses in surgical pathology: genitourinary system. Lippincott Williams & Wilkins, 2014.

Case 10

Case 10: A 56-year-old man presented with a mediastinal mass and resection was performed. One representative section. Image of immunohistochemistry for CK AE1&3 is attached.

Targeted Diagnosis: **Metaplastic thymoma**



Case 10

Submitted Diagnoses by Participating Institutions	Number	
Metaplastic thymoma	23	Acceptable
Thymoma (type AB or others)	2	Acceptable
Thymic squamous cell carcinoma	1	
Biphasic synovial sarcoma	1	

Educational notes:

1. This mediastinal tumor is encapsulated and biphasic, composed of anastomosing strands of epithelial cell component with intervening spindled cell component. The epithelial cell component shows moderately abundant eosinophilic cytoplasm with mild to moderate nuclear pleomorphism. The spindled cell component shows fascicular and storiform patterns with generally bland looking to plump mild cytological atypical nuclei. Hemorrhagic necrosis is observed at the tumor center. Mitotic figure is scanty. Immunohistochemistry shows contrasting staining between the epithelial cell and spindled cell components for CK AE1&3. These features are those of metaplastic thymoma.
2. Metaplastic thymoma is a biphasic tumor confined to the thymus. It is usually well-circumscribed or encapsulated, lacking the lobulation and fibrous bands of conventional thymomas. It consists of anastomosing epithelial cell strands and trabeculae in a background of spindled cell component. Lymphocyte infiltration is typically sparse and plasma cells can be present occasionally. Strikingly, mitotic activity is sparse. Metaplastic thymoma follows an indolent clinical course, with only rare reports of recurrence or malignant transformation.
3. Although biphasic synovial sarcoma is a reasonable differential diagnosis, epithelial component of biphasic synovial is usually pale or columnar cells with rare focal squamous differentiation. Spindle cell component in biphasic synovial sarcoma shows characteristic hemangiopericytoma-like vessels and ropy collagen fibers.
4. In this case, presence of tumor necrosis raises the suspicion of sarcomatoid thymic carcinoma, and rarely focal high-grade transformation of metaplastic thymoma into sarcomatoid carcinoma have been reported. Nonetheless, in sarcomatoid carcinoma, in addition to malignant epithelial component, a high-grade spindle cell component with significant nuclear atypia, frequent mitotic figures, and commonly prominent coagulative necrosis is invariably present.

Reference

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