FINAL REPORT

QUALITY ASSURANCE PROGRAM
GENERAL DIAGNOSTIC HISTOPATHOLOGY
CYCLE 02/2023

NOTES FROM THE COORDINATOR

1. For this cycle 02/2023, a total of 28 institutions responded online by the closing date of 15 November 2023.

2. Excerpts of previously circulated information about this quality assurance program are reproduced here:
    - **IAP-MD QAP provides a platform via 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 02/2023 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. Emerita Dr. Nor Hayati Othman, Prof. Dato Dr. Norain Karim, Dr. Hakimah Mahsin, Datin Dr. Nik Raihan Nik Mustapha, Dr. Razmin Ghazali, Dr. Noraini Mohd Dusa, Dr. Suhaila Abdullah, Dr Farveen Marican, Dr. Nurwahyuna Rosli and Dr. Amizatul Aini Salleh.

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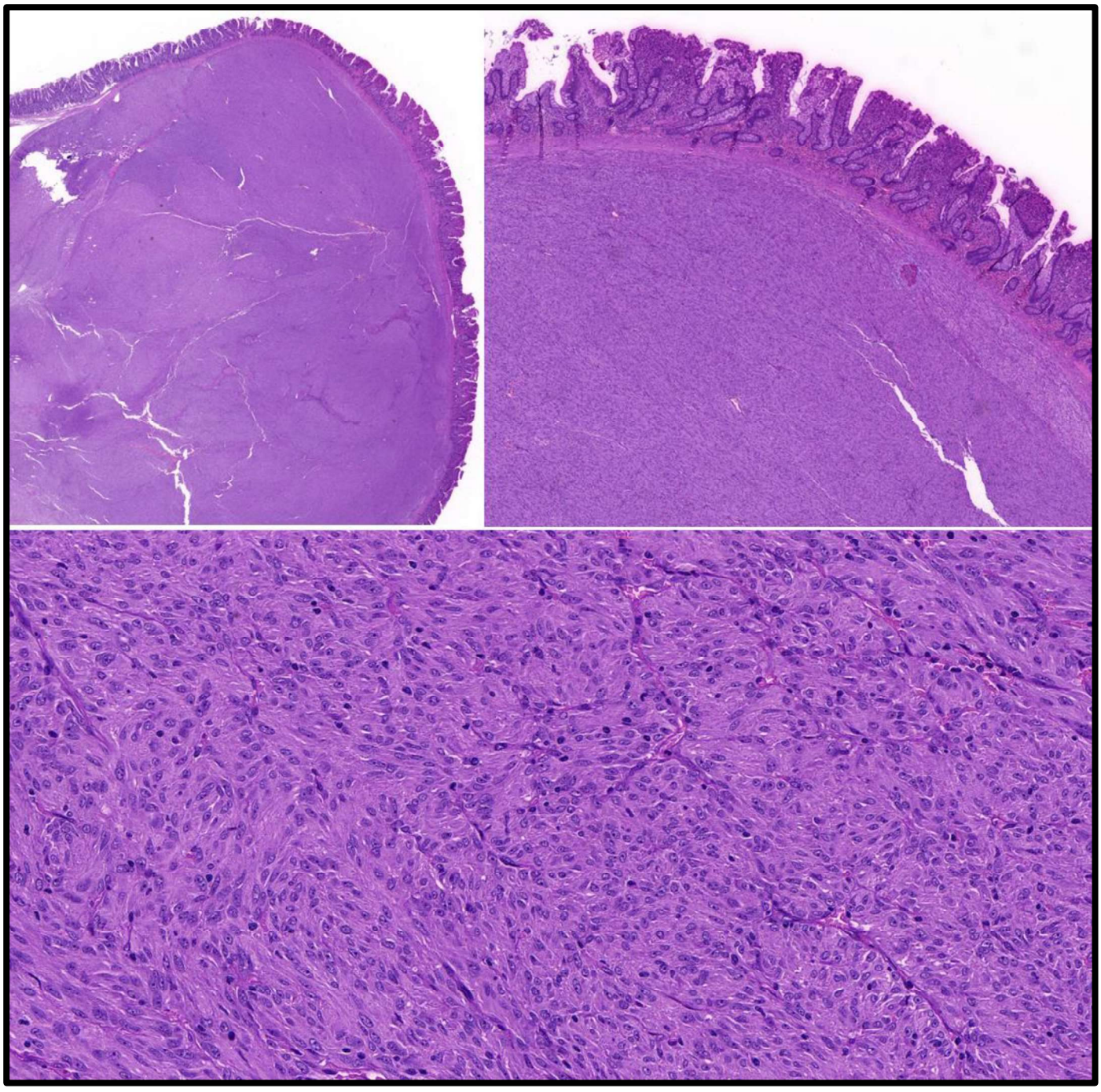
Case 1

Case 1: A 24-year-old female presented with epigastric pain and vomiting. CT scan showed small bowel obstruction.

Targeted Diagnosis: **Gastrointestinal stroma tumor (GIST)**



Case 1

Submitted Diagnoses by Participating Institutions	Number	
Gastrointestinal stromal tumor (GIST).	17	Acceptable
GIST, high/low risk, AFIP category 1	3	Acceptable
GIST for IHC (DOG-1, CD117), GIST with other differentials including IMT, Leiomyoma/Leiomyosarcoma	8	Acceptable

Educational notes:

1. The resection specimen shows a submucosal tumor in the small intestine composed of short fascicles of spindle cells arranged in a focal vague storiform pattern. The spindle cells exhibit moderate nuclear pleomorphism with plump oval nuclei and amphophilic cytoplasm. The histological features are consistent with gastrointestinal stromal tumor (GIST) of small intestine.
2. GIST is a mesenchymal tumor characterized by differentiation towards the interstitial cells of Cajal, which express KIT(CD117) and DOG1. More than 95% of GIST express KIT and 50% of KIT-negative GIST express DOG1. Molecularly, 75% of GIST harbor gain-of-function mutations in KIT gene and 10% in PDGFRA gene. About 5-10% have SDH dysfunction due to alternations in SDH subunit genes, the so-called SDH-deficient GIST.
3. Clinically, GIST has a variable behavior; the relapse risk after surgery is assessed based on (1) tumor mitotic rate (per $5mm^2$), (2) tumor size, and (3) tumor anatomical location (stomach, duodenum, jejunum/ileum, rectum). The relapse risk is best applied to KIT/PDGFRA-mutant GIST but not SDH-deficient GIST. GIST occurs in other sites is best assessed following the criteria for jejunum/ileum GIST.
4. To exclude GIST histologic mimics, the following basic panel is recommended: KIT(CD117), DOG1, Desmin, S100 protein, and CD34. To screen for SDH-deficient GIST, immunostaining for SDHB is performed as it is lost in all SDH-deficient GIST, irrespective of the SDH-subunit that is inactivated.

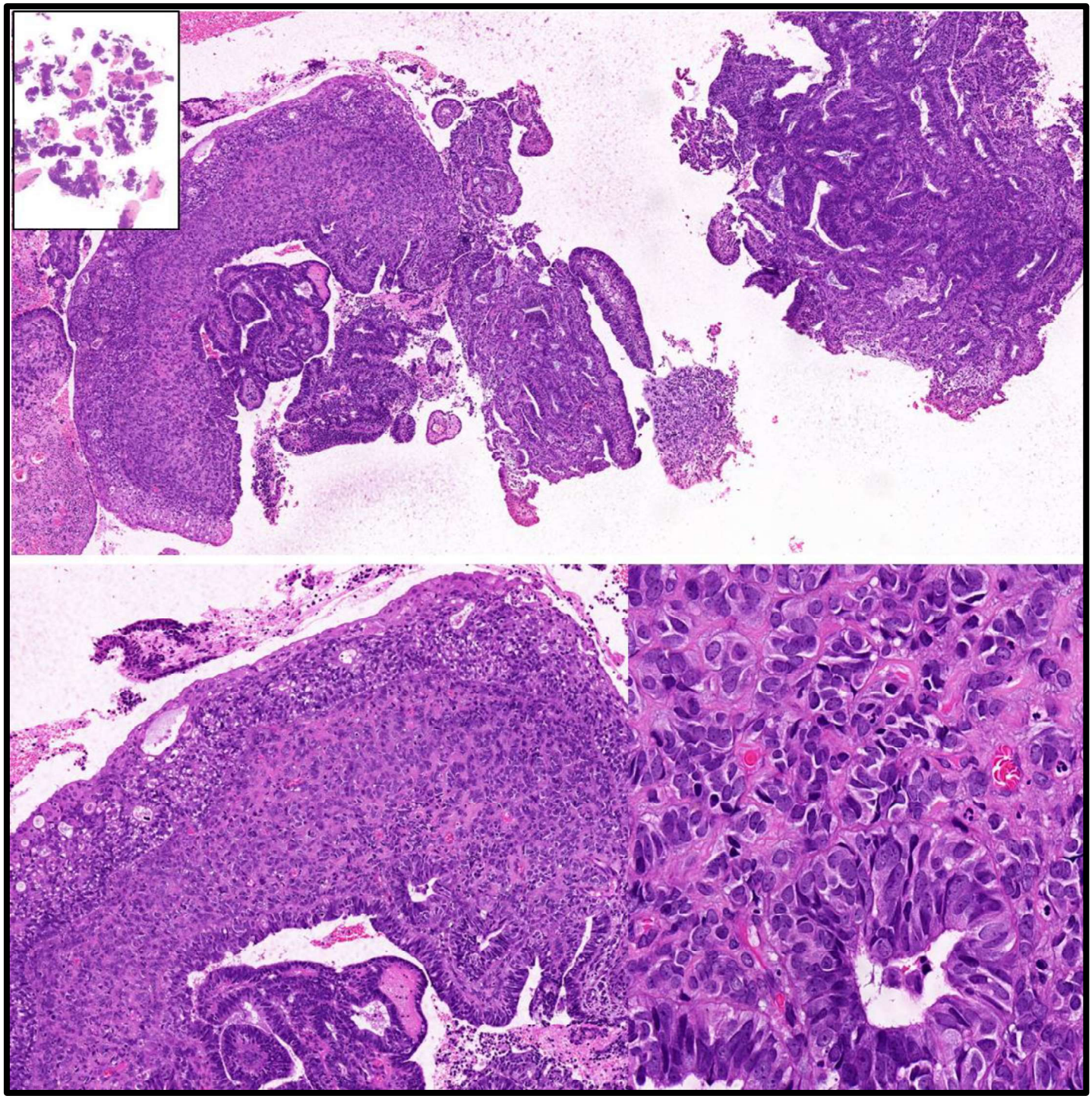
Reference:

1. WHO Classification of Tumours Editorial Board. Digestive system tumours. Lyon (France), WHO classification of tumours series, 5th ed., 2019
2. Protocol for the Examination of Resection Specimens From Patients With Gastrointestinal Stromal Tumor (GIST), Version: 4.3.0.0, December 2022

Case 2

Case 2: A 37-year-old woman presented with prolonged menses. Pipelle sample.

Targeted Diagnosis: **Corded and hyalinized endometroid carcinoma (CHEC)**



Case 2

Submitted Diagnoses by Participating Institutions	Number	
Corded and hyalinized endometrioid carcinoma (CHEC), FIGO grade 1/2; endometrial carcinoma with foci of CHEC pattern	21	Acceptable
Endometroid carcinoma FIGO Grade 1/2; endometrioid carcinoma at least FIGO Grade 2 with solid area of atypical cells, suggest IHC for confirmation	3	Acceptable
Atypical hyperplasia with focal endometrioid carcinoma; atypical hyperplasia with focal intramucosal carcinoma; endometrioid carcinoma with background atypical hyperplasia	3	Acceptable
Endometrioid carcinoma FIGO Grade 1 with neuroendocrine differentiation, further staining needed	1	

Educational notes:

1. Several fragments of the endometrial tissue show epithelioid cells arranged in cords, surrounded by a myxoid stroma. The remaining tissue fragments show conventional endometrioid carcinoma. Both the endometrioid and corded epithelial components, as well as the stroma show low-grade nuclei. The features are diagnostic of corded and hyalinized variant of endometroid carcinoma (CHEC).
2. CHEC is characterized by the presence of epithelioid and/or spindled cells arranged in cords, small clusters, or as single elements. The cells are immersed in a hyaline stroma and merge imperceptibly with a conventional endometrioid component. The stroma commonly appears myxoid and a discrete percentage of cases may show osteoid or chondroid matrix.
3. The biphasic pattern of CHEC may raise the concern of carcinosarcoma. In most cases, the endometrioid component shows low-grade features; the corded/spindled cells as well as the stromal component display bland appearance and a low mitotic index. A minor subset of CHEC may contain either a high-grade endometrioid component or a corded component with increased nuclear atypia, making distinction from carcinosarcoma and dedifferentiated carcinoma a challenge. Features that favor CHEC include (i) anastomosing cords of epithelioid cells merging with an endometrioid component with prominent squamous/morular differentiation, (ii) superficial localization of the corded/spindled component, and (iii) a lower mitotic index in the corded/spindled component as compared to the endometrioid component.
4. CHEC appears clinically and molecularly similar to classical endometrioid carcinoma and mostly shows No Specific Molecular Profile (NSMP) phenotype. The majority of the CHECs reported in the literature showed a favorable outcome. Therefore, CHEC has been considered as a variant of low-grade endometrioid carcinoma.

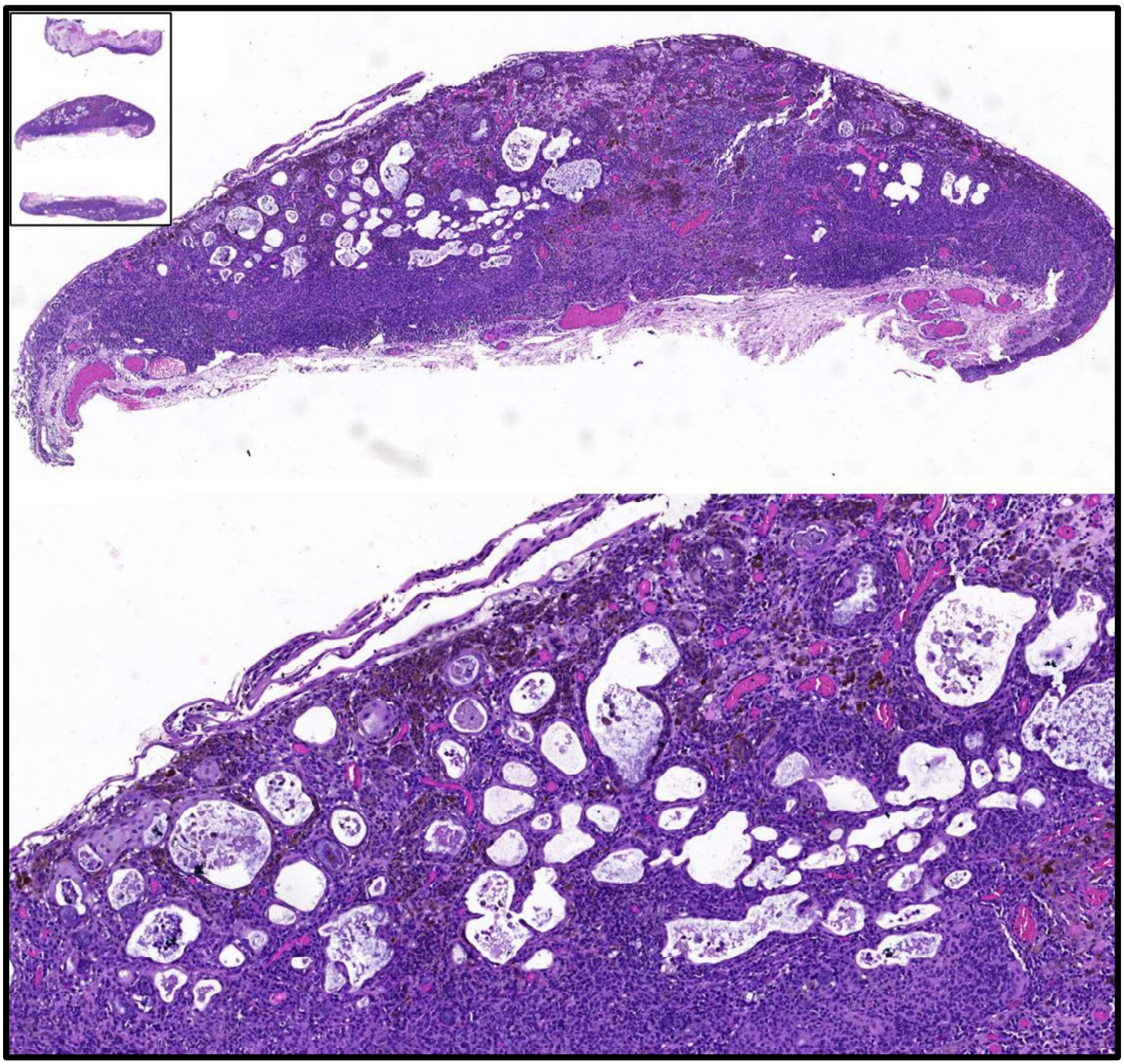
Reference:

1. Travaglino, Antonio, et al. "Corded and hyalinized endometrioid carcinoma: summary of clinical, histological, immunohistochemical and molecular data." Pathology-Research and Practice (2023): 154515.

Case 3

Case 3: A 13-year-old girl presented with a painless right conjunctival pigmented lesion. The lesion had been present since she was 6 years old, but recently increased in size.

Targeted Diagnosis: **Inflammatory juvenile conjunctival nevus (IJCN)**



Case 3

Submitted Diagnoses by Participating Institutions	Number	
Inflammatory juvenile conjunctival nevus (IJCN); Inflamed juvenile conjunctival nevus; Inflammatory juvenile congenital nevus	20	Acceptable
Conjunctival nevus; compound nevus; melanocytic nevus; juvenile conjunctival nevus; compound conjunctival nevus	7	Acceptable
Atypical compound nevus	1	Acceptable

Educational notes:

1. The biopsy shows proliferation of nests of round nevus cells within the epithelium and substantia propria. The nevus cells display mild nuclear atypia, rare mitoses, and retention of melanin; they are surrounded by dense infiltration by lymphocytes, plasma cells and eosinophils. Cystic epithelial rests and scattered goblet cells are present. The clinical and histological features are diagnostic of inflammatory juvenile conjunctival nevus (IJCN).
2. IJCN may manifest as a rapidly growing lesion, which raises the concern of malignancy. Histologically, IJCN may mimic melanoma because the former frequently shows confluent growth of the junctional component, a certain degree of atypia and reverse maturation, i.e. melanocytes displaying nuclear and cytoplasmic size greater in depth than in the junctional component. The presence of epithelial solid or cystic inclusions and the preservation of PAS positive goblet cells supports a benign melanocytic lesion.
3. Cytological features that support a diagnosis of melanoma are marked nuclear pleomorphism, hyperchromasia, presence of nucleoli, spindle cell morphology and mitotic activity in the stromal component. Immunohistologically, the tumor cells frequently express S100 and MelanA. HMB45 is positive in the superficial layer only. Other differential diagnoses include lymphoma and IgG4-related disease.
4. Treatment for IJCN is complete excision, and the prognosis is excellent.

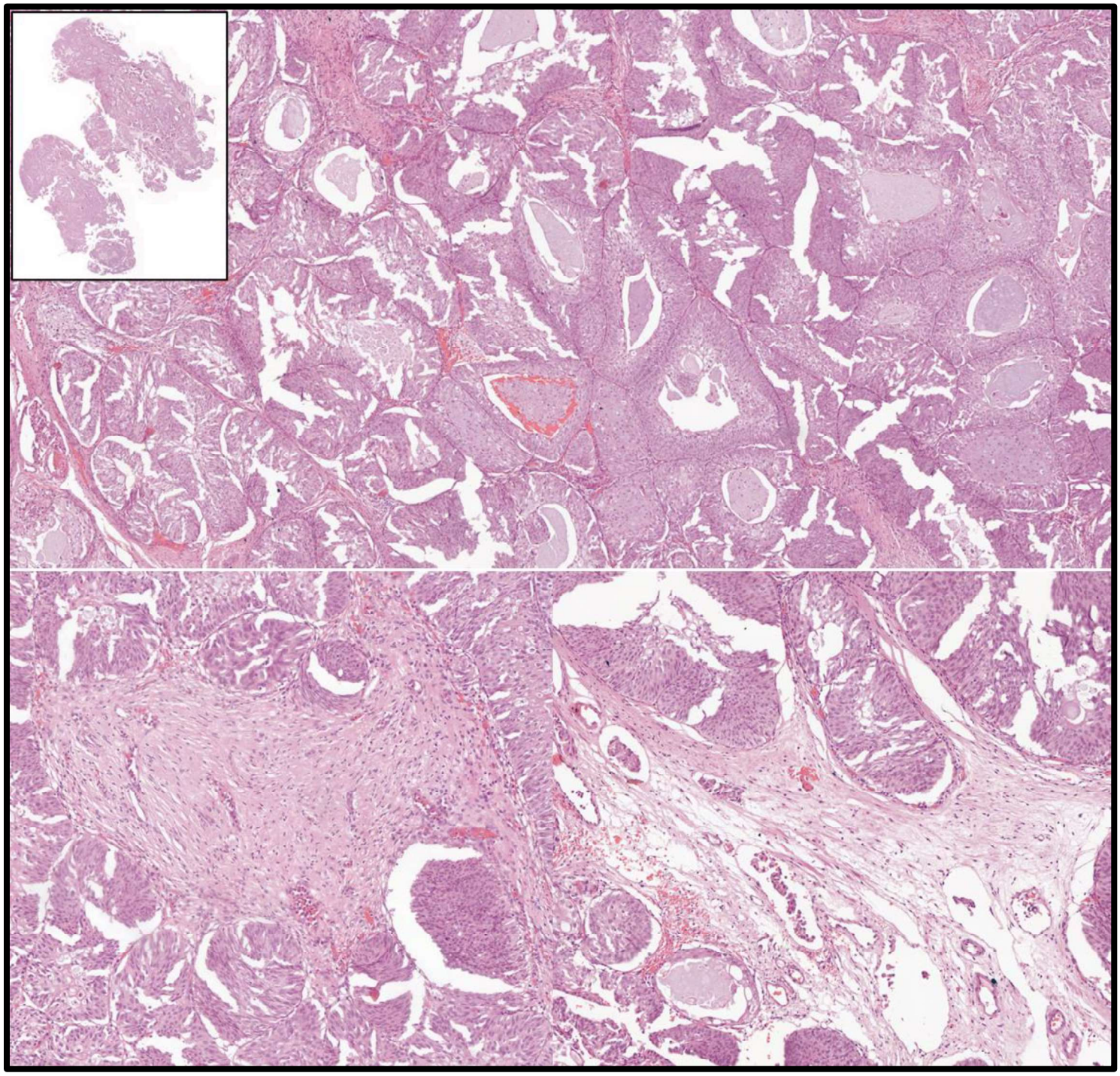
Reference

1. Nebot, L., et al. (2019). Search for histopathological characteristics of inflammatory juvenile conjunctival nevus in conjunctival nevi related to age: Analysis of 33 cases. Saudi Journal of Ophthalmology, 33(3), 214-218.
2. Choi, E. K., & Chévez-Barrios, P. (2014). Inflamed conjunctival nevi: histopathological criteria. Archives of Pathology & Laboratory Medicine, 138(9), 1242-1246.

Case 4

Case 4: A 68-year-old male presented with frequent hematuria and underwent TURBT.

Targeted Diagnosis: **Invasive urothelial carcinoma, low grade, large nested subtype**



Case 4

Submitted Diagnoses by Participating Institutions	Number	
Invasive urothelial carcinoma; invasive urothelial carcinoma, low grade; invasive urothelial carcinoma, nested subtype	19	Acceptable
Inverted papilloma with area of suspicious invasion; inverted urothelial papilloma, unable to exclude infiltrating urothelial carcinoma, nested variant.	2	Acceptable
Non-invasive papillary urothelial carcinoma, high grade (inverted) with stromal Invasion, suspects nested variant invasive urothelial carcinoma	1	Acceptable
Inverted urothelial papilloma; inverted urothelial papilloma with cystitis cystica et glandularis; inverted urothelial neoplasm with low malignant potential.	3	
florid von Brunn nest; florid von Brunn nest with cystitis cystica	3	

Educational notes:

1. These tissue fragments show an inverted growth of urothelial cells arranged in confluent nests of medium to large size. Microcysts are observed in some nests. The nests are mostly rounded with circumscribed border. These constituent urothelial cells show limited cytological atypia. Lamina propria invasion is evident by presence of desmoplastic stroma with inflammatory infiltrates and retraction artifact. Lymphovascular invasion is noted. These features are consistent with invasive urothelial carcinoma, low grade, large nested subtype.
2. Inverted/endophytic urothelial lesions pose diagnostic difficulties as the differential diagnoses range from von Brunn nests to invasive urothelial carcinoma, nested (including large nested) subtype. The diagnostic approach needs to take into consideration of both architectural and cytological features, namely the type of inverted pattern (i.e., nests versus trabeculae), number of cellular layers, degree of atypia (including polarity assessment), and mitotic index.
3. Architecturally, von Brunn nests are less packed and have a flat base. Inverted papilloma predominantly shows a trabecular inverted pattern with orderly polarized cells. Inverted urothelial neoplasm with low malignant potential and inverted noninvasive papillary urothelial carcinoma both feature broad-front verrucous carcinoma-like growth or inverted papilloma-like growth or a mixture of both patterns. Unequivocal stromal invasion is absent.
4. Cytologically, there is a group of deceptively bland invasive urothelial carcinomas, including the nested subtype and the microcystic subtype. Recognizing this group of invasive urothelial carcinoma is important to avoid confusion with commonly occurring benign proliferations.
5. Large nested subtype of invasive urothelial carcinoma as in this case consists of large confluent nests but has an overall bland histologic features. It is distinguished from other benign or noninvasive mimickers by presence of muscular propria invasion, irregularly infiltrating nests, or stromal reaction.

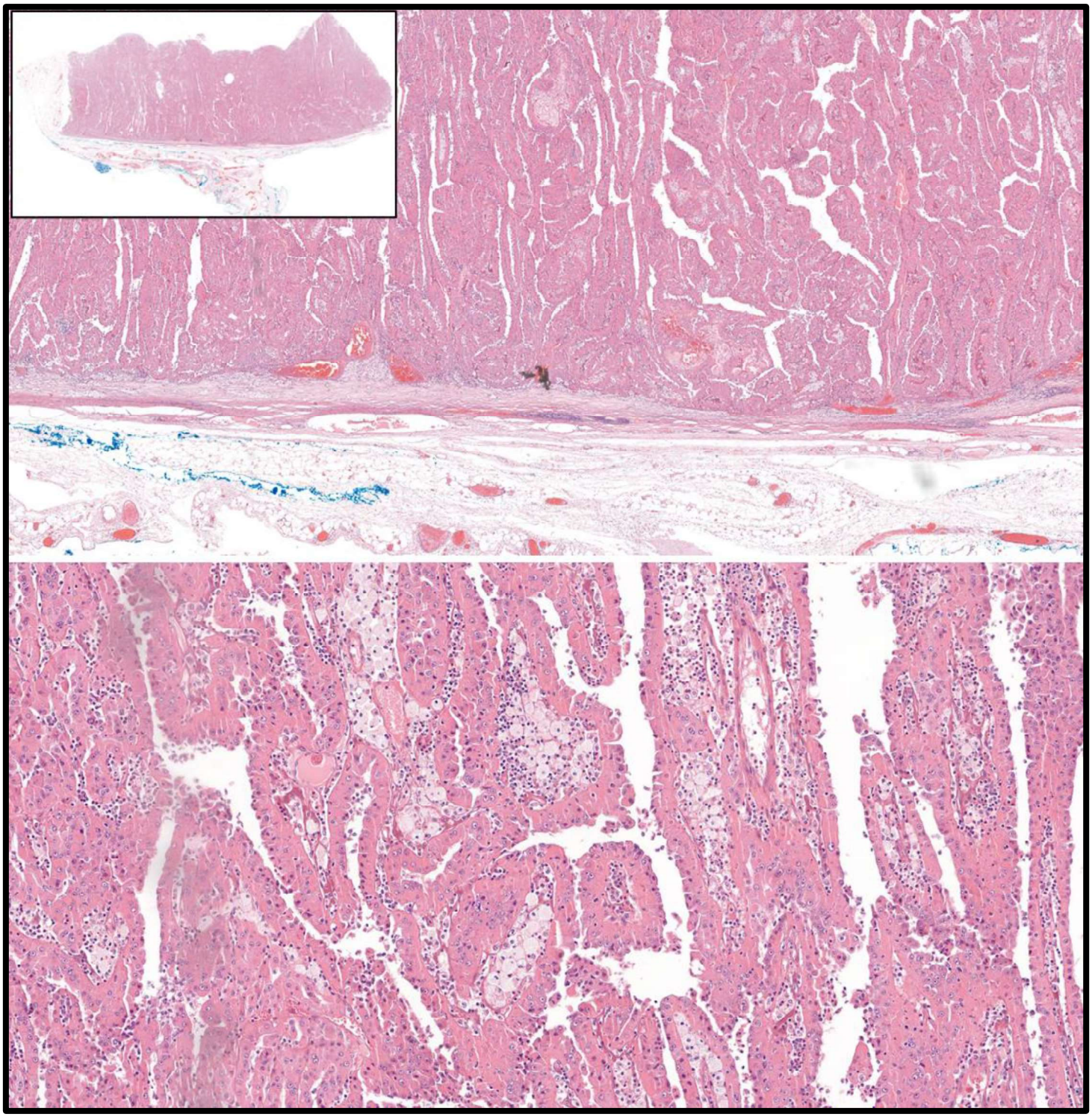
Reference

1. Biopsy Interpretation of the Bladder. Jonathan I. Epstein, et al. 4th edition, 2024.
2. Cox, R., & Epstein, J. I. (2011). Large nested variant of urothelial carcinoma: 23 cases mimicking von Brunn nests and inverted growth pattern of noninvasive papillary urothelial carcinoma. The American journal of surgical pathology, 35(9), 1337-1342.

Case 5

Case 5: A 60-year-old female presented with a renal mass and underwent nephrectomy.

Targeted Diagnosis: **Papillary renal cell carcinoma**



Case 5

Submitted Diagnoses by Participating Institutions	Number	
Papillary renal cell carcinoma; papillary renal cell carcinoma, WHO/ISUP grade 3; papillary renal cell carcinoma for IHC (AMACR)	16	Acceptable
Papillary renal neoplasm with reversed polarity for IHC	3	Acceptable
Papillary renal cell carcinoma, oncocytic variant	5	Acceptable
Papillary renal cell carcinoma, NOS most likely type 2; papillary renal cell carcinoma type 2	4	

Educational notes:

1. This renal tumor is well-demarcated and shows papillary architecture. The papillae are lined by a pseudostratified layer of columnar cells displaying WHO/ISUP grade 3 nucleolar prominence and abundant eosinophilic cytoplasm. There are characteristic foamy histiocytes located in the papillary cores. These histological features are consistent with papillary renal cell carcinoma.
2. Recent classification of renal cell neoplasia has restricted the diagnosis of papillary renal cell carcinoma (PRCC) to a more defined entity by exclusion of the previously known “type 2 PRCC”; therefore, subclassification of “type 1” and “type 2 PRCC” is no longer required.
3. PRCC shows a spectrum of morphological and molecular features, ranging from low to high grade tumors. Classic PRCC shows papillae with vascular cores, foamy histiocytes and psammoma bodies. Nonetheless, the spectrum of PRCC has expanded to include different patterns such as biphasic (alveolar/squamoid) PRCC, oncocytic low-grade PRCC, Warthin-like PRCC, solid PRCC and papillary renal neoplasm with reverse polarity (PRNRP). These patterns are currently not considered as separate subtypes of PRCC.
4. The differential diagnoses of high-grade PRCC such as this case include fumarate hydratase (FH)-deficient RCC and microphthalmia-associated transcription factor (MITF) family translocation RCC. Morphological pattern heterogeneity would favor these differential diagnoses and requires further immunohistochemical surrogates or molecular studies.
5. Although it is considered a pattern of PRCC, PRNRP is increasingly recognized as an entity with characteristic features such as GATA3 positivity and KRAS mutation. Nevertheless, in contrast to the current case, PRNRP shows apically located WHO/ISUP grade 1 - 2 nuclei.

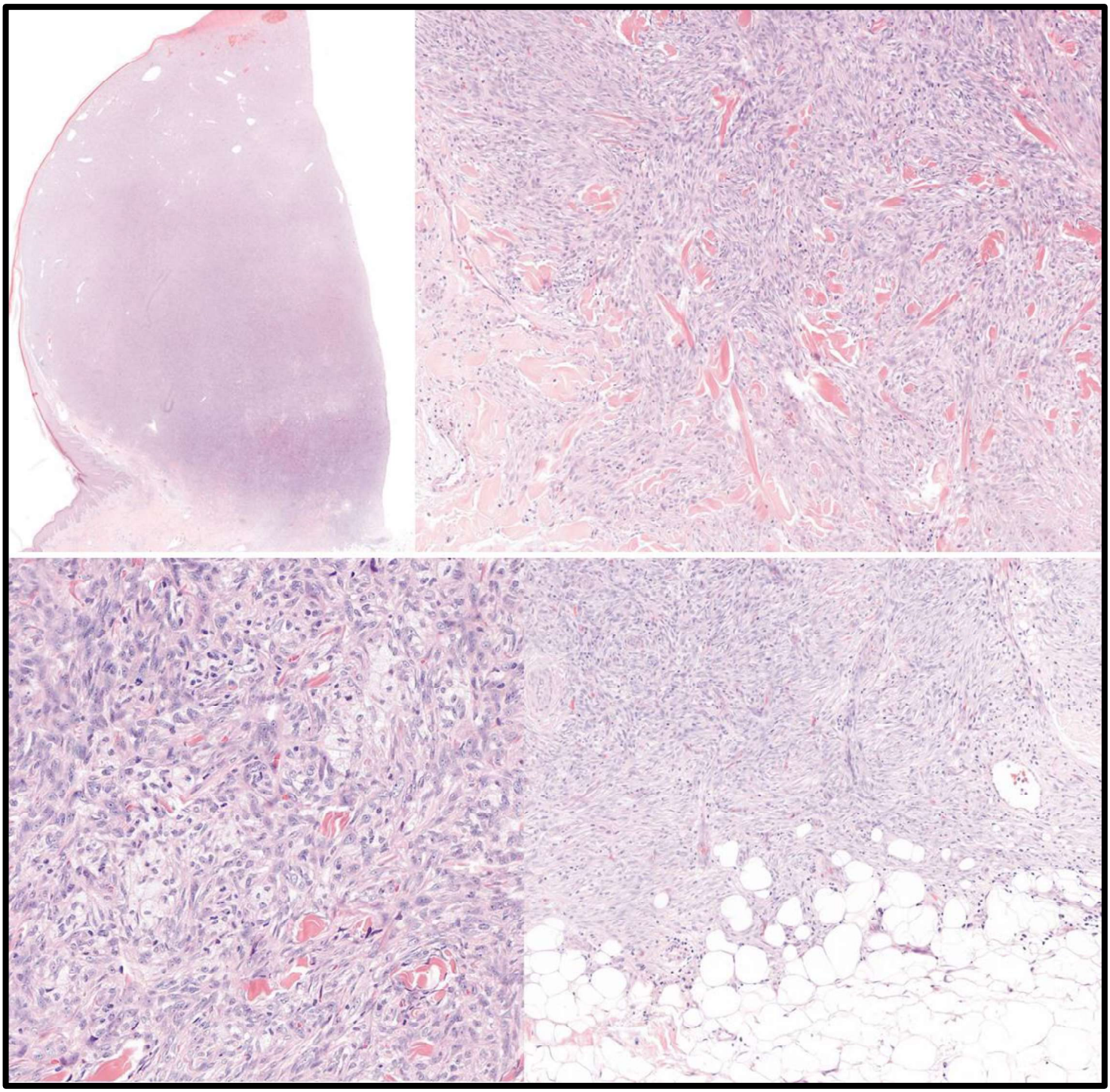
Reference

1. Trpkov, Kiril, et al. New developments in existing WHO entities and evolving molecular concepts: The Genitourinary Pathology Society (GUPS) update on renal neoplasia. Modern Pathology 34, 7 (2021): 1392-1424.
2. WHO Classification of Tumours Editorial Board. Urinary and male genital tumours. Lyon (France): 2022, WHO classification of tumours series, 5th ed.

Case 6

Case 6: A 49-year-old man presented with a pedunculated mass at thigh.

Targeted Diagnosis: **Cellular dermatofibroma/ fibrous histiocytoma**



Case 6

Submitted Diagnoses by Participating Institutions	Number	
Dermatofibroma; cellular dermatofibroma; aneurysmal dermatofibroma; benign fibrous histiocytoma	15	Acceptable
Spindle cell lesions, differential diagnosis of cellular dermatofibroma, dermatofibrosarcoma protruberans, for IHC	9	Acceptable
Dermatofibrosarcoma protuberans, DFSP for IHC, DFSP versus solitary fibrous tumor	3	
Solitary fibrous tumour	1	

Educational notes:

1. This dermal-based tumor mass is cellular and composed of spindle cells arranged in a storiform pattern. The spindle cells show plump oval nuclei with scattered mitoses. The overlying epidermis is ulcerated. At the lateral side of the tumor, collagen bundle entrapment is evident. There are focal foamy histiocytes admixed in this tumor. This tumor infiltrates minimally into the subcutis at one focus. These histological features are those of cellular dermatofibroma/ fibrous histiocytoma.
2. Although this dermatofibroma is cellular, it shows characteristic collagen bundle entrapment at the lateral side of the tumor and focal reactive foamy histiocytes. There is focal minimal infiltration into the subcutis; this feature is nevertheless common for cellular dermatofibroma.
3. The major differential diagnosis for this cellular dermatofibroma is dermatofibrosarcoma protruberans (DFSP). DFSP shows diffuse infiltration of dermis as well as infiltration into subcutaneous tissue with a typical “honeycomb” architecture. The diagnosis is further supported by strong diffuse positivity for CD34 in DFSP in contrast to lack of CD34 or focal/patchy CD34 positivity in cellular dermatofibroma.
4. Cutaneous solitary fibrous tumor is exceedingly rare, and it usually presents as a subcutaneous nodule. Histologically, cellular solitary fibrous tumor shows spindle cells embedded in focally hyalinized stroma with pericytomatous vessels. STAT6 positivity is highly sensitive and specific for solitary fibrous tumor.

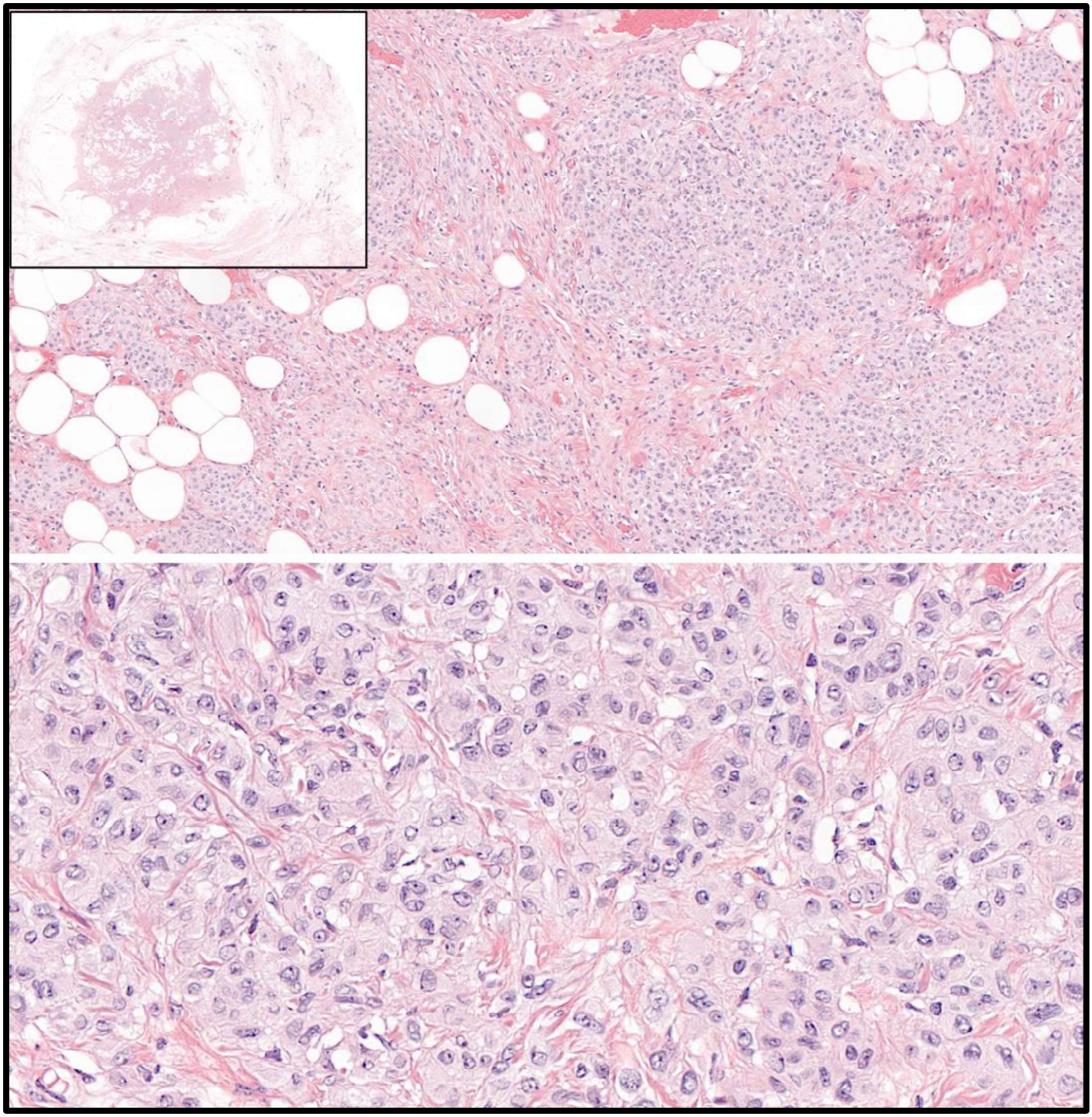
Reference

1. Hornick, J. L. (2020). Cutaneous soft tissue tumors: how do we make sense of fibrous and “fibrohistiocytic” tumors with confusing names and similar appearances? Modern Pathology, 33, 56-65.
2. Vincek, V., et al. (2022). Cutaneous solitary fibrous tumor: Report of three cases with review of histopathological mimics. Journal of Cutaneous Pathology, 49(2), 167-171.

Case 7

Case 7: A 55-year-old female has a previous history of breast cancer with lumpectomy and had a separate breast mass. Excision. Immunohistochemistry provided: Desmin, ER.

Targeted Diagnosis: **Myofibroblastoma**



Case 7

Submitted Diagnoses by Participating Institutions	Number	
Myofibroblastoma	27	Acceptable
Epithelioid angiomyolipoma	1	

Educational notes:

1. The mass is fairly circumscribed and composed of broad anastomosing fibrous bands mixed with adipocytes. In the fibrous bands, there are epithelioid cells displaying abundant pale eosinophilic cytoplasm and round to oval nuclei with inconspicuous nucleoli and occasional nuclear grooves. At areas, these epithelioid cells are arranged in clusters. These epithelioid cells are strong positive for Desmin and positive for estrogen receptor. These features are diagnostic of myofibroblastoma.
2. Mammary myofibroblastoma is a rare benign mesenchymal tumor showing fibroblastic, myofibroblastic and less frequently myoid differentiation. There is no epimyoepithelial component and it shows low mitotic count with no atypical mitosis and no necrosis. Nonetheless, myofibroblastoma can adopt a variety of histological patterns, including lipomatous, myxoid, fibrous/collagenized, epithelioid/deciduoid, and palisading/Schwannian-like. Immunohistochemically, myofibroblastoma coexpresses CD34 and desmin as well as hormonal receptors (estrogen receptor, progesterone receptor and androgen receptor). Molecularly, myofibroblastoma carries deletion of 13q that results in the loss of RB1 expression by immunohistochemistry.
3. Epithelioid myofibroblastoma may sometimes show nuclear pleomorphism, which may be confused with an invasive carcinoma; negative cytokeratin immunostaining would help in this distinction.
4. Lipomatous myofibroblastoma may be confused with other spindle cell tumors that contain a lipomatous component. Although angiomyolipoma shows histological overlap with presence of myoid perivascular cells, adipose tissue, and blood vessels, it is extremely rare with only a single mammary angiomyolipoma case report in literature. Immunohistochemically, angiomyolipoma is positive for HMB45 but negative for CD34.

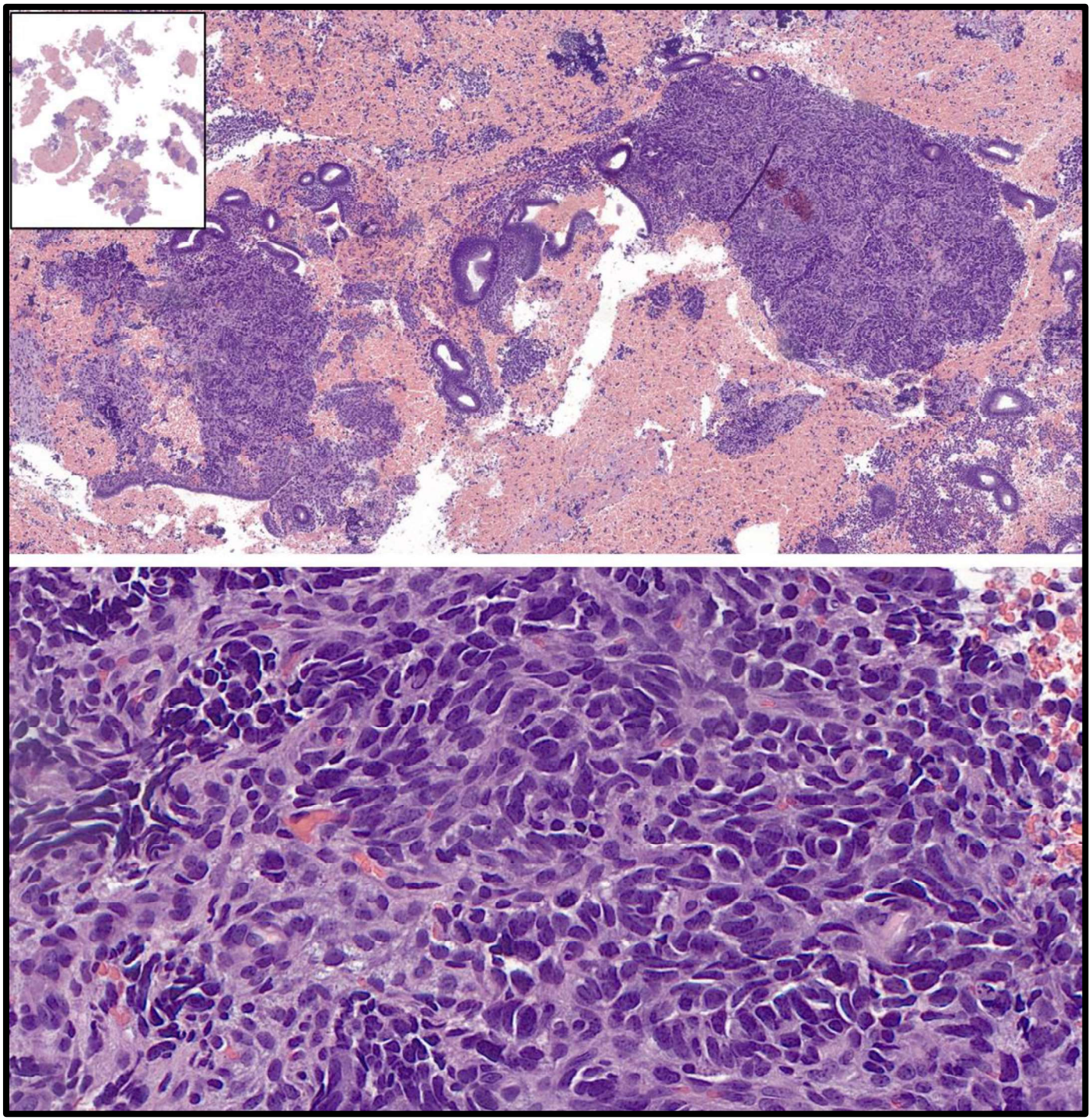
Reference

1. Magro, G. (2008). Mammary myofibroblastoma: a tumor with a wide morphologic spectrum. Archives of pathology & laboratory medicine, 132(11), 1813-1820.
2. 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
3. Damiani, S., Chiodera, P., Guaragni, M., & Eusebi, V. (2002). Mammary angiomyolipoma. Virchows Archiv, 440, 551-552.

Case 8

Case 8: A 54-year-old woman was recently diagnosed with lung adenocarcinoma, currently presented with abnormal uterine bleed. Pipelle sample. Immunohistochemistry provided: ER, TTF1, Synaptophysin, Chromogranin, Ki-67.

Targeted Diagnosis: **Small cell neuroendocrine carcinoma (indeterminate for tumor origin)**



Case 8

Submitted Diagnoses by Participating Institutions	Number	
Small cell neuroendocrine carcinoma with a comment on limitation to determine primary solely based on TTF1 immunohistochemistry	3	Acceptable
Small cell neuroendocrine carcinoma; small cell neuroendocrine carcinoma to exclude metastasis; small cell carcinoma	11	Acceptable
Neuroendocrine carcinoma; Neuroendocrine carcinoma, metastatic lesion cannot be excluded	2	
Metastatic small cell carcinoma; metastatic small cell lung carcinoma, metastatic neuroendocrine carcinoma of lung origin, small cell neuroendocrine carcinoma of the uterus	12	

Educational notes:

1. Infiltrating cords, trabeculae and cohesive clusters of malignant cells are seen in between benign endometrial glands. These malignant cells display hyperchromatic and stippled nuclei, inconspicuous nucleoli, scanty cytoplasm, nuclear molding and smearing artefact. Immunohistochemically they are positive for synaptophysin, chromogranin and TTF-1. ER is negative. The features are diagnostic of small cell neuroendocrine carcinoma (SCNEC). The origin of this tumor (gynecology tract versus lung) is indetermined.
2. The diagnosis of SCNEC requires morphologically prototypic features of small cell carcinoma, i.e. high-grade tumor cells with hyperchromatic nuclei and scanty cytoplasm. Immunohistochemical confirmation of neuroendocrine differentiation is desirable but not required for diagnosis when the histological criteria are met.
3. SCNECs of the female genital tract are rare highly aggressive tumors, which show a high propensity for systemic spread and poor prognosis. They occur mostly as mixed carcinomas of SCNECs and non-neuroendocrine carcinomas, with the exception for vulva SCNECs, which commonly present as a pure type. SCNECs are more common in the cervix where they are associated with high-risk HPV infection, primarily with HPV 16 and 18. In the uterine corpus, endometrial neuroendocrine carcinomas are often mixed with FIGO grade 1 or 2 endometrioid carcinoma or may be a part of the carcinoma component of carcinosarcoma.
4. When confronted by the issue of assigning the site of tumor origin for SCNECs, immunohistochemical positivity of TTF-1 should be interpreted with caution. TTF-1 might be helpful in differentiating pulmonary carcinoid tumors from extrapulmonary carcinoids. However, for high-grade tumors, TTF-1 positivity should not be used as a marker of lung origin, as positive expression has been described in numerous primary extrapulmonary SCNECs including prostate, bladder, intestinal and gynecological organs. In such cases, clinical and radiological correlation as well as multi-disciplinary discussion are essential to arrive at a consensus diagnosis.

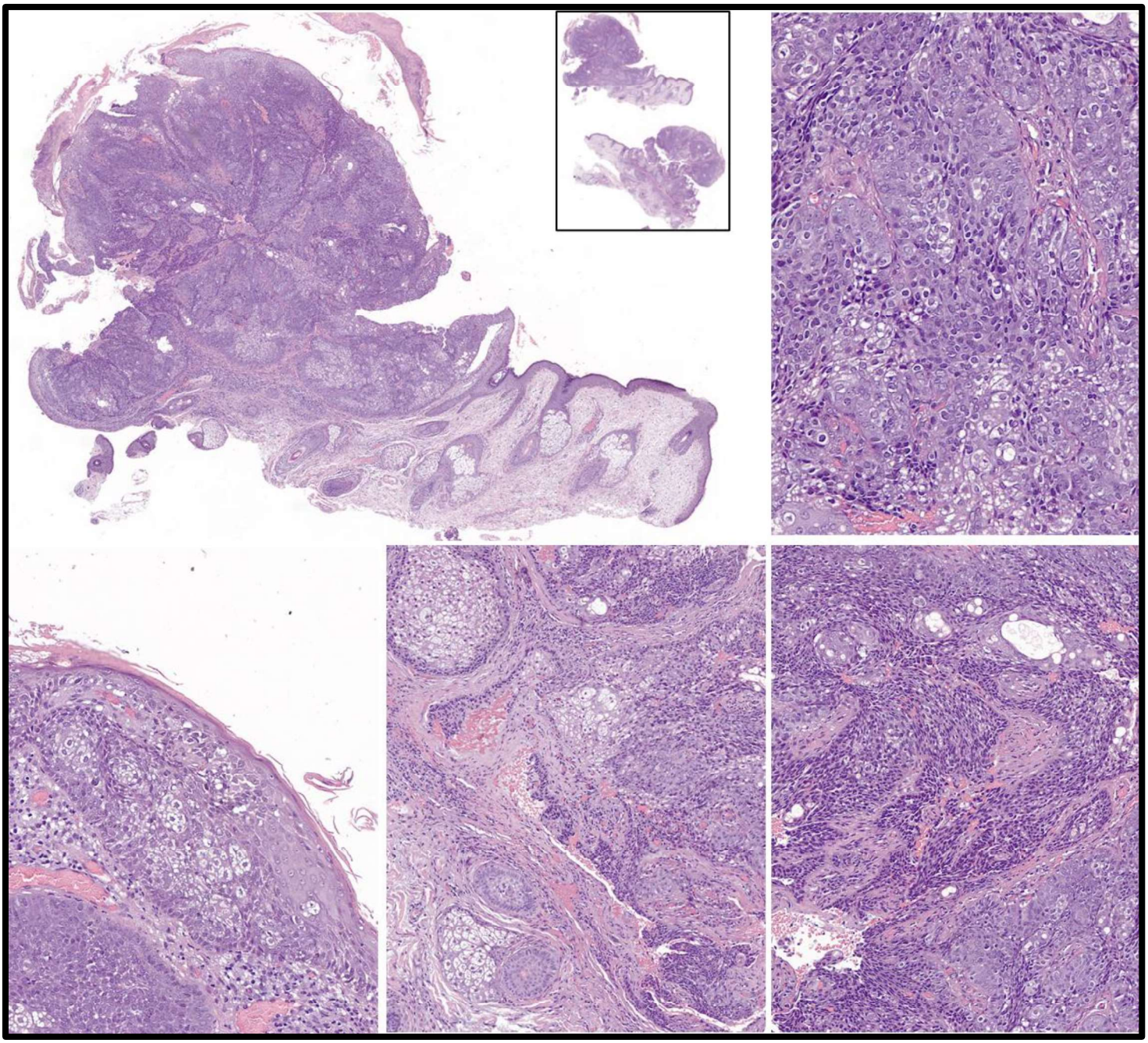
Reference

1. Verset, L., Arvanitakis, M., Loi, P., Closset, J., Delhaye, M., Remmelink, M., & Demetter, P. (2011). TTF-1 positive small cell cancers: Don't think they're always primary pulmonary!. World Journal of Gastrointestinal Oncology, 3(10), 144.
2. Talia, K. L., & Ganesan, R. (2022). Neuroendocrine Neoplasia of the Female Genital Tract. Surgical Pathology Clinics, 15(2), 407-420.

Case 9

Case 9: A 54-year-old man presented with a right upper eyelid mass for 9 months.

Targeted Diagnosis: **Sebaceous carcinoma**



Case 9

Submitted Diagnoses by Participating Institutions	Number	
Sebaceous carcinoma	12	Acceptable
Sebaceous neoplasm, differentials include sebaceous carcinoma/suspicious of malignancy	2	Acceptable
Sebaceoma; sebaceous adenoma	12	
sebaceous neoplasm; sebaceous neoplasm favor sebaceoma	2	

Educational notes:

1. The eyelid mass is composed of irregular lobules of basophilic germinative sebocytes admixed with more mature sebocytes. There is a dermal growth pattern with pushing borders with focal areas demonstrating infiltrative cords. The tumor cells display enlarged, atypical nuclei with a high nuclear: cytoplasmic ratio, vesicular chromatin, and prominent nucleoli. Cells with more mature sebaceous differentiation display abundant intracytoplasmic vacuoles, imparting a foamy appearance. The vacuoles impinge on the nucleus creating scalloping. The features are that of well to moderately differentiated sebaceous carcinoma.
2. This tumor is a sebaceous neoplasm as evidenced by neoplastic sebocytes as well as formation of neoplastic sebaceous ducts.
3. The benign sebaceous adenoma on one spectrum is composed of a mixture of germinative, immature sebocytes and mature sebocytes whereby the mature sebocytes occupy more than 50%. Sebaceoma is another benign sebaceous neoplasm. While maintaining its organoid growth patterns as in sebaceous adenoma, sebaceoma is predominantly composed of (more than 50%) germinative, immature sebocytes.
4. Sebaceous carcinoma on the malignant spectrum can adopt various architectural patterns, including well-circumscribed lobules with pushing borders, comedo necrosis, papillary and highly infiltrative cords; combinations of these patterns are often observed. Malignant features such as prominent cytologic atypia, an infiltrative pattern of growth, and intraepidermal involvement (with pagetoid extension) distinguish sebaceous carcinoma from its benign counterparts.
5. Sebaceous adenoma, sebaceoma, and sebaceous carcinoma may serve as markers for Muir-Torre syndrome (MTS) as MTS is characterized by presence of a sebaceous tumor and a visceral malignancy. MTS results from germline mutations affecting genes involved in DNA mismatch repair (MMR) pathways. Therefore, loss of MMR proteins by immunohistochemistry and subsequent MMR germline testing may be indicated in selected cases.

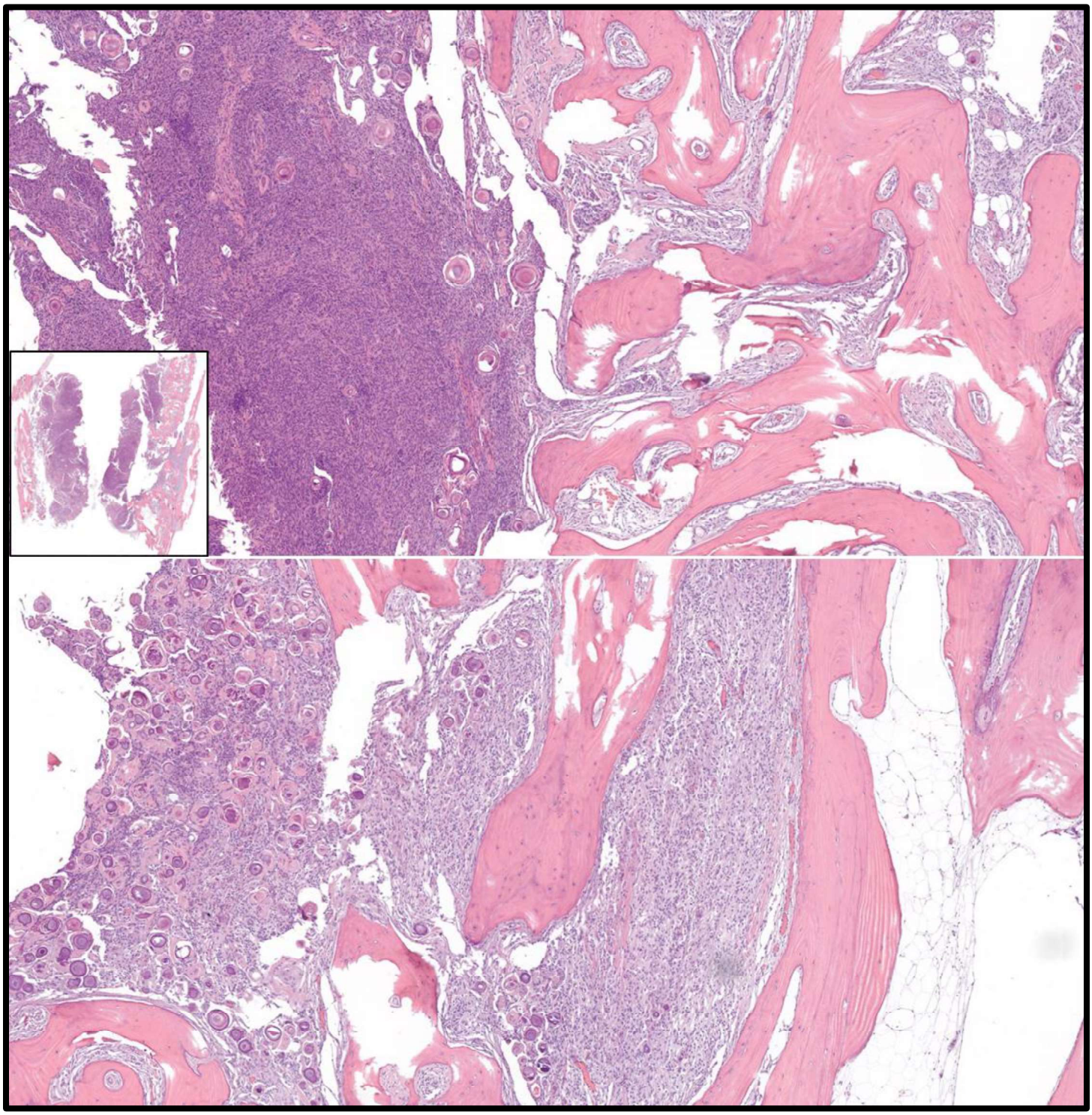
Reference

1. Flux, K. (2017). Sebaceous neoplasms. Surgical pathology clinics, 10(2), 367-382.
2. Tetzlaff, M. T., North, J., & Esmaeli, B. (2019). Update on sebaceous neoplasia: the morphologic spectrum and molecular genetic drivers of carcinoma. Diagnostic Histopathology, 25(3), 102-109.

Case 10

Case 10: A 61-year-old woman with a T11 spinal tumor. Intraoperatively noted a hard tumor attached to posterior part of dura and compressing the spinal cord.

Targeted Diagnosis: **Transitional meningioma, WHO grade 1**



Case 10

Submitted Diagnoses by Participating Institutions	Number	
Transitional meningioma, WHO grade I	1	Acceptable
Psammomatous meningioma WHO grade 1; psammomatous meningioma; meningioma, psammomatous, grade 1 with invasion into the bone; meningothelial meningioma, WHO Grade I	26	Acceptable
Meningioma, WHO grade 1.	1	Acceptable

Educational notes:

1. The spinal tumor shows an admixture of tumor patterns, predominantly composed of monomorphic epithelioid cells arranged in lobules and whorls, displaying abundant eosinophilic cytoplasm and round to oval nuclei with nuclear holes. Focal bundles of spindled fibrous tumor cells and transitional areas are also present. Numerous psammoma bodies are embedded in between the tumor cells. Features of higher grade such as increased mitosis or cellularity, small cells with high N:C ratio, nucleoli prominence, sheeting, spontaneous necrosis are absent. The features favor transitional meningioma, WHO grade I.
2. Like cranial meningioma, there is a wide morphological spectrum of histological subtypes of spinal meningioma, the most common being meningothelial, psammomatous, and transitional meningiomas. All three subtypes share similar molecular features, particularly 22q deletions, NF2 mutations, and epigenetic profiles. Psammomatous meningioma has predominance of psammoma bodies over viable tumor cells, so much so that actual meningioma cells can be rare to virtually absent. In contrast, transitional meningioma predominantly contains meningothelial, fibrous and transitional tumor cells, and may show frequent psammoma bodies. In contrast, whorls and psammoma bodies are rarer in the meningothelial subtype.
3. Most spinal meningiomas correspond to CNS WHO grade 1. Features of more aggressive growth can arise in any of the different morphological patterns. CNS WHO grade should be assigned by applying the specific criteria for CNS WHO grade 2 to assign atypical meningioma or CNS WHO grade 3 to assign anaplastic meningioma, regardless of the underlying morphological subtype.

Reference

1. WHO Classification of Tumours Editorial Board. Central nervous system tumours. Lyon (France): WHO classification of tumours series, 5th ed.; vol. 6.