International Academy of Pathology
Malaysian Division

FINAL REPORT

QUALITY ASSURANCE PROGRAM
GENERAL DIAGNOSTIC HISTOPATHOLOGY
CYCLE 01/2023

NOTES FROM THE COORDINATOR

1. For this cycle 01/2023, a total of 29 institutions responded online by the closing date of 15 June 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 01/2023 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 and Dr. Nurul Akmar Misron.

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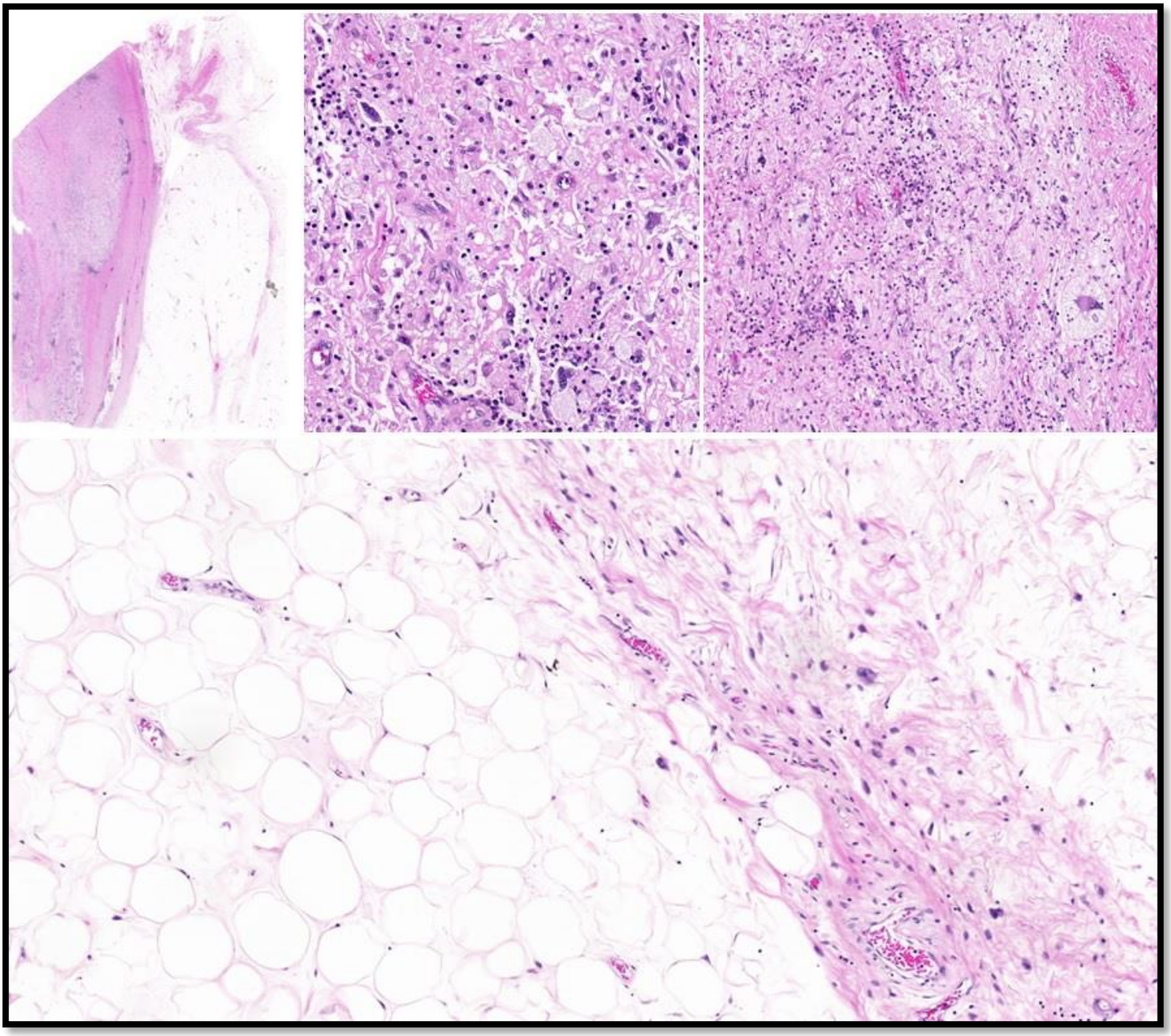
Coordinators for IAP-MD QAP

Case 1

Case 1: A 55-year-old man presented with a left para-testicular mass.

Targeted Diagnosis: **Dedifferentiated liposarcoma**



Case 1

Submitted Diagnoses by Participating Institutions	Number	
Dedifferentiated liposarcoma	14	Acceptable
Liposarcoma (LPS)	12	Acceptable
Well-differentiated LPS/ Well-differentiated LPS, inflammatory type	2	Acceptable
Inflammatory myofibroblastic tumor	1	

Educational notes:

1. This para-testicular mass is a dedifferentiated liposarcoma (LPS) showing transition of a well-differentiated liposarcoma LPS to non-lipogenic sarcoma. The dedifferentiated lipomatous component is composed of scattered marked pleomorphic malignant cells set in an edematous inflammatory stroma. Some of the malignant cells are in multinucleated form. The nature of this malignant tumor is revealed with the presence of the adjacent well-differentiated LPS. The well-differentiated LPS is composed of mostly mature adipose showing marked variation in size and shape. Atypical stromal cells displaying enlarged hyperchromatic nuclei are seen within the fibrous septa. Occasional adipocytes with atypical enlarged hyperchromatic nuclei are also seen.
2. Dedifferentiated LPS is usually a non-lipogenic sarcoma of variable histological grades. The diagnosis of dedifferentiated LPS lies in recognition of progression of an atypical lipomatous tumor/ well-differentiated LPS in the primary or in a recurrence.
3. Nonetheless, the well-differentiated component may not be identifiable in some cases. Diffuse nuclear expression of MDM2 and/or CDK4 immunohistochemistry or demonstration of MDM2 gene amplification by FISH would be helpful to differentiate dedifferentiated LPS from other high-grade sarcomas in the appropriate setting, especially in the case of sarcomas arising in the retroperitoneum and spermatic cord.
4. Dedifferentiated LPS has a high local recurrence (at least 40%) and develops distant metastases in 15-20%. Nevertheless, as compared to the other high-grade sarcomas, dedifferentiated LPS has a less aggressive clinical course.

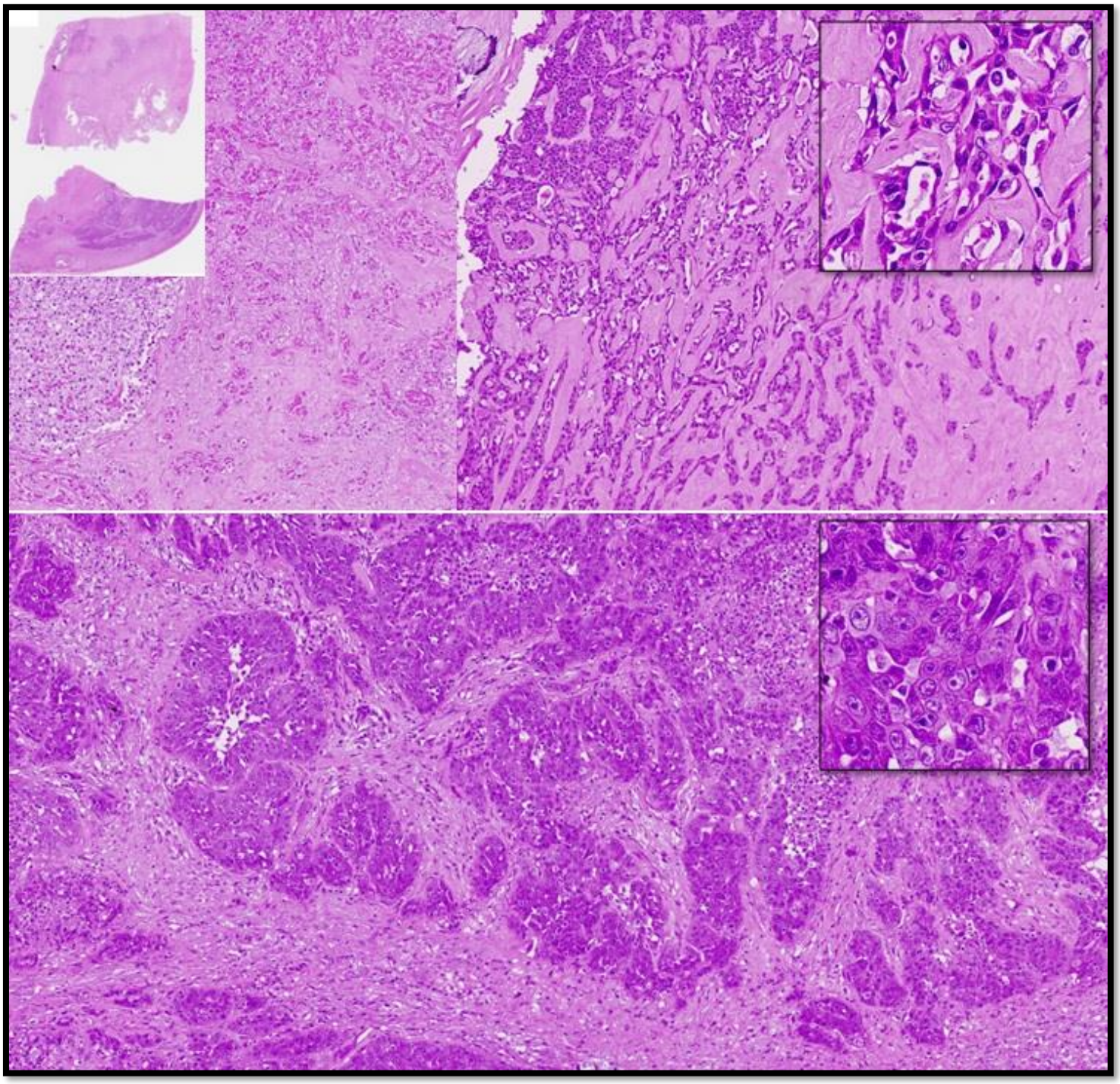
Reference:

1. WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2020

Case 2

Case 2: A 75-year-old woman presented with dysphagia and hoarseness of voice due to a thyroid mass.

Targeted Diagnosis: **Anaplastic thyroid carcinoma with associated papillary thyroid carcinoma**



Case 2

Submitted Diagnoses by Participating Institutions	Number	
Anaplastic thyroid carcinoma (ATC) with papillary thyroid carcinoma/ ATC/ ATC with squamous differentiation/ ATC with a differential of MTC/ ATC versus MTC	11	Acceptable
Mixed medullary thyroid carcinoma (MTC) and ATC/ Mixed MTC and PDTC	4	Acceptable
Poorly differentiated thyroid carcinoma (PDTC)/ High-grade follicular cell derived non-anaplastic thyroid carcinoma	8	
MTC	4	
Squamous cell carcinoma with a differential of MTC	1	
Metastatic adenocarcinoma ?primary site	1	

Educational notes:

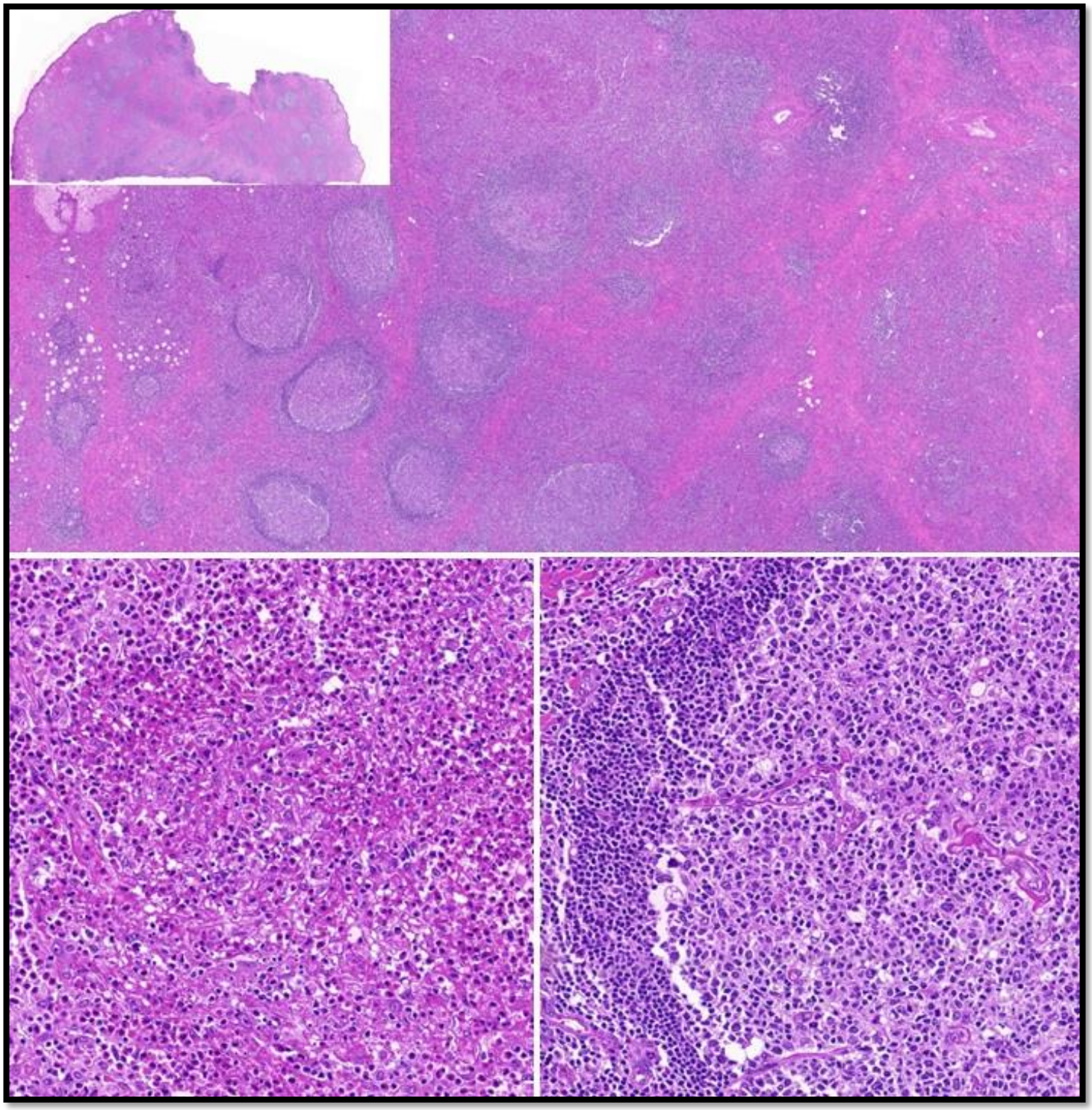
1. This tumor shows large areas of stromal hyalinization with silhouette of neoplastic nuclei. The viable tumor areas show focally anastomosing glandular structures intermingled with hyalinized stroma. Characteristic nuclei of papillary thyroid carcinoma (PTC), i.e., enlarged nuclei with irregular nuclear membrane and nuclear grooves are seen. At other area, tumor cells arranged in bands and trabeculae display large pleomorphic nuclei with prominent nucleoli. These features are those of an anaplastic thyroid carcinoma with associated PTC.
2. Anaplastic thyroid carcinomas (ATCs) show a variety of microscopic patterns and cellular morphologies. Nonetheless, all ATCs display pleomorphic nuclei. Essentially, diagnosis of ATC requires focal features of thyroid follicular differentiation and/or a past differentiated thyroid carcinoma in the context of undifferentiated malignant cells. In addition, other undifferentiated malignancies are considerably excluded. In this case, extensive stromal hyalinization reasonably doubts amyloid deposition of medullary thyroid carcinoma (MTC). Although Congo red histochemistry could confirm amyloid deposition, cytological features of the undifferentiated malignant cells harboring prominent nucleoli are incompatible with the usual fine chromatin pattern of nuclei in MTCs. Immunohistochemistry (IHC) is helpful as the majority of MTCs would be positive for calcitonin and CEA. For ATC, IHC is used to confirm epithelial differentiation with focal weak positivity for cytokeratin. Thyroglobulin and TTF-1 are commonly negative in ATC.
3. High-grade follicular cell-derived non-anaplastic thyroid carcinoma is a recently introduced category of carcinoma with high grade features, i.e., high mitotic count and tumor necrosis. It consists of (1) the poorly differentiated thyroid carcinoma diagnosed following the usual Turin criteria, and (2) differentiated high-grade thyroid carcinoma (DHGTC), which shows the features of well-differentiated thyroid carcinoma, but elevated mitotic activity and/or tumor necrosis. DHGTC does not show nuclear pleomorphism. Histological features of this case are beyond the Turin criteria.

Reference:
1. WHO Classification of Tumours Editorial Board. Endocrine and neuroendocrine tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2022.

Case 3

Case 3: A 14-year-old boy presented with a painless posterior auricular lesion.

Targeted Diagnosis: **Kimura disease**



Case 3

Submitted Diagnoses by Participating Institutions	Number	
Kimura disease	25	Acceptable
Angiolymphoid hyperplasia with eosinophilia (AHLE)/ AHLE with a differential of Kimura disease	4	

Educational notes:

1. The lesion shows multiple reactive lymphoid follicles in the subcutis with fibrosis. Germinal centers of the lymphoid follicles show the spectrum of eosinophilic infiltrates, eosinophilic folliculolysis and eosinophilic microabscess. Vascularization and proteinous depositions in the germinal centers are noted. These features are those of Kimura disease.
2. Kimura disease is a benign disease occurring predominantly in Asian peoples with a predilection for young males. It usually presents as a soft tissue swelling at the head and neck region associated with lymphadenopathy, eosinophilia, and increased serum levels of IgE. Histologically, Kimura disease is characterized by three components: cellular inflammatory infiltrates containing eosinophils and reactive follicular hyperplasia, stromal sclerosis, and proliferation of postcapillary venules.
3. In the past, angiolymphoid hyperplasia with eosinophilia (ALHE) or epithelioid hemangioma (EH) has been regarded within the spectrum of Kimura Disease with overlapping clinicopathological features. ALHE/EH is now considered a separate entity that histologically, it is distinguishable from Kimura disease by its prominent lobules or aggregates of vascular proliferation. The vessels are lined by plump endothelial cells with epithelioid or histiocytoid changes. Inflammatory infiltrates including eosinophils in ALHE/EH diffusely surround and may infiltrate the blood vessels. Similarly, reactive follicular hyperplasia may be observed in ALHE/EH.
4. EH is the recommended terminology over ALHE in the new WHO classification of vascular tumors. EH is benign but local recurrence is common following incomplete surgical excision.

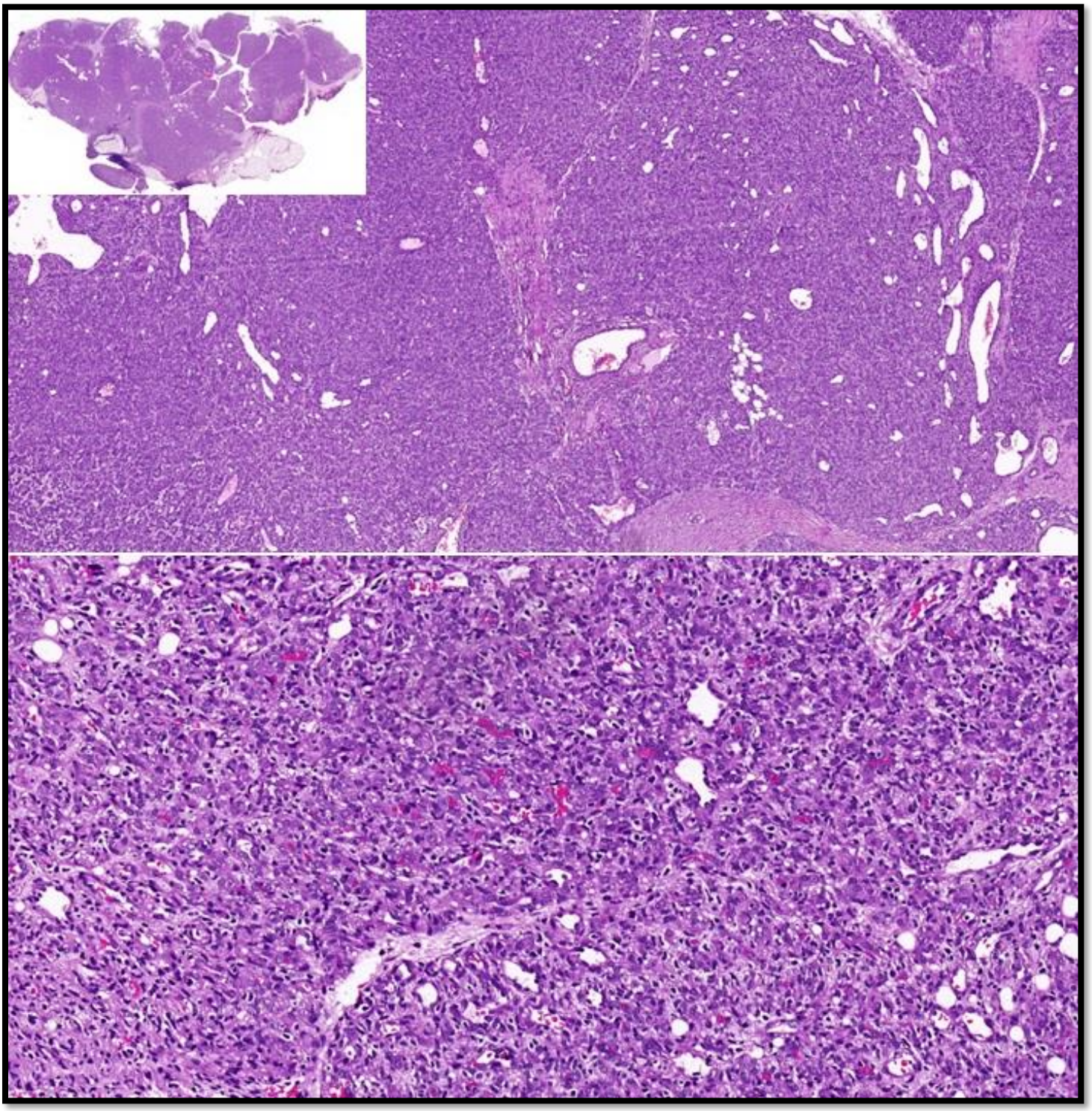
Reference

1. Guo R, Gavino AC. Angiolymphoid hyperplasia with eosinophilia. Arch Pathol Lab Med. 2015 May;139(5):683-6.
2. Chen H, et al. Kimura disease: a clinicopathologic study of 21 cases. Am J Surg Pathol. 2004 Apr;28(4):505-13.
3. WHO Classification of Tumours Editorial Board. Paediatric tumours [Internet; beta version ahead of print]. Lyon (France): International Agency for Research on Cancer; 2022

Case 4

Case 4: A premature infant with an axillary swelling present at birth.

Targeted Diagnosis: **Infantile hemangioma**



Case 4

Submitted Diagnoses by Participating Institutions	Number	
Infantile hemangioma (IH)/ IH for GLUT1 IHC	24	Acceptable
Infantile or Congenital hemangioma/ Congenital hemangioma	3	Acceptable
Kaposiform hemangioendothelioma	1	
Non Hodgkin Lymphoma, probably primary immunodeficiency (PID).	1	

Educational notes:

1. Section shows large cellular lobules in the subcutis. The cellular lobules are composed of closely packed capillaries with mostly inconspicuous lumina except at the periphery of the lobules. The capillaries are composed of plump endothelial cells and pericytes, that are cytologically uniform. These histological features are consistent with infantile hemangioma.
2. Infantile hemangioma (IH) affects about 5% of infants and reaches its greatest size around 10 months of age and involutes over several years. Clinically, it usually presents as a solitary red tumor. Extensive segmental infantile hemangioma in the head and neck and in the lumbosacral and perineal regions may have syndromic association.
3. The histological appearance of IH depends on the growth phases. In the proliferative phase as in this current case, the capillaries are closely packed with inconspicuous lumina. In the involutional phase, the capillaries are dilated and lined by flattened endothelial cells associated with interstitial fibrosis and adipose tissue. In the end stage, the lesion is replaced mostly by fibrofatty tissue with sparse residual larger vessels.
4. The major differential diagnosis is Kaposiform hemangioendothelioma(KHE), which also occurs in infants and young children. In contrast to IH, KHE appears as ill-defined large vascular nodules composed of fascicles of spindle endothelial cells with elongated slit-like lumina. Tufted angioma (TA), a related vascular tumor, on the other hand, is composed of multiple small discreet intradermal lobules of capillaries distributed in a cannonball pattern. Both KHE and TA are immunohistochemically negative for GLUT1 as opposed to GLUT1 cytoplasmic positivity in IH.
5. Congenital hemangioma (CH) as a differential diagnosis shows lobules of capillaries with round or stellate lumens separated by dense fibrous tissue and contain draining dysmorphic veins. CH is also GLUT1 negative.
6. The prognosis of IH is excellent with complete regression in 90% of the cases.

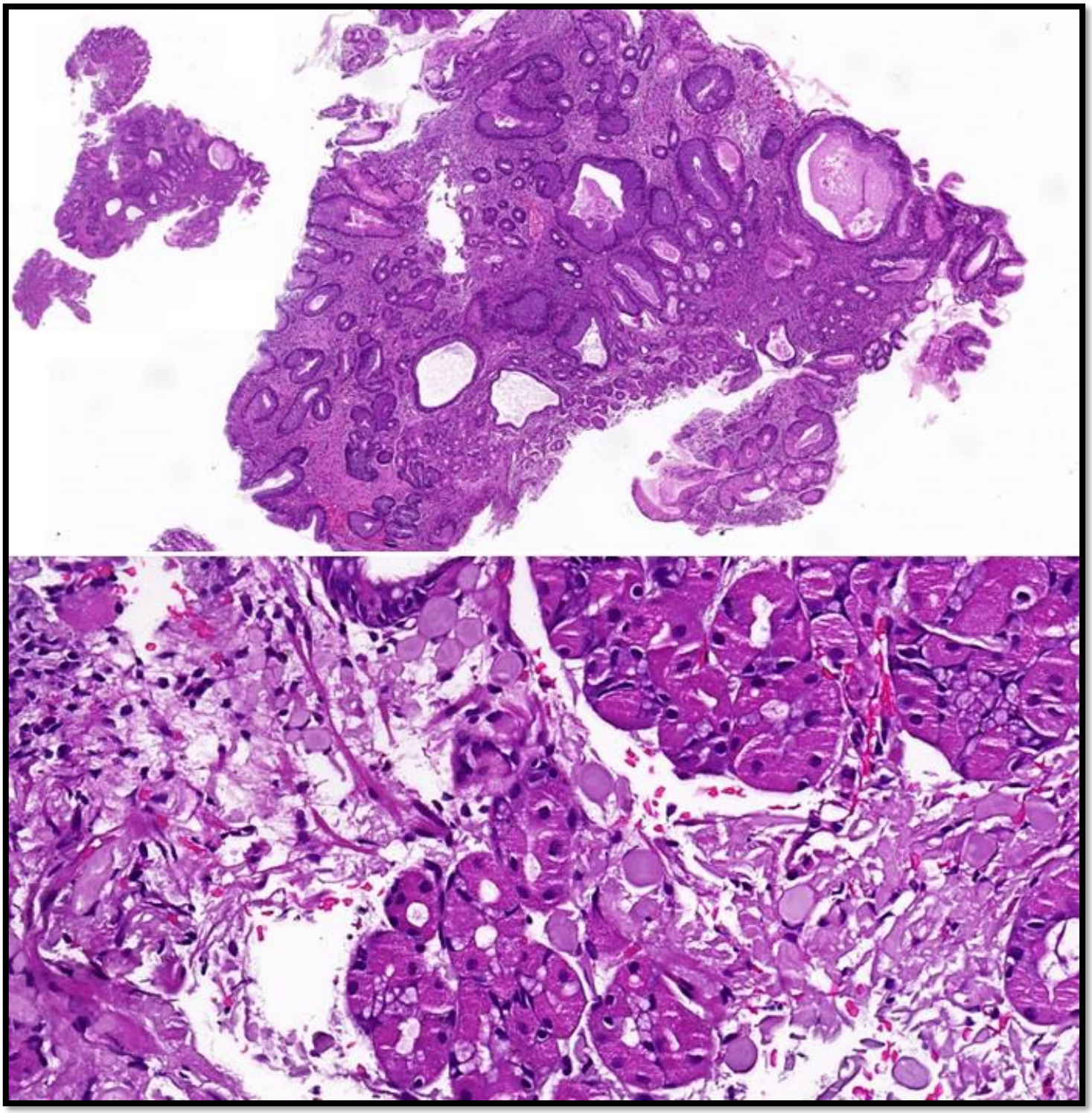
Reference

1. WHO Classification of Tumours Editorial Board. Paediatric tumours [Internet; beta version ahead of print]. Lyon (France): International Agency for Research on Cancer; 2022

Case 5

Case 5: A 72-year-old woman presented with epigastric pain. OGDS showed a stomach polyp.

Targeted Diagnosis: **Fundic gland polyp and gastric amyloidosis**



Case 5

Submitted Diagnoses by Participating Institutions	Number	
Fundic gland polyp (FDP) and gastric amyloidosis	5	Acceptable
Hyperplastic polyp (HP) and amyloidosis	2	Acceptable
FDP, to rule out amyloidosis and signet-ring cell carcinoma with further stains	4	Acceptable
FDP/HP to rule out signet-ring carcinoma	4	
FDP/HP/HP with proton pump inhibitor effect/ HP with glandular atrophy	7	
FDP with low grade dysplasia and amyloidosis	1	
Gastritis cystica polyposa	1	
Signet ring carcinoma/ poorly differentiated carcinoma in FDP/HP	5	

Educational notes:

1. There are small polypoid fragments of gastric oxyntic-type mucosa with variably dilated glands lined predominantly by mucinous foveolar cells, and a small portion of flattened parietal cells and chief cells. The fibrotic lamina propria contains moderate lymphoplasmacytic infiltrates as well as globules of amorphous materials in one focus, consistent with amyloid deposition. There is no dysplasia or intestinal metaplasia of the lining epithelium. These features are that of fundic gland polyp and gastric amyloidosis.
2. Fundic gland polyp (FDP) is a benign cystic hyperplastic proliferation of oxyntic glands. The cystic dilated glands are lined not only by chief cell and parietal cells, but also mucinous foveolar cells in FDP. In contrast, the hyperplastic polyp of the stomach shows hyperplastic foveolar epithelium with cystic dilatations and corkscrew appearance.
3. Most of the amyloid involvement of the gastrointestinal tract is a result of systemic amyloidosis with dominant gastrointestinal involvement (80%). A minority (21%) occurs as localized amyloidosis to the gastrointestinal tract without an associated plasma cell dyscrasia or other organ involvement. The amyloid deposits are confirmed by Congo red histochemistry (stained red) and they produce apple-green birefringence under polarized light. Histologically, muscularis mucosae was the most common location of amyloid deposition in gastric biopsies. In this current case, the amyloid appears as globular deposits, which is rare in gastrointestinal tract except in globular hepatic amyloidosis. This type of globular amyloid deposits could occur as intracellular amyloid globules, giving rise to signet-ring appearance of the cells. Nevertheless, transition to extracellular laminated globules up to 40 um in diameter helps in its recognition.

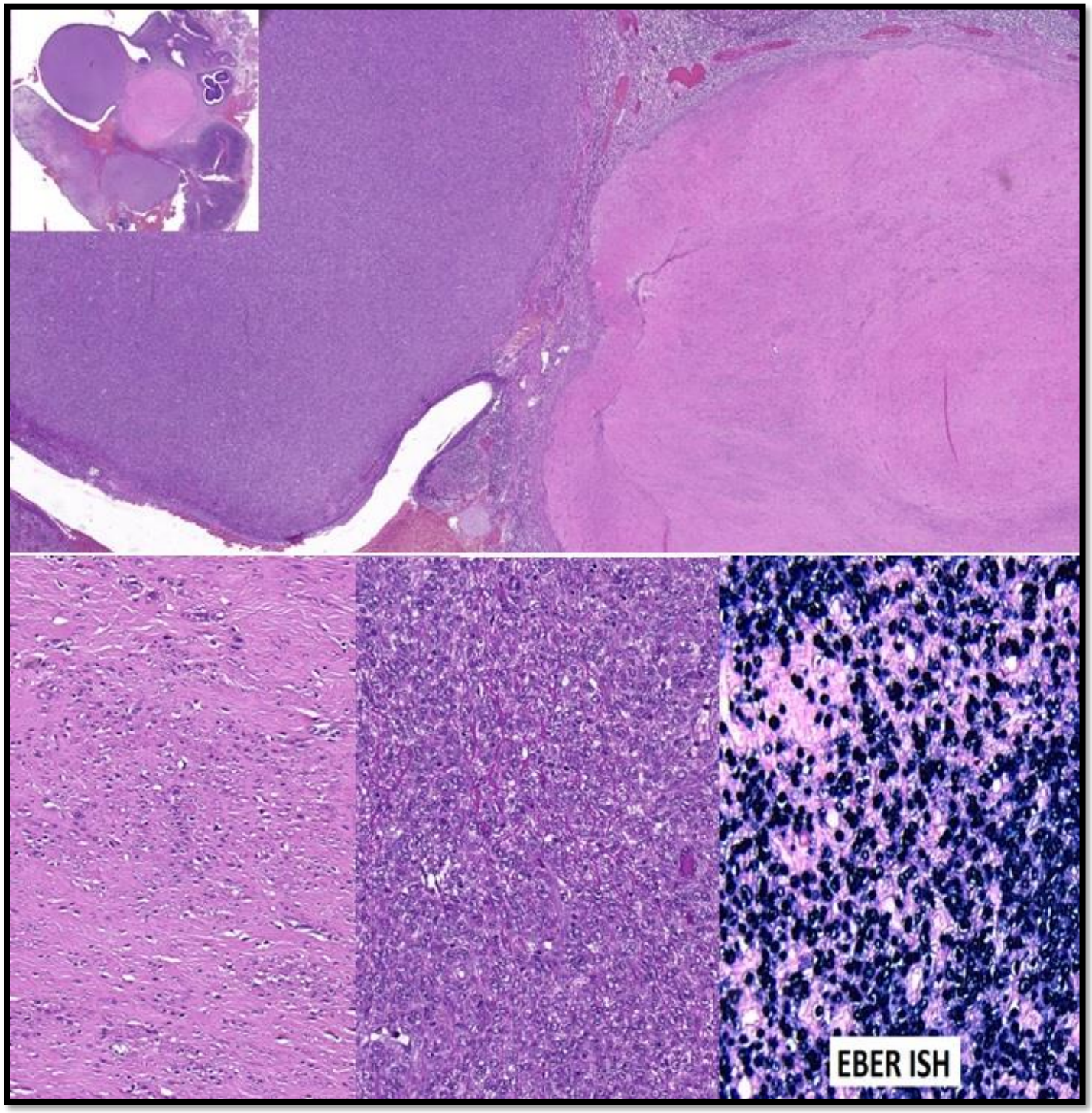
Reference

1. Demirhan B, et. al. Globular amyloid deposits in the wall of the gastrointestinal tract: report of six cases. Amyloid. 2002 Mar;9(1):42-6.
2. Makhlouf HR, Goodman ZD. Globular hepatic amyloid: an early stage in the pathway of amyloid formation: a study of 20 new cases. Am J Surg Pathol. 2007 Oct;31(10):1615-21.
3. Said SM, Grogg KL, Smyrk TC. Gastric amyloidosis: clinicopathological correlations in 79 cases from a single institution. Hum Pathol. 2015 Apr;46(4):491-8.

Case 6

Case 6: A 51-year-old man with underlying retroviral disease presented with a right tonsillar mass. State the diagnosis and one other stain to perform for confirmation of diagnosis.

Targeted Diagnosis: **Epstein-Barr virus-associated smooth muscle tumor. Stain: EBER ISH.**



Case 6

Submitted Diagnoses by Participating Institutions	Number	
EBV-associated smooth muscle tumor. Stain: EBV stain/EBER-ISH	26	Acceptable
EBV-associated smooth muscle tumor.	1	Acceptable
Kaposi sarcoma. Stain: LANA	1	
Epithelioid Leiomyosarcoma	1	

Educational notes:

1. There are several circumscribed nodules formed by intersecting fascicles of spindle cells with ample eosinophilic cytoplasm and blunt ended nuclei. In other areas, the tumor displays compact, round, oval and epithelioid nuclei, open nuclear chromatin, and small nucleoli. Mitotic activity is low. There is no tumor necrosis. Immunohistochemistry shows diffuse positivity for Vimentin and SMA. The cells are negative for Desmin, S100, CKAE1/AE3, LCA and CD30. The features suggest Epstein-Barr virus (EBV)–associated smooth muscle tumor (EBV-SMT). Evidence of EBV infection is diagnostic.
2. EBV-SMTs is suspected when smooth muscle tumors arise in setting of immunosuppression states such as HIV/AIDS, posttransplant-related immunosuppression, and congenital immunodeficiency. The tumor shares some morphological features with conventional leiomyomas, in addition to having a second population of more primitive looking, small, round tumor cells and a contingent of intratumoral lymphocytes.
3. Immunophenotypically, there is typical smooth muscle differentiation (SMA, Caldesmon). Desmin can sometimes be positive; when it happens, the expression is usually focal. EBER-ISH has emerged as the most reliable and specific method of separating EBV-SMTs from other SMTs on tissue biopsy.
4. Leiomyosarcoma is characterized by higher degree of hypercellularity, more nuclear atypia, increased mitotic rate, and tumor cell necrosis, although these features can occasionally be seen in EBV-SMTs, especially in association with HIV. Demonstration of EBV infection allows distinction from other SMA-expressing tumors.
5. Nodule-stage Kaposi Sarcoma may also exhibit “myoid” histomorphology and contain a sprinkling of intralesional inflammatory cells. Features to support Kaposi Sarcoma include presence of hyaline globules, slit-like spaces containing erythrocytes and peripheral ectatic vessels.

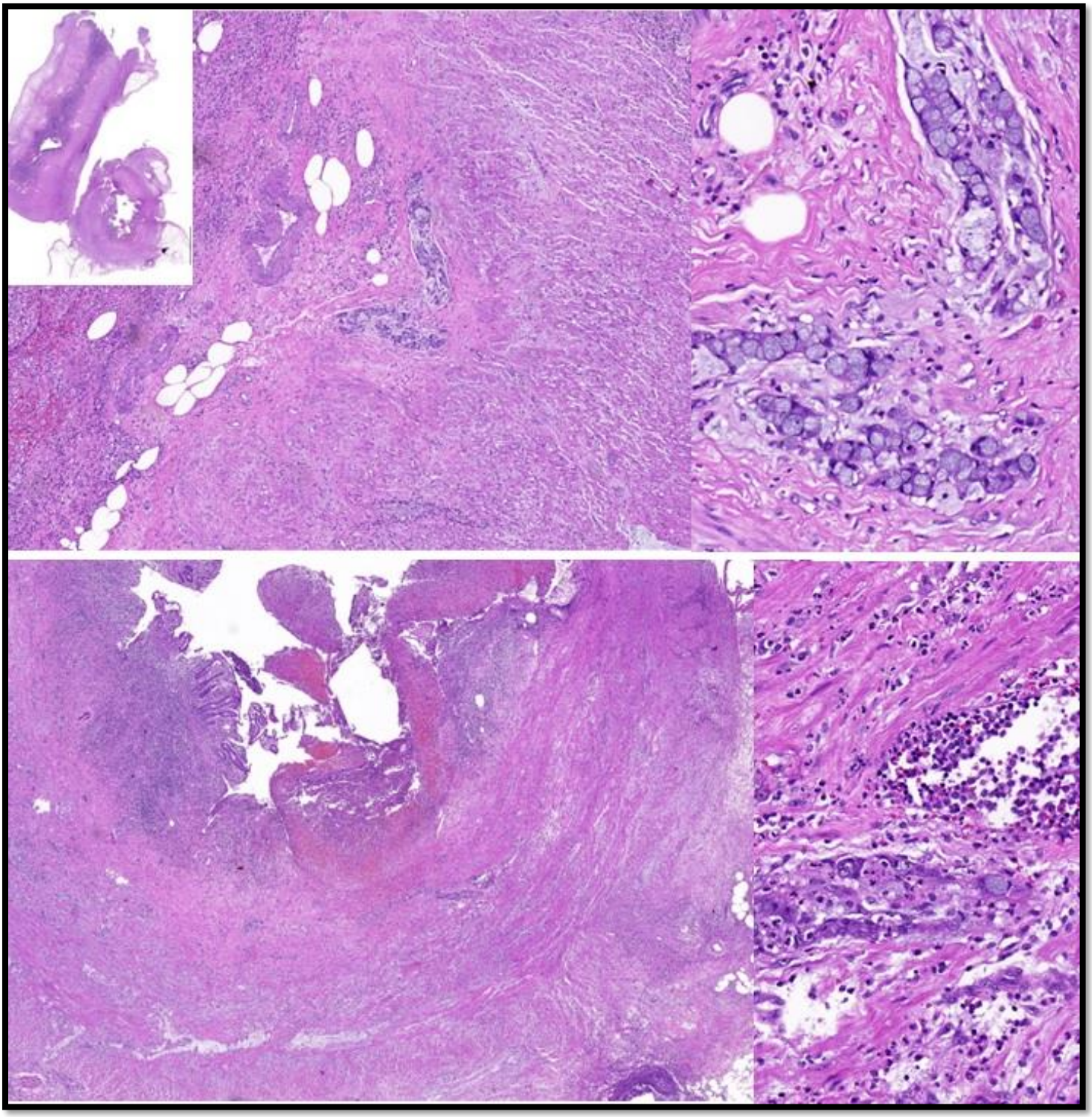
Reference

1. Tirelo M. Pitjadi, Wayne Grayson; Epstein-Barr Virus-Associated Smooth Muscle Tumour: A Case Series with a Significant Proportion of Tumours Showing Proclivity for Cutaneous Soft Tissues. Dermatopathology 28 June 2019; 6 (2): 133–146.
2. Magg T, Schober T, Walz C, et al. Epstein-Barr Virus-Smooth Muscle Tumors as Manifestation of Primary Immunodeficiency Disorders. Front Immunol. 2018;9:368.

Case 7

Case 7: A 43-year-old man underwent an appendicectomy for acute appendicitis.

Targeted Diagnosis: **Appendiceal goblet cell adenocarcinoma, low grade**



Case 7

Submitted Diagnoses by Participating Institutions	Number	
Goblet cell adenocarcinoma/Goblet cell carcinoma/Goblet cell adenocarcinoma low grade/Goblet cell carcinoma high grade/Goblet cell adenocarcinoma with background acute appendicitis	26	Acceptable
Signet ring cell adenocarcinoma in background of acute appendicitis	1	
Signet ring type neuroendocrine tumor	1	
Chronic non-specific appendicitis	1	

Educational notes:

1. This appendix is involved by goblet cell adenocarcinoma (GCA), displaying infiltration by scattered goblet-like cells and occasional endocrine cells that are arranged as small cohesive clusters. The cells show low-grade nuclear atypia and abundant mucinous cytoplasm. Extracellular mucin pools are observed. Mitotic figures are infrequent. Dense transmural mixed acute and chronic inflammatory cells in the background are seen, but not stromal desmoplasia.
2. GCA is no longer considered to be a subtype of neuroendocrine neoplasm; previously used terminologies such as goblet cell carcinoid, crypt cell carcinoma, microglandular carcinoma and adenocarcinoid are also no longer recommended by WHO.
3. GCA is diagnosed by the presence of the low-grade component. Histologically, the low-grade pattern is formed by tubules recapitulating intestinal crypts, or more commonly, small cohesive clusters lacking recognizable lumina. Circumferential infiltration of the appendiceal wall by tumor clusters in a concentric fashion without eliciting desmoplastic reaction is a hallmark.
4. GCA also shows high-grade patterns that deviate from the simple clustered or tubular low-grade patterns. These include single infiltrative cells, complex anastomosing tubules, cribriform, sheets or large aggregates of goblet or signet ring-like cells. Typically, obvious nuclear atypia, frequent mitoses and stromal desmoplasia are associated with these high-grade patterns.
5. Signet-ring cell adenocarcinoma in the appendix shows widespread (> 50%) discohesive and disorganized growth of signet-ring cells with high-grade cytological features. The presence of a low-grade GCA component in the same tumor helps to distinguish high-grade GCA from signet-ring cell adenocarcinoma.

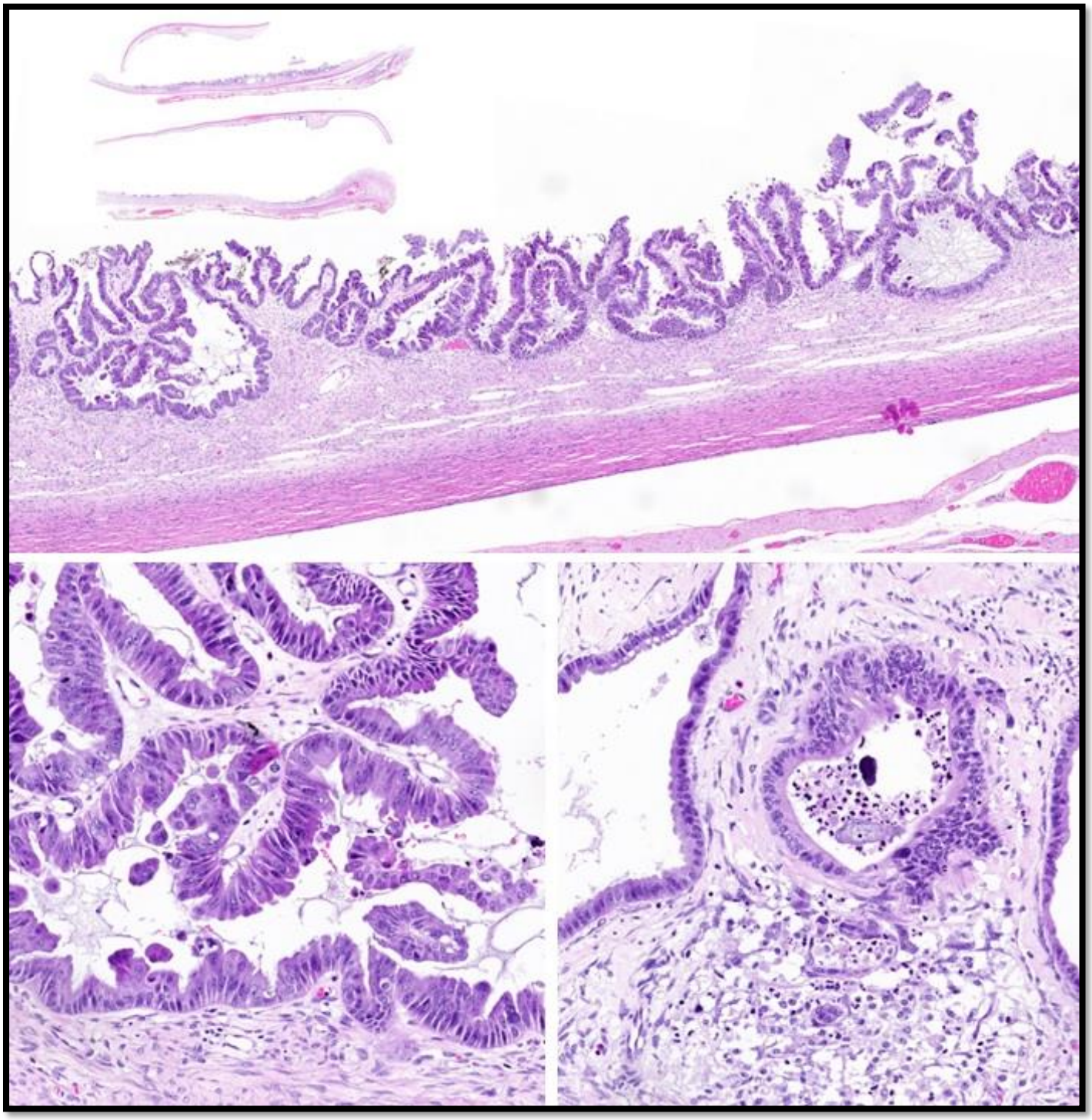
Reference

1. Wang HL. Goblet Cell Adenocarcinoma of the Appendix: Diagnosis, Prognosis and Nomenclature. J Clin Transl Pathol. 2022;2(3):69-74.
2. WHO Classification of Tumours Editorial Board. Digestive system tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2019

Case 8

Case 8: A 44-year-old woman presented with a left ovarian cyst measuring 220mm.

Targeted Diagnosis: **Microinvasive carcinoma arising in a background of mucinous borderline tumor with intraepithelial carcinoma**



Case 8

Submitted Diagnoses by Participating Institutions	Number	
Microinvasive carcinoma in background of mucinous borderline tumor (MBT)/ MBT with microinvasive carcinoma/ MBT with intraepithelial carcinoma and microinvasive carcinoma/ Mucinous neoplasm with intraepithelial carcinoma and microinvasive carcinoma	6	Acceptable
MBT with microinvasion /MBT with intraepithelial carcinoma and microinvasion/ MBT with focal microinvasion/ MBT with intraepithelial carcinoma and suspicious of microinvasion	10	Acceptable
Seromucinous borderline tumour with microinvasive carcinoma	1	Acceptable
MBT with intraepithelial carcinoma	8	Acceptable
MBT	3	
Seromucinous borderline tumour	1	

Educational notes:

1. The ovarian cyst wall is lined by mucinous epithelium displaying a variable degree of nuclear atypia. There are areas showing epithelial stratification forming papillary structures and intraluminal tufting with low-grade nuclear atypia, consistent with mucinous borderline tumor (MBT). At focal areas, intraepithelial carcinoma is evidenced by the presence of marked enlarged, hyperchromatic nuclei with prominent nucleoli and loss of nuclear polarity. Focal infiltrative stromal invasion (measuring less than 5mm) associated with stromal reaction by the marked atypical neoplastic cells is observed. These features are that of microinvasive carcinoma arising in a background of MBT with intraepithelial carcinoma.
2. MBT of the ovary is lined by gastrointestinal-type mucinous epithelium (gastric pyloric epithelium, goblet cells and rarely Paneth cells). It shows architectural abnormalities by a variable degree of stratification, tufting, and villous or slender filiform papillae. The lining epithelial cells show low-grade nuclear atypia. When small foci of stromal invasion (< 5 mm in the greatest linear extent) are seen in MBT, such a tumor is designated as MBT with microinvasion only if the infiltrative neoplastic cells exhibit similar degree of limited nuclear atypia.
3. However, when focal or patchy marked cytological atypia is observed, a diagnosis of intraepithelial carcinoma is warranted. When there is stromal invasion of <5mm in the greatest linear and the invasive foci display marked cytological atypia, a diagnosis of microinvasive carcinoma is rendered.
4. When diffuse marked cytological atypia is observed, a diagnosis of mucinous carcinoma (primary or metastatic) should be considered.
5. Seromucinous borderline tumors are characterized by papillae exhibiting hierarchical branching and lined by an admixture of Mullerian-type epithelia without stromal invasion. The stromal cores are variably edematous or fibrous. Usually, these tumors are associated with endometriosis.

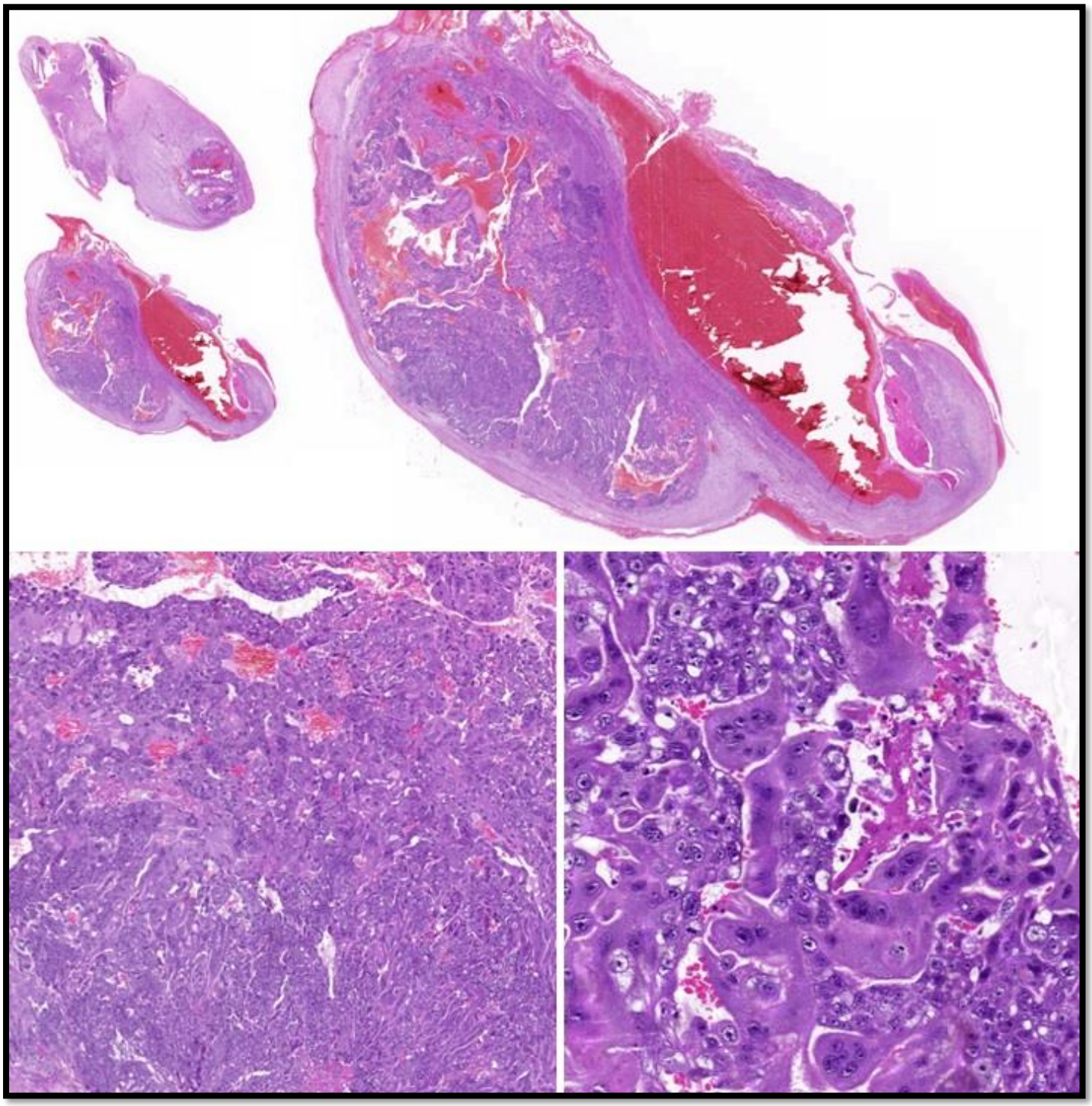
Reference

1. WHO Classification of Tumours Editorial Board. Female genital tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2020

Case 9

Case 9: A 34-year-old woman underwent wedge resection of the right ovary and salpingectomy for an ectopic pregnancy.

Targeted Diagnosis: **Gestational choriocarcinoma**



Case 9

Submitted Diagnoses by Participating Institutions	Number	
Gestational choriocarcinoma/ extrauterine gestational choriocarcinoma/ Gestational choriocarcinoma involving the ovary with coexisting hemorrhagic corpus luteal cyst	7	Acceptable
Choriocarcinoma/ Extrauterine choriocarcinoma/ Tubal choriocarcinoma/ Choriocarcinoma with hemorrhagic corpus luteal cyst	21	Acceptable
High grade serous carcinoma	1	

Educational notes:

1. Sections from the ovarian tissue show infiltration by trophoblastic cells forming irregular and infiltrative mass surrounded by fibrin hemorrhage. The neoplastic trophoblasts are composed mainly of syncytiotrophoblasts with interspersed areas of mononuclear and intermediate cytotrophoblasts forming sheets. Prominent nuclear atypia, frequent mitoses and tumor necrosis are observed. Chorionic villi are not identified. No other germ cell components are present. This represents gestational choriocarcinoma.
2. Gestational ovarian choriocarcinoma may represent metastasis from uterine choriocarcinoma or arise from an ovarian ectopic pregnancy. It is characterized by bilaminar pattern of mononuclear villous cytotrophoblast and intermediate trophoblast rimmed by multinucleated syncytiotrophoblast.
3. Choriocarcinoma of germ cell origin is morphologically indistinguishable from their gestational counterpart. However, the former more commonly occurs in children and younger adult age group. Thorough sampling is important to look for other co-existing germ cell tumors which would imply a non-gestational etiology.
4. Somatic carcinoma (including high-grade serous carcinoma) with trophoblastic differentiation is a less likely differential diagnosis. Histologically, distinct carcinomatous area with epithelial differentiation is discernible in such a somatic carcinoma.
5. Genotyping is helpful in problematic cases by identifying the presence of unique paternal alleles of the index gestation, supporting the diagnosis of gestational choriocarcinoma. In non-gestational choriocarcinoma of germ cell origin and somatic carcinoma with trophoblast differentiation, they show biallelic germ cell pattern and biallelic somatic cell pattern, respectively.

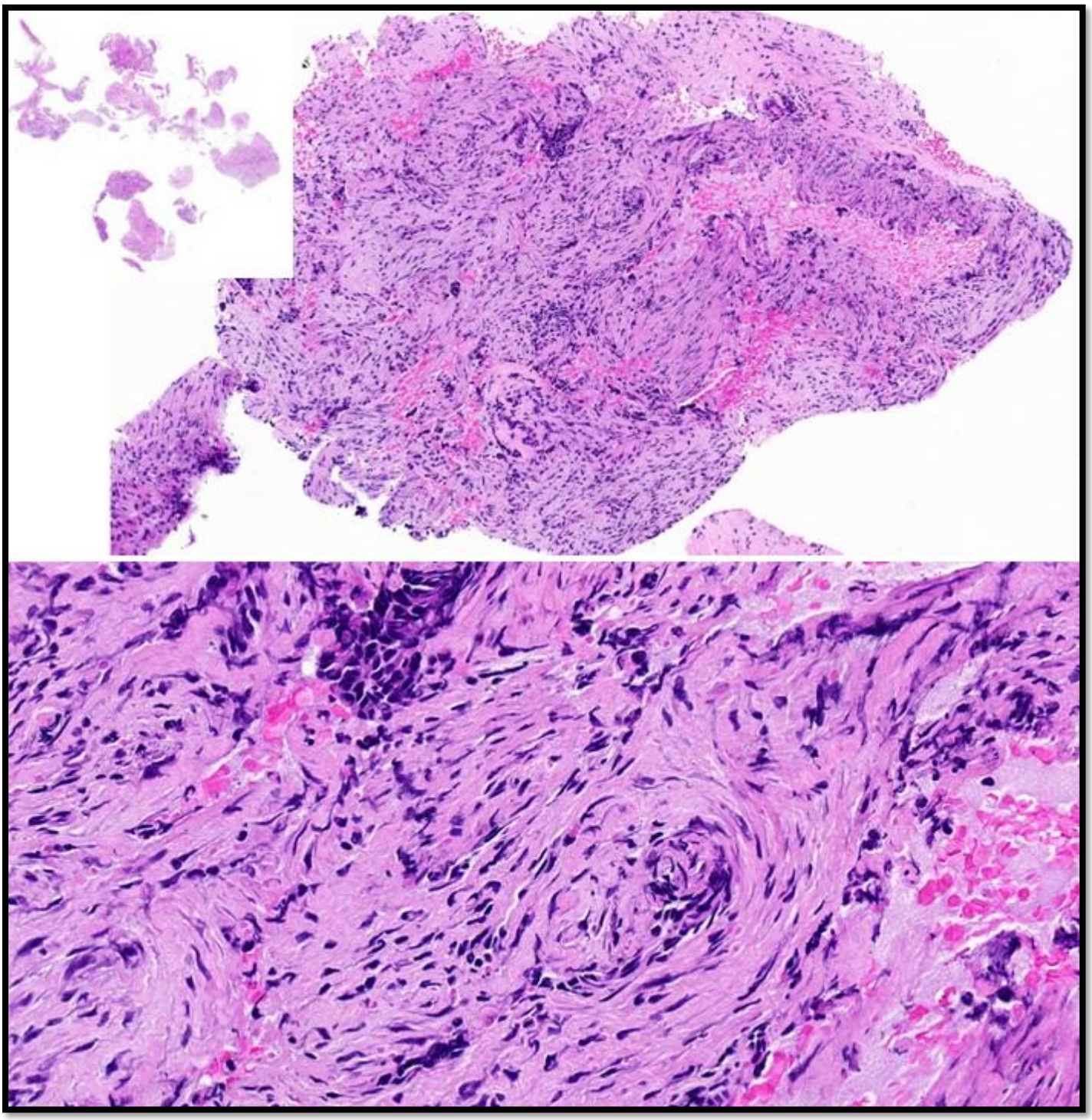
Reference

1. Jia N, et. al. A gestational choriocarcinoma of the ovary diagnosed by DNA polymorphic analysis: a case report and systematic review of the literature. J Ovarian Res. 2017 Jul 20;10(1):46.
2. Sadiq Q, et. al. High-grade serous carcinoma of ovary with choriocarcinomatous differentiation: a case report and review of literature. Journal of Clinical Gynecology and Obstetrics. 2020 Sep 9;9(3):53-9.

Case 10

Case 10: A 6-month-old boy presented with a rapidly growing mass at his right second toe swelling for 3 months.

Targeted Diagnosis: **Inclusion body fibromatosis**



Case 10

Submitted Diagnoses by Participating Institutions	Number	
Inclusion body fibromatosis/ Inclusion body infantile digital fibromastosis/ Infantile digital fibromatosis / Infantile digitial fibroma	28	Acceptable
Neurofibroma	1	

Educational notes:

1. There are multiple pieces of tumor tissue composed of spindle cells arranged in fascicles and whorls with collagenous stroma. These spindle cells have elongated, slender and bland wavy nuclei with tapered end, finely dispersed chromatin, inconspicuous nucleoli, and ill-defined eosinophilic cytoplasm. Some cells have intracytoplasmic perinuclear rounded eosinophilic inclusion. Mitotic figures and tumor necrosis are not observed. The features are diagnostic of Inclusion body fibromatosis.
2. Inclusion body fibromatosis classically occurs in children younger than 5 years as a single lesion on the dorsal or lateral aspects of the digits, sparing the thumb and the great toe. Less commonly, it presents as multiple synchronous or metachronous lesions and rarely involves extradigital sites such as arm, breast, tongue, and thigh.
3. Inclusion body fibromatosis is composed of intradermal proliferation of bland fibroblasts/ myofibroblasts characteristically arranged in fascicles perpendicular to the epidermis, surrounding adnexa, and occasionally infiltrating deeper tissues. The hallmark feature is the presence of rounded, pale pink to red intracytoplasmic inclusion. The inclusions are frequently paranuclear, indenting the nucleus and can be highlighted by trichrome (red), phosphotungstic acid–hematoxylin (dark purple), and Movat (pink) stains.
4. Neurofibroma is composed of bland spindle cells with thin, wavy nuclei embedded within a variably loose myxoid stroma containing carrot-shredded collagen bundles. Perineurial and perineurial-like cells, fibroblasts, and mast cells are frequently identifiable, but intracytoplasmic inclusion bodies are not a feature.

Reference

1. Agnihotri MA, Sathe PA. Inclusion body fibromatosis - A report of four cases and review of literature. J Postgrad Med. 2021;67(1):24-26.