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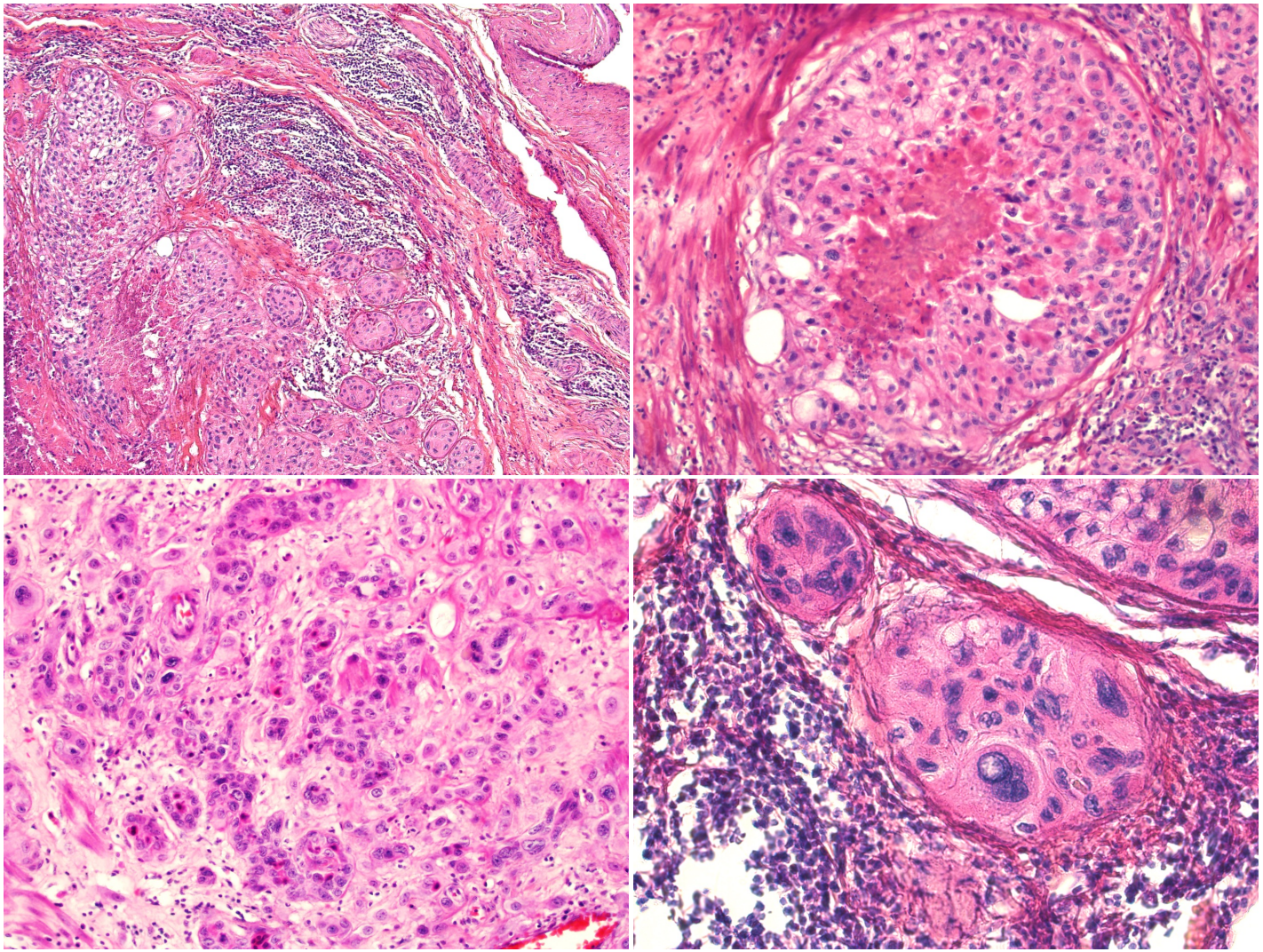
Yale Pathology

Case Presentation

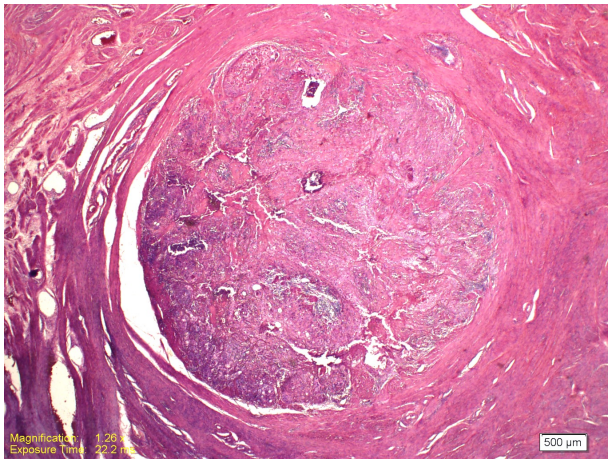
44-year-old woman G1P1 presented with vaginal bleeding and a cervical mass, which was biopsied and interpreted as poorly differentiated carcinoma. The patient underwent radical hysterectomy, bilateral salpingo-oophorectomy and pelvic lymph node dissections. The hysterectomy specimen showed a 4.0 cm fungating cervical mass extending to the parametrium. A post-operative work-up for extrauterine disease was negative.

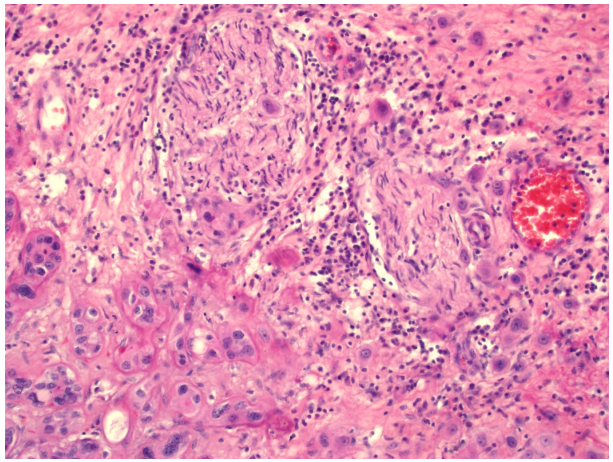


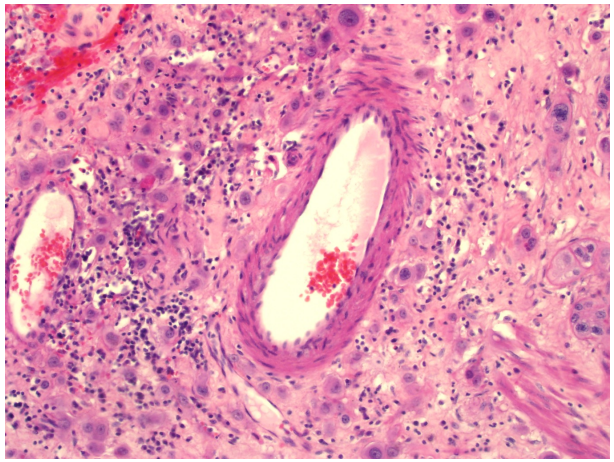
Differential diagnoses

A. Squamous cell carcinoma
B. Epithelioid leiomyosarcoma
C. Epithelioid trophoblastic tumor (ETT)
D. Placental site trophoblastic tumor (PSTT)

Additional Histological Images







The tumor was positive for hCG and hPL in a focal, individual cell fashion at the initial workup. Serum hCG level was not considered. Retrospective p63 immunostain shows a diffuse positivity and Ki-67 labelling index is 10% among tumor cells.

Final Diagnosis: Epithelioid Trophoblastic Tumor (ETT)

The patient received post-operative external pelvic radiotherapy with an additional right parametrial boost. She also received irradiation to the vaginal cuff and 12 cycles of methotrexate, 5FU and leucovorin. She has been followed clinically and without evidence of tumor metastasis or recurrence 34 years afterward.

Discussion

Epithelioid trophoblastic tumor (ETT) is a rare tumor of the chorionic type intermediate trophoblast in women usually of 15 to 48 years of age. ETT forms discrete, invasive nodules or cystic hemorrhagic masses with frequent ulceration and fistula formation. Histologically, the tumor is characterized by well circumscribed, nodular proliferation of relatively uniform, medium-sized trophoblastic cells arranged in nests, cords, or large sheets. Moderate nuclear atypia is usually present and mitotic counts are variable. Extensive "geographic" necrosis with associated calcification is often present. 50% of the tumors involve the cervix or lower uterine segment. The tumor cells may colonize cervical epithelium simulating high-grade squamous intraepithelial lesion. Major differential diagnoses include squamous cell carcinoma and PSTT. ETT has a far more favorable prognosis comparing with SCC. High index of suspicion is crucial to avoid misinterpretation of ETT as squamous cell carcinoma.

Table 2. Differential Diagnosis of Epithelioid Trophoblastic Tumor vs. Squamous Cell Carcinoma

Clinicopathologic Parameters	Epithelioid Trophoblastic tumor	Squamous Cell Carcinoma
Presentation	young patient with vaginal bleeding and recent pregnancy	older patient with history of HPV infection and/or cervical dysplasia
Serum hCG	elevated although at low levels (<2500 mIU/ml)	not increased
Cervical intraepithelial neoplasia	unassociated	Usually present
Histology	nodular proliferation with hyalinizing changes	squamous carcinoma nests with true keratin formation
Cytology	polygonal cells with convoluted nuclei and abundant clear to eosinophilic cytoplasm	tumor cells at various stages of squamous differentiation including cell bridges
Decidualized stromal cells	frequently present	absent, unless with concurrent or recent pregnancy
Immunohistochemistry	tumor cells positive for inhibin, HLA-G, CK18, hPL and hCG	tumor cells negative for inhibin, HLA-G, CK18, hPL and hCG
Clinical follow-up after hysterectomy	<25% recurrence rate	aggressive clinical course depending on the tumor stage