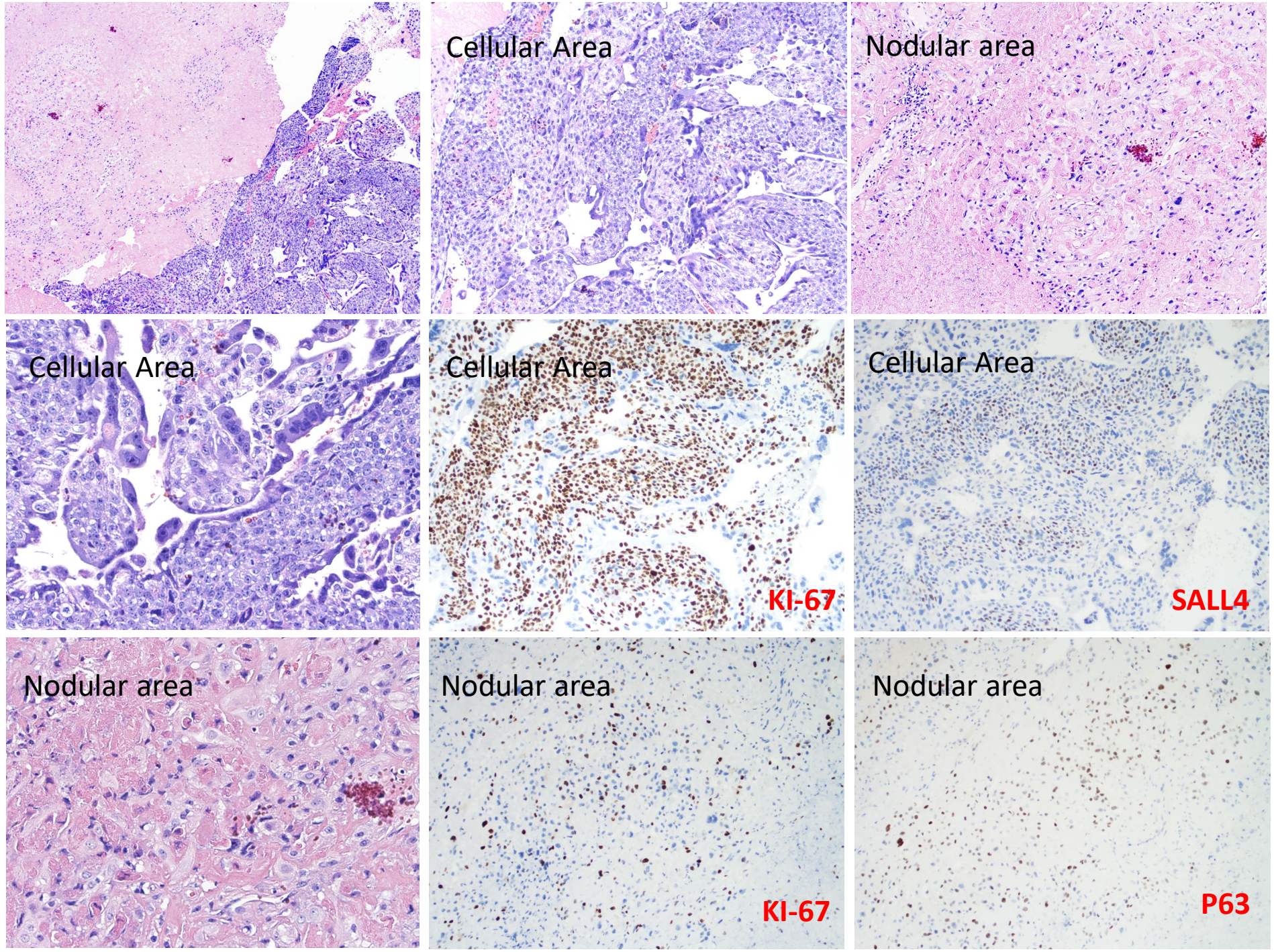
Where Knowledge is Created and Shared
Yale Pathology

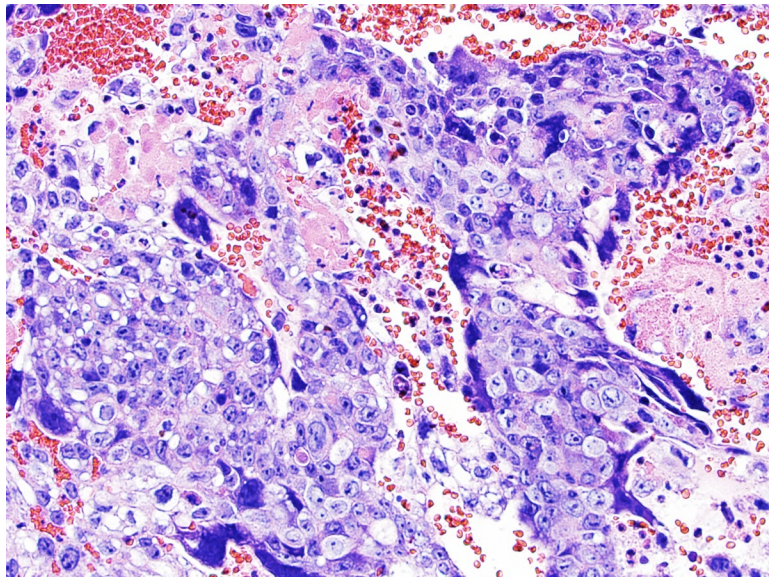
39-year-old woman presenting with amenorrhea and serum hCG of 46,485 mIU/mL. D/C was performed.

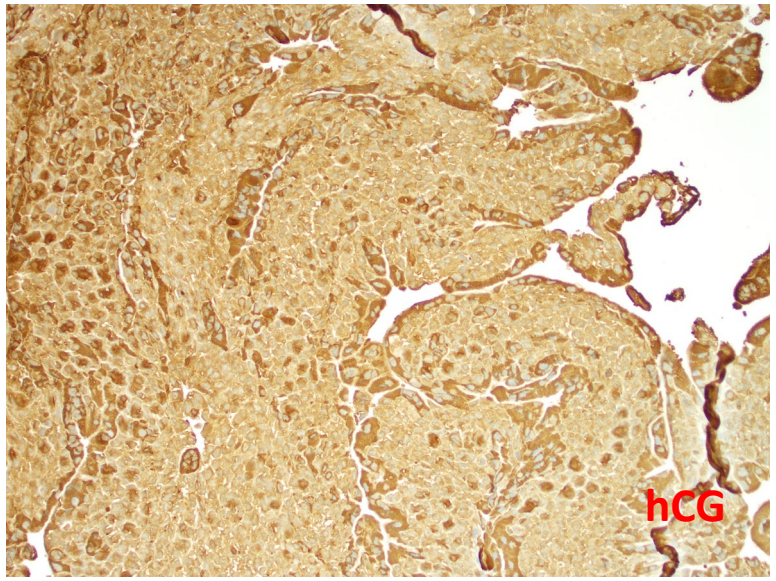

Cellular Area
Nodular area
Cellular Area
Cellular Area
KI-67
Cellular Area
SALL4
Nodular area
Nodular area
KI-67
Nodular area
P63

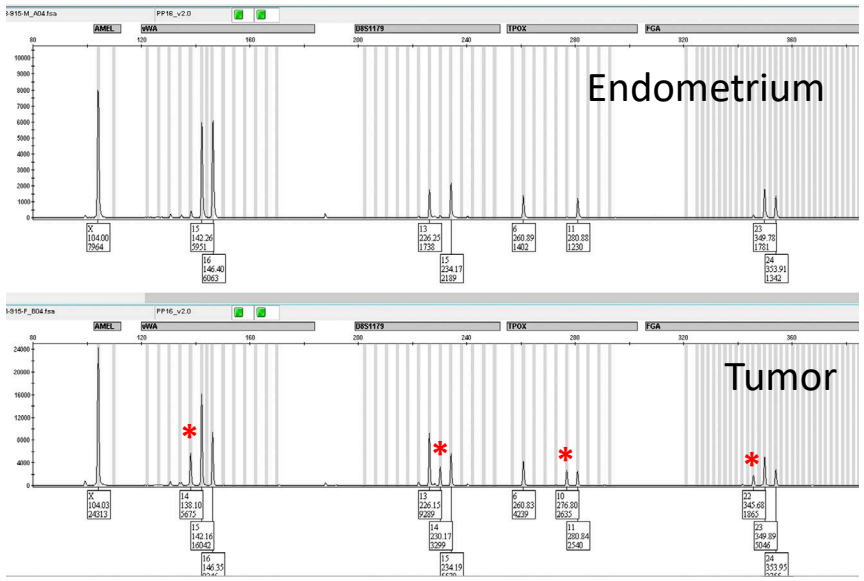
# Diagnostic Options

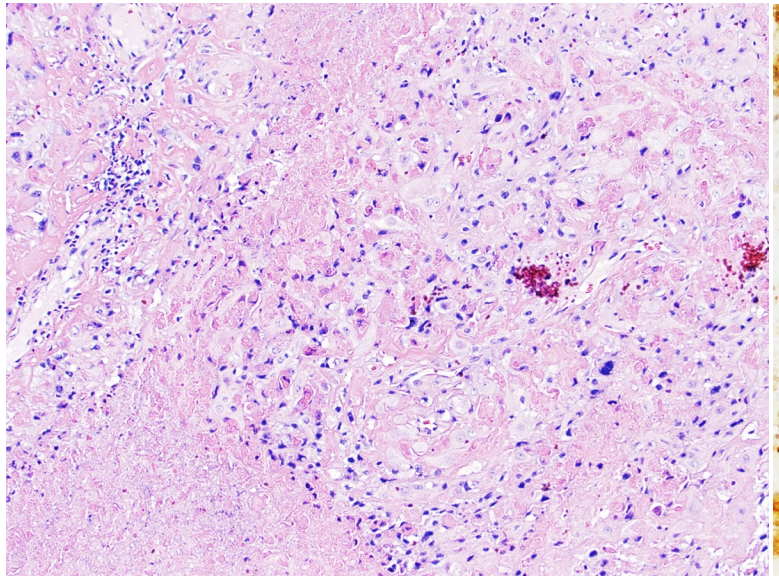
A: Choriocarcinoma (CC)
B: ETT
C: Mixed CC and ETT
D: Mixed CC and PSTT

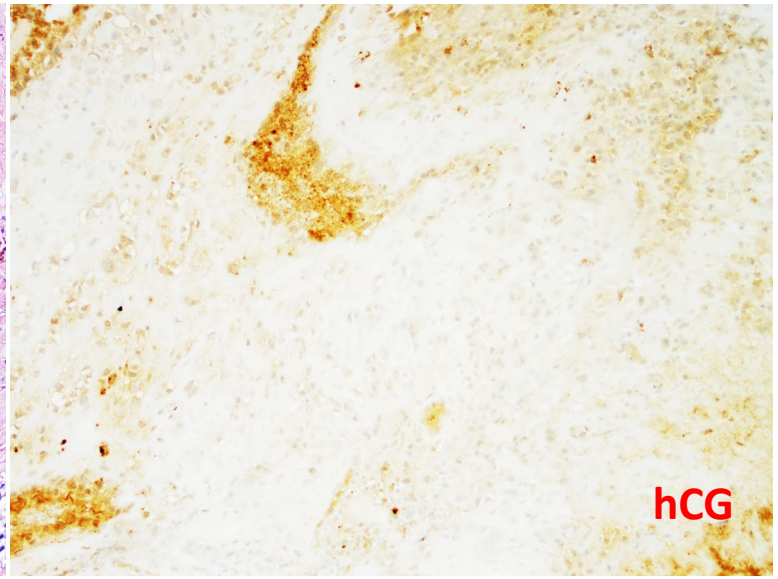
# Additional Histological, Immunohistochemical and STR Genotyping Images








STR genotyping identified the presence of distinct paternal alleles (indicated by asterisks) in the tumor.

The endometrial curettage demonstrates two distinct tumor components: a highly cellular biphasic proliferation of choriocarcinoma (CC) and a nodular epithelioid trophoblastic proliferation embedded in a hyalinized matrix (ETT). The choriocarcinoma cells are diffusely positive for beta-HCG, variably positive for hPL, p63 and SALL4. The ETT tumor cells are positive for CAM5.2 and p63 along with a Ki67 labeling index of over 10%. STR genotyping reveals an identical genetic profile in the two tumor components with the presence of distinct paternal alleles at multiple STR loci, confirming a clonal neoplastic proliferation of gestational nature with divergent differentiation.

Final Diagnosis: Mixed gestational choriocarcinoma and epithelioid trophoblastic tumor

Mixed gestational trophoblastic tumor is the rarest form of GTN, with less than 40 reported cases in the literature. The most common histological combination is choriocarcinoma and ETT (49%), followed by CC with PSTT (32%), ETT with PSTT (12%), and CC with both ETT and PSTT (7%). All published cases had an elevated serum beta-hCG level, which is the single most useful biomarker for diagnostic consideration and clinical monitoring of treatment response and disease progression. The functional tumor cells producing beta-hCG are the neoplastic syncytiotrophoblast in CC or syncytiotrophoblast-like cells in PSTT and ETT. Patients with pure CC usually have a very high serum beta-hCG due to the presence of large number of syncytiotrophoblast, generally over 10,000 mIU/ml and can reach extreme levels of over 100,000 mIU/ml. In contrast, patients with pure PSTT or ETT generally present with lower levels of serum beta-hCG from less than 1,000 mIU/mL to undetectable. Mixed trophoblast tumors have a highly variable serum hCG level depending on the tumor histological subtypes and their proportions. Pathological diagnosis of mixed trophoblastic tumors can be challenging due to their rarity, elusive clinical presentations, and a wide range of histomorphology. However, an accurate and timely diagnosis is essential as each distinct trophoblastic tumor component in a mixed trophoblastic tumor dictates the tumor biology, clinical treatment options, and patient outcome. The presence of choriocarcinoma component must be ruled out when a gestational trophoblastic tumor presents with a very high serum beta-hCG level.